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SWEDRES | SVARM

Sales of antibiotics and occurrence of antibiotic resistance in Sweden

Folkhälsomyndigheten
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SVA NATIONAL VETERINARY INSTITUTE

A report on Swedish Antibiotic Sales and Resistance in Human Medicine (Swedres) and Swedish Veterinary Antibiotic Resistance Monitoring (Svarm)

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Preface

Welcome to the eleventh joint Swedish report on antibiotic resistance and use in humans and animals.

Although antibiotic resistance in Sweden has gradually increased in several bacterial species, we are convinced that our collaboration in monitoring antibiotic use and resistance both in animals and humans has contributed to slowing this process. Colleagues in both animal and human medicine have benefitted from and been inspired by colleagues in the other sector. Communication of results, to professionals as well as to the public, has improved and is more thorough because of this collaboration. Surveillance and monitoring are essential in the work against antibiotic resistance. It is nessesary to pinpoint areas for actions and to follow effects of implemented actions. In addition, antibiotic resistance data is required to develop treatment guidelines.

Another key component in the efforts against antibiotic resistance is collaboration and cooperation of all the relevant expert areas such as antibiotic stewardship (called "Strama work" in human medicine in Sweden), surveillance, infection prevention and control, clinical microbiology, and communicable disease control.

As described in previous reports, the Covid-19 pandemic had a great impact on notifiable antibiotic resistance and antibiotic use in humans, but less so on resistance levels in common clinical pathogens isolated from blood cultures. During the initial years of the Covid-19 pandemic work against antibiotic resistance was hampered. During 2022, as the pandemic gradually subsided, the systematic promotion, prevention and controlefforts to prevent the spread of antibiotic resistance rebounded. Unfortunately, this is also true for the levels of notifiable antibiotic resistance and antibiotic use as they have both increased during 2022.

In forthcoming years, we also look forward to involving the environmental sector in the work against antibiotic resistance. Additionally, we hope to develop this report to a more digital format. One example of this is that for this report, some historical data emanating from the monitoring in the veterinary field (i.e. the Svarm part) is presented as open data on the web.

Work within the European Union has also accelerated over the last years. In January 2022, a new EU regulation on veterinary medicinal products came into force. The regulation provides several important tools that aim to support prudent use of antibiotics for animals.

We hope the 2022 Swedres-Svarm report will be useful in the continued work against antibiotic resistance.

Solna and Uppsala, June 2023

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The national surveillance of antibiotic resistance would not have been possible without the contribution of data and active support of all the Swedish clinical microbiology laboratories.

Epidemiological information on clinical notifications was checked and updated by the Regional Departments for Communicable Disease Control.

Contributions to Svarm
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Content

Sammanfattning/Summary

Sammanfattning

Under lång tid har Sverige haft en gynnsam situation jämfört med många andra länder när det gäller antibiotikaresistens hos bakterier från människor. Det läget kvarstår fortfarande. En av anledningarna är att vi har effektiva strategier för att främja en ansvarsfull användning av antibiotika och begränsa spridningen av antibiotikaresistens. Trots det goda läget finns det problem med kontinuerligt ökande antibiotikaresistens och smittspridning inom sjukvården. Viktiga exempel är de återkommande utbrotten av vankomycinresistenta enterokocker på sjukhus och ett ökande antal vårdrelaterade kluster av ESBL-CARBA. Detta poängterar vikten av ett kontinuerligt arbete inom Strama, vårdhygien och smittskydd för att förebygga infektioner och ökande antibiotikaresistens.

Antibiotikaförsäljningen inom humanmedicinen i Sverige ökade under 2022, efter att ha minskat kraftigt under 2020 och 2021.

Inom veterinärmedicinen har antibiotikaförsäljningen minskat kraftigt sedan mitten av åttiotalet för att de senare åren ha stabiliserats på en jämförelsevis låg nivå.

Förekomsten av resistens bland bakterier från djur har generellt sett varit stabilt låg. För vissa substanser och bakterier har förekomsten över tid till och med minskat. Ett sådant exempel är ESBL-bildande Escherichia coli hos slaktkyckling. Det finns dock undantag, exempelvis har förekomsten av resistens mot ampicillin, sulfonamider och trimetoprim ökat hos slumpmässigt utvalda E. coli hos såväl slaktkyckling som slaktgris.

Viktiga fynd 2022

- Den totala antibiotikaförsäljningen inom humanmedicinen i Sverige ökade med 8,2 procent under 2022 jämfört med 2021. Det återspeglas inom både recept och rekvisitioner, inklusive för akutsjukhus. Försäljningen av antibiotika inom tandvården minskade med 0,8 % procent under samma period.
- Antibiotikaförsäljningen inom öppenvården ökade under året jämfört med samma period året innan. Framför allt bidrog förskrivning av luftvägsantibiotika till barn under tredje och fjärde kvartalet till denna ökning.
- Sedan 2020 används resistens mot cefotaxim hos Escherichia coli och andelen meticillinresistenta Staphylococcus aureus (MRSA) isolerade från blod som indikatorer på antibiotikaresistens i Sverige. Både andelen MRSA och andelen E. coli som är resistenta mot cefotaxim har långsamt ökat under en tioårsperiod till nuvarande 1,9 respektive 7 procent. För båda indikatorerna ser ökningen ut att stanna av under de senaste åren.
- Under pandemin minskade antalet fall av flertalet typer av anmälningspliktig antibiotikaresistens. För de flesta av dessa ses nu tydliga ökningar, mest markant för ESBL-CARBA, där 240 fall rapporterades, mot 137 år 2021. Resistensnivåer bland kliniska isolat från människor påverkades inte av pandemin.
- En ökning av resistensen hos Streptococcus pyogenes mot klindamycin startade våren 2020. Den har under hösten 2022 gradvis återgått till ursprungliga nivåer, under 5 procent.
- Ett kluster av vårdrelaterad ESBL-CARBA och fem vårdrelaterade kluster med smittspridning utomlands rapporterades 2022. Elva sjukhusrelaterade smittspridningar av vankomycinresistenta enterokocker rapporterades under 2021.
- Försäljningen av antibiotika för användning till djur är stabilt låg och domineras av penicillin med smalt spektrum.
- MRSA är ovanliga hos både lantbrukets djur och sällskapsdjur.
- ESBL-bildande E. coli är generellt sett ovanliga hos både lantbrukets djur och sällskapsdjur samt på kött.
- Bakterier som bildar ESBL-CARBA har inte bekräftats hos tamdjur i Sverige.

Försäljning av antibiotika

Antibiotikaförsäljning inom humanmedicin

Den totala mängden antibiotika som såldes i Sverige ökade med 8,2 procent under 2022 och ligger nu på 10,2 DDD per 1 000 invånare och dag. I detta innefattas all antibiotika som sålts på recept till individer och på rekvisition till olika vårdinrättningar och särskilda boenden.

Öppenvård

Antalet antibiotikarecept som hämtades ut på apotek under året låg på 251 recept per 1 000 invånare, en ökning med 9 procent jämfört med 2021. Bland landets 21 regioner uppnådde 10 regioner det nationella målet på högst 250 recept per 1 000 invånare. Försäljningen ökade i samtliga åldersgrupper, och den var högst i gruppen barn i åldern 0–4 år där den ökade med 33,9 procent jämfört med året innan. Tydligast var ökningen under det fjärde kvartalet. Denna ökning bestod framför allt av antibiotika som ofta används vid luftvägsinfektioner.

Försäljningen av antibiotika på recept inom tandvården minskade marginellt med 0,8 procent under 2022 jämfört med året innan, och utgör 6,6 procent av alla uthämtade antibiotikarecept under året. Sedan år 2007 har antibiotikaförsäljningen inom tandvården minskat med hälften.

Sjukhus och andra vårdformer

Den totala försäljningen av antibiotika på rekvisition till vårdinrättningar ökade under 2022 jämfört med 2021. Även antibiotikaförsäljningen till akutsjukhusen ökade jämfört med året innan, mätt både i DDD per 100 vårdtillfällen och 100 vårddagar, och låg på den högsta försäljningen på 5 år. Den ökade försäljningen noterades framför allt för bredspektrumantibiotika, betalaktamaskänsliga och betalaktamasresistenta penicilliner. Liksom tidigare år fanns stora regionala variationer i användningen av bredspektrumantibiotika vid akutsjukhusen.

Antibiotikaförsäljning inom veterinärmedicin

I samband med att data för 2022 började analyseras upptäcktes en substantiell minskning jämfört med 2021 varför bortfall av data misstänktes. Undersökningar för att utreda detta inleddes och ett antal avvisade datarapporter från apotek identifierades. Dessa korrigerades av apoteken. I denna rapport har därför data från 2017 uppdaterats. Skillnaden mellan 2021 och 2022 var dock fortfarande oväntat hög (-12 procent) men trots omfattande undersökningar för att hitta andra oupptäckta fel kunde inga sådana påvisas. Någon förklaring till den plötsliga minskningen har inte identifierats. Uppgifter om försäljning 2022 bör därför tolkas med försiktighet. Om ännu oupptäckta felkällor skulle identifieras framöver kommer data uppdateras och publiceras på SVA:s webb.

Försäljningen av antibiotika för djur från apotek i Sverige uppgick 2022 till 8 865 kilogram, varav 60 procent var penicillin med smalt spektrum. Försäljningen av antibiotika som bör användas särskilt restriktivt (fluorokinoloner, tredje generationens cefalosporiner och polymyxin) har minskat kraftigt sedan 2013. Under hela tioårsperioden har andelen produkter för behandling av enstaka djur varit över 90 procent av den totala försäljningen.

Den totala försäljningen av antibiotika för djur har minskat med över två tredjedelar sedan 1986, när användningen av tillväxtbefrämjande antibiotika upphörde. Detta är korrigerat för att antalet djur av olika arter har förändrats genom åren. Under 90-talet minskade användningen av antibiotika som läkemedel till hela djurgrupper, och under det senaste decenniet ses också en minskad användning av antibiotika för behandling av enstaka djur.

Jämförelse av försäljning inom human- och veterinärmedicin

Under 2022 såldes 59,3 ton antibiotika för behandling av människor och 8,8 ton för behandling av djur (inkluderar inte produkter för intramammärt eller intrauterint bruk). Uttryckt i relation till kroppsvikt (milligram aktiv substans per skattad kilogram biomassa) var försäljningen 84,6 milligram per kilo-gram för människor och 11,3 milligram per kilogram för djur. Försäljning inom humanmedicin dominerade för alla analyserade antibiotikaklasser.

Anmälningspliktig resistens

ESBL-bildande Enterobacterales

ESBL-bildande Enterobacterales hos människor har varit anmälningspliktigt sedan 2007. Det är den vanligaste av de anmälningspliktiga resistenstyperna.

Resultat 2022, Enterobacterales med ESBL

- Antal rapporterade fall: 9 611 (föregående år 7 860), relativ förändring: 22 procent ökning.
- Antal fall med blodförgiftning: 818 (föregående år 719).
- Som tidigare år var E. coli den vanligaste arten, 82 procent, följt av Klebsiella pneumoniae, 10 procent.
- Andelen E. coli från blododling som är resistenta mot tredje generationens cefalosporiner var fortsatt 7 procent, såsom 2021.

Resultat 2022, Enterobacterales med ESBL-CARBA

- Antal rapporterade fall: 240 (föregående år 137), relativ förändring: 75 procent ökning.
- Antal fall med blodförgiftning: 14 (föregående år 7).
- E. coli var den vanligaste arten, 56 procent, följt av K. pneumoniae, 31 procent.
- Antalet E. coli från blododling som är resistenta mot meropenem är 3 av 10 541, jämfört med 6 av 10 624 under 2021.
- Fjorton kluster, med mellan två och sju fall vardera, har identifierats med helgenomsekvensering. Bland fyra av dessa förekom inhemsk smitta.

Bakterier som bildar ESBL är inte anmälningspliktiga vid fynd hos djur. Sådana bakterier är generellt sett ovanliga hos djur i Sverige. Tidigare var förekomsten hos slaktkyckling hög men den har minskat under senare år. Under 2022 undersöktes förekomsten av ESBL-bildande E. coli i tarm- och köttprov från slaktkyckling och kalkon samt i tarmprov från värphöns med selektiva metoder.

Sådana bakterier hittades i 2 procent av tarmproven från slaktkyckling respektive värphöns men inte i något tarmprov från kalkon. Vidare hittades sådana bakterier inte i några av proven av kalkonkött eller kycklingkött med svenskt ursprung. Däremot var 25 procent av proven av kycklingkött med utländskt ursprung positiva för ESBL-bildande E. coli. Antalet undersökta prov av utländskt ursprung är dock begränsat varför resultatet ska tolkas med försiktighet.

Bakterier som bildar ESBL-CARBA har inte bekräftats hos tamdjur i Sverige.

Staphylococcus aureus resistenta mot meticillin (MRSA)

Samhällsförvärvad smitta är sedan länge den vanligaste typen hos människor smittade med MRSA i Sverige, med hälften av fallen. Från 2015 rapporteras familje-/hushållssmitta och samhällsförvärvad smitta separat. Familje-/hushållssmitta och samhällsförvärvad smitta utgjorde 28 procent respektive 19 procent av fallen.

Resultat 2022

- Antal rapporterade fall: 3 340 (föregående år 2 895), relativ förändring: 15 procent ökning.
- Antal fall med blodförgiftning: 96 (föregående år 97).
- Andelen MRSA bland S. aureus från blododling har minskat till 1,9 procent, från 2,0 procent 2021.

Förekomsten av MRSA hos djur i Sverige är fortfarande låg, vilket begränsar risken för spridning till människor. Under året isolerades MRSA sporadiskt från djurslagen hund, häst, katt och papegoja. Hos hundar och katter dominerar samma typer av MRSA som hos människor, vilket tyder på att människor är smittkällan. Hos hästar sjönk antalet MRSA-fall till 13 jämfört med 2020-21 (27 respektive 23 fall), vilket antas bero på att det de tidigare två åren förekom utbrott av MRSA på hästsjukhus, men inte under 2022.

Staphylococcus pseudintermedius resistenta mot meticillin (MRSP)

Under 2022 var antalet anmälda fall av meticillinresistenta Staphylococcus pseudintermedius (MRSP) hos djur på ungefär samma nivå som de senaste åren. Totalt anmäldes 54 fall av MRSP till Jordbruksverket, varav 52 fall från hund samt ett från katt och ett från orangutang. Samtliga isolat fanns tillgängliga för vidare undersökning. De första åren efter att MRSP hade hittats hos djur i Sverige var i princip alla fall av en viss sekvenstyp (ST71). På senare år förekommer fler olika sekvenstyper, (33 olika 2022) varav ST551 är den vanligaste.

MRSP är inte anmälningspliktig vid förekomst hos människor.

Streptococcus pneumoniae med nedsatt känslighet för penicillin (PNSP)

Resultat 2022

- Antal rapporterade fall: 146 (föregående år 92), relativ förändring: 59 procent ökning.
- Antal fall med blodförgiftning: 9 (föregående år 3).
- Andelen S. pneumoniae med nedsatt känslighet för penicillin (PNSP) från blododling har ökat till 7,7 procent, från 6,3 procent 2021.

Enterococcus faecium och Enterococcus faecalis resistenta mot vankomycin (VRE)

Resultat 2022

- Totalt antal rapporterade fall: 236 (föregående år 209), relativ förändring: 13 procent ökning.
- Antalet fall av VRE kan variera kraftigt mellan år beroende på hur många och hur stora smittspridningar som förekommit på sjukhus.
- Antal rapporterade fall av E. faecium med vankomycinresistens: 227 (föregående år 204), relativ förändring: 11 procent ökning.
- Antal rapporterade fall av E. faecalis med vankomycinresistens: 4 (föregående år 1).
- Fem fall av VRE rapporterades med både E. faecium och E. faecalis.
- Antal fall med blodförgiftning: 5 (föregående år 2).
- Sexton smittspridningar rapporterades under året med 2–28 fall. Av dessa var sex större sjukhusrelaterade utbrott med 8–28 fall vardera. År 2021 rapporterades elva sjukhusrelaterade smittspridningar.
- Andelen VRE hos enterokocker från blododling är låg, 0,3 procent för E. faecium och 0,1 procent för E. faecalis.

Resistens hos zoonotiska bakterier

Salmonella är ovanligt hos djur i Sverige och isolerade stammar är oftast känsliga för antibiotika. Resistens mot fluorokinoloner är ovanlig. Bland 115 isolat från tamdjur 2022 fanns endast tre isolat med resistens mot ett antibiotikum vardera och inget var resistent mot fluorokinoloner. För salmonellaarter var resistensen bland faecesisolat från människor högst mot fluorokinoloner, 24 procent. Ingen resistens mot karbapenemer rapporterades. Salmonella från invasiva infektioner hos människor är mer resistenta än isolat från djur i Sverige. Detta beror troligen på att en stor andel av fallen hos människor är smittade utomlands eller via importerade livsmedel.

Campylobacter från djur i Sverige är oftast känsliga för relevanta antibiotika och exempelvis är resistens mot erytromycin mycket ovanligt. Hos Campylobacter jejuni från människor var resistensen mot ciprofloxacin 55 procent och mot tetracyklin 27 procent 2022. En halv procent var resistenta mot erytromycin.

Vanligtvis behandlas inte infektioner som orsakas av salmonella eller campylobacter med antibiotika, hos vare sig människor eller djur. Hos människor resistensbestäms därför endast en liten andel av isolaten, varav de flesta gäller allvarliga infektioner.

Resistens hos kliniska isolat från människor

Alla data för dessa sammanställningar samlas in automatiserat via Svebar, ett samarbete mellan de kliniska mikrobiologiska laboratorierna och Folkhälsomyndigheten.

- Escherichia coli: Resistens hos blodisolat mot ceftazidim och cefotaxim var 6 respektive 7 procent. Antalet anmälningar av E. coli ESBL från blod 2022 var 605. Resistens mot ciprofloxacin är nu 14 respektive 10 procent hos isolat från blod respektive urin, ett observandum vid val av empirisk behandling av febril urinvägsinfektion.
- Vid ålders- och könsfördelning av resultat för E. coli från urin ses vissa skillnader mellan grupperna. Speciellt tydligt är den höga ciprofloxacinresistensen (17–19 procent) hos män, 20 år och äldre.
- Klebsiella pneumoniae: Resistens hos blodisolat mot cefotaxim och ceftazidim var 6 respektive 7 procent. Antalet anmälningar av K. pneumoniae ESBL från blod 2022 var 122. Liksom för E. coli är resistensen mot ciprofloxacin nu relativt hög, 12 respektive 10 procent hos isolat från blod och urin.
- Staphylococcus aureus: Resistens mot cefoxitin (som indikerar MRSA) hos isolat från blod och prover från hud- och mjukdelar var 1,9 respektive 2,3 procent. Antalet anmälningar av MRSA från blod 2022 var 96.
- Enterococcus faecalis och Enterococcus faecium: Vankomycinresistensen hos isolat från blod är fortsatt låg (0,1 respektive 0,3 procent) och höggradig aminoglykosidresistens är fortfarande på en lägre nivå jämfört med 2017.
- Clostridioides difficile: Incidensen har legat relativt stabilt sedan 2018, men har nu ökat från 61 fall till 65 fall per 100 000 invånare och år. Antibiotikaresistens har inte undersökts 2022.

Resistens hos kliniska isolat från djur

Bakterier som orsakar sjukdom hos djur är fortfarande oftast känsliga för de antibiotika som vanligen används. Till exempel är bakterier som orsakar luftvägsinfektioner hos lantbrukets djur och hästar generellt känsliga för bensylpenicillin men resistens förekommer exempelvis hos Pasteurella multocida från kalv. Penicillin-resistens är däremot vanligt hos Staphylococcus pseudintermedius från hundar, Staphylococcus hyicus från grisar och förekommer hos S. aureus från hästar samt S. felis från katter, men är ovanligt hos S. schleiferi från hundar. Resistens hos E. coli från olika djurslag förekommer också och är vanligast hos isolat från träckprover från unga kalvar och grisar. Resistensundersökning är motiverat för val av lämpligt antibiotikum vid behandling, särskilt för stafylokocker, E. coli och Brachyspira spp.

Indikatorbakterier från friska djur

Resistens hos E. coli i tarmfloran hos friska djur kan användas som indikator för utbredningen av antibiotikaresistens hos bakteriefloran i en djurpopulation och indirekt som indikator på omfattningen av antibiotikaanvändning till djuren. I Sverige är förekomsten av resistens hos dessa indikatorbakterier låg hos de flesta undersökta djurslagen och situationen är gynnsam ur ett internationellt perspektiv. Till exempel var 69 respektive 64 procent av E. coli från friska slaktkycklingar och slaktgrisar i de senast gjorda undersökningarna känsliga för alla testade substanser.

Summary

For a long time, Sweden has had a favourable situation compared to many other countries when it comes to antibiotic resistance in bacteria from humans, which remains true. One contributing factor is that we have effective strategies to promote the responsible use of antibiotics and limit the spread of antibiotic resistance. Despite the favourable situation, there are problems with continuously increasing antibiotic resistance and the spread of infections in healthcare. Important examples are the recurrent outbreaks of vancomycin-resistant enterococci in hospitals and an increasing number of healthcare-associated clusters of $ESBL_{CARBA}$. This emphasises the importance of continuous work within Strama, infection prevention and control as well as infection prevention in the community to prevent increasing antibiotic resistance.

Antibiotic sales for humans increased in 2022 after a considerable reduction in 2020 and 2021 as an effect of the COVID-19 pandemic. In past decades, consumption has shifted from broad-spectrum antibiotics towards narrow-spectrum antibiotics. However, this development seems to have been disrupted in the recent years.

In veterinary medicine, sales of antibiotics have decreased markedly since the mid-1980s, and in recent years sales seem to have stabilised at a comparatively low level. The occurrence of resistance among bacteria from animals has generally been stable at low or moderate levels. For some substances and in some bacteria the occurrence of resistance is even declining. One example of this is a significant decline of the occurrence of ESBL-producing *Escherichia coli* among broilers. There are however exceptions, and for example resistance to ampicillin, sulphonamides and trimethoprim has increased in indicator *E. coli* from both broilers and pigs.

Key findings 2022

- Total sales of antibiotics for humans in Sweden increased by 8.2% in 2022 compared to 2021, as measured in DDD per 1 000 inhabitants per day. The increase was reflected in both outpatient and inpatient care, as well as in acute care hospitals. Antibiotic sales in dentistry decreased by 0.8% in 2022.
- Antibiotic sales in outpatient care increased during 2022 compared to 2021. Sales of antibiotics commonly used for respiratory tract infections in children during the third and fourth quarters of the year especially contributed to this increase.
- Since 2020, resistance to cefotaxime in *Escherichia coli* and the proportion of methicillin-resistant *Staphylococcus aureus* (MRSA) isolated from blood are used as indicators of antibiotic resistance in Sweden. Both the proportion of MRSA and the proportion of *E. coli* that are resistant to cefotaxime have slowly increased over a ten-year period to the current 1.9 and 7 percent respectively. For both indicators, the increase appears to have slowed down in recent years.
- During the pandemic, the number of cases of most types of notifiable antibiotic resistance decreased. For most of these, clear increases are now seen, most markedly for $ESBL_{CARBA}$, where 240 cases were reported, compared to 137 in 2021. Resistance levels among clinical isolates from humans were not affected by the pandemic.
- An increase in resistance among *Streptococcus pyogenes* to clindamycin starting in the spring of 2020 has been noted, during the fall 2022 the resistance returned to previous levels, below 5%.
- One cluster of health care-related $ESBL_{CARBA}$ and five health care-related clusters with transmission abroad were reported in 2022.
- Eleven hospital-associated outbreaks of vancomycin-resistant enterococci were reported in 2021.
- Sales of antibiotics for animals are stable at a low level and are dominated by narrow-spectrum penicillin.
- MRSA is uncommon among both farm and companion animals.
- ESBL-producing *E. coli* is generally uncommon among farm and companion animals as well as on meat.
- $ESBL_{CARBA}$-producing bacteria have not been confirmed in domestic animals in Sweden.

Sales of antibiotics

Sales of antibiotics for humans

The total sales of antibiotics for humans in Sweden increased by 8.2% in 2022 and was estimated at 10.2 DDD per 1 000 inhabitants per day. This figure encompasses all antibiotics sold on prescription to individuals and all antibiotics sold to hospitals and other health- and social care facilities.

Outpatient care

In 2022, 251 prescriptions per 1 000 inhabitants were dispensed at pharmacies in Sweden, an increase of 9% compared to 2021. Among the 21 regions in Sweden, 10 regions achieved the national long-term target of 250 or fewer prescriptions per 1 000 inhabitants and year. Antibiotic sales increased in all age groups with the highest increase in children aged 0-4 years, where sales increased by 33.9% compared to the year before. The most substantial increase occurred during the fourth quarter of 2022. This increase consisted primarily of antibiotics commonly used to treat respiratory tract infections.

The sales of antibiotics in dentistry decreased marginally by 0.8% in 2021, and accounted for 6.6% of all antibiotic prescriptions during the year. Since 2007, the prescription of antibiotics by dentists has decreased by half.

Hospitals and other health- and social care facilities

In 2022, the sales of antibiotics on requisition, including all antibiotics sold to hospitals and other health- and social care facilities, increased. Antibiotic sales to acute care hospitals increased during 2022, as measured both in DDD per 100 admissions and per 100 patient days, reaching the highest

levels observed over the last five years. In particular, sales of broad-spectrum antibiotics increased, as well as sales of beta-lactamase sensitive and resistant penicillins. Large regional variations were observed in the consumption of broad-spectrum antibiotics, which is consistent with previous years.

Sales of antibiotics for animals

When retrieving data for 2022, a substantial decrease compared to 2021 was noted, and a lack of completeness was suspected. Investigations to resolve the issue was initiated and a number of rejected data reports from pharmacies were identified and corrected by the pharmacies. Therefore, in this report, data since 2017 has been updated. The difference between 2021 and 2022 was still inexplicably large (-12%) and a thorough search for yet undiscovered errors was undertaken but none was identified. No explanation for this sudden decrease in sale has been identified. Hence, the results should be assessed with caution. Furthermore, if at a later stage some yet unidentified error causing a lack of completeness is discovered, data will be updated and published online on the SVA web page.

In 2022, reported sales of antibiotics for animals from pharmacies in Sweden were 8 865 kg, of which around 60% were narrow-spectrum penicillins. Sales of antibiotics that should be used with special restrictions (fluoroquinolones, third generation cephalosporins and polymyxins) have decreased considerably since 2013. During the past decade, the proportion of products for the treatment of individual animals has been over 90% of the total sales.

Since the withdrawal of growth-promoting antibiotics from the Swedish market in 1986, the total sales of antibiotics corrected for population sizes over time have decreased by more than two thirds. During the 1990s, sales of veterinary products for medication of groups of animals decreased, and in the past decade there has also been a decrease in sales of products for use in individual animals.

Comparing sales of antibiotics in human and veterinary medicine

In 2022, a total of 59.3 tonnes of antibiotics were sold for human use and 8.8 tonnes were sold for animal use (excluding products for intramammary or intrauterine use). Measured as milligrams of active substance per kilogram biomass, the sales were 84.6 and 11.3 milligrams per kilogram, respectively. Antibiotic sales for humans still dominate for all analysed classes of antibiotics.

Notifiable resistance

ESBL-producing Enterobacterales

ESBL-producing Enterobacterales in humans has been subject to mandatory notification since 2007. It is the most common type of notifiable antibiotic resistance.

Results 2022, Enterobacterales with ESBL

- Number of reported cases: 9 611 (previous year 7 860), relative change +22%.
- Number of bloodstream infections: 818 (previous year 719).
- As in previous years, *Escherichia coli* was the most common species, (82%), followed by *Klebsiella pneumoniae*, (10%).
- The proportion of *E. coli* from blood cultures that are resistant to third-generation cephalosporins were 7% as in 2021.

Results 2022, Enterobacterales with $ESBL_{CARBA}$

- Number of reported cases: 240 (previous year 137), relative change +75%.
- Number of bloodstream infections: 14 (previous year 7).
- Among Enterobacterales with $ESBL_{CARBA}$, *E. coli* was the most common species, (56%) followed by *Klebsiella pneumoniae* (31%).

The number of *E. coli* from blood cultures resistant to meropenem was 3 out of 10 541, compared to 6 out of 10 624 in 2021.

ESBL-producing Enterobacterales are generally rare among animals in Sweden. Previously, the occurrence in intestinal samples from broilers was high but it has decreased in recent years. In 2022, the occurrence of ESBL-producing *E. coli* in intestinal samples from broilers, fattening turkeys and laying hens, as well as samples of broiler and turkey meat was investigated with selective methods. Such bacteria were isolated from 2% of the intestinal samples from broilers and laying hens, respectively but not in any intestinal samples from fattening turkeys. Furthermore, such bacteria were not isolated from any of samples of turkey meat or broiler meat of Swedish origin. However, 25 % of broiler meat samples of non-Swedish origin were positive for ESBL-producing *E. coli*, although the number of samples are limited and hence the results should be assessed with caution.

Bacteria that produce $ESBL_{CARBA}$ have not been confirmed in domestic animals in Sweden.

Methicillin-resistant Staphylococcus aureus (MRSA)

Community-acquired infection has long been the most common type in humans, accounting for half of the cases. In 2015, community-acquired infection was divided into family/household-related infection and community-acquired infection. Family/house-hold-related infections and community-acquired infections accounted for 28% and 19% of the cases, respectively.

Results 2022

- Number of reported cases: 3 340 (previous year 2 895), relative change +15%.
- Number of bloodstream infections: 96 (previous year 97).
- The proportion of MRSA among *Staphylococcus aureus* isolated from blood has decreased to 1.9%, compared to 2.0% in 2021.

The occurrence of MRSA in animals in Sweden is still low, which limits the spread from animals to humans. MRSA was found sporadically in horses, dogs, cats and one parrot. The increase of MRSA cases, compared to previous years, seen in horses in 2020 (n=27) and 2021 (n=23) was partly explained by outbreaks in equine hospitals. Consequently, in 2022 the figures dropped to 13 cases, as there were no outbreaks. In companion animals, the same types of MRSA as in humans dominate, indicating a human source of MRSA in these animals.

Methicillin-resistant Staphylococcus pseudintermedius (MRSP)

In 2022, the number of reported cases of methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) in animals was around the same level as in previous years. In total 54 cases of MRSP were notified to the Swedish Board of Agriculture, including 52 from dogs, one from a cat and one from a orangutan. All isolates were available for further investigations. When MRSP first occurred among animals in Sweden, the sequence type ST71 dominated. However, for several years the isolates of MRSP have been more diverse with several sequence types occurring.

MRSP in humans is not notifiable.

Streptococcus pneumoniae with reduced susceptibility to penicillin (PNSP)

Results 2022

- Number of reported cases: 146 (previous year 92), relative change +59%.
- Number of bloodstream infections: 9 (previous year 3).
- The proportion of *S. pneumoniae* with reduced susceptibility to penicillin (PNSP) among bloodstream infections increased to 7.7% from 6.3% 2021.

Vancomycin-resistant enterococci (VRE)

Results 2022

- Total number of reported cases: 236 (previous year: 206), relative change +13%.
- The number of cases of VRE can vary greatly between years depending on the number and magnitude of hospital outbreaks.
- Number of reported cases of *E. faecium* with vancomycin resistance: 227 (previous year: 204), relative change +11%
- Number of reported cases of *E. faecalis* with vancomycin resistance: 4 (previous year: 1)
- There were five cases infected with both *E. faecium* and *E. faecalis*.
- Number of bloodstream infections: 5 (previous year: 2)
- Sixteen clusters were reported during the year with 2-28 cases each. Out of these, six were large hospital-related outbreaks with 8-28 cases each. In 2021, eleven hospital-related outbreaks were reported.
- The proportion of VRE among bloodstream infections is low at, 0.3% for *E. faecium* resistant to vancomycin and 0.1% for *E. faecalis* resistant to vancomycin.

Zoonotic pathogens

Salmonella is rare in animals in Sweden. Furthermore, only a few of the notified cases involve antibiotic-resistant strains. Resistance to fluoroquinolones is rare. Among 115 isolates from domestic animals in 2022 only 3 were resistant to one antibiotic each and none was resistant against fluoroquinolones.

For *Salmonella* species isolated from human faeces, the highest occurrence of resistance was to fluoroquinolones, (24%). No resistance to carbapenems was reported. Isolates from human invasive infections with *Salmonella* are markedly more resistant, probably due to the large proportion of cases acquired abroad.

Campylobacter from animals in Sweden are generally susceptible to relevant antibiotics, and resistance to erythromycin, for example, is most uncommon. In *Campylobacter jejuni* from humans, resistance to ciprofloxacin was 55% and resistance to tetracycline was 27% in 2022, and a half percent of the isolates were resistant to erythromycin.

Infections, either in humans or in animals, caused by *Salmonella* and *Campylobacter* are usually not treated with antibiotics. In humans, only a small proportion of the isolates, most of which are related to serious infections, are tested for antibiotic susceptibility.

Human clinical isolates

All data for these compilations are collected automatically via Svebar, a collaboration between the clinical microbiology laboratories and the Public Health Agency.

Escherichia coli: Resistance in blood isolates to ceftazidime and cefotaxime was 6 and 7% respectively. The number of reported *E. coli* ESBL from blood was 605 cases in 2022. Resistance to ciprofloxacin is now 14% and 10%, respectively, in isolates from blood and urine. This needs to be considered when choosing empirical treatment for febrile urinary tract infection.

When *E. coli* from urine are divided by age and gender, some differences in resistance are seen. Most prominent is the high ciprofloxacin resistance (17-19%) seen among men 20 years and older.

Klebsiella pneumoniae: resistance in blood isolates to cefotaxime and ceftazidime was 6 and 7% respectively. The number of reported *K. pneumoniae* ESBL from blood was 122 cases in 2022. As for *E. coli*, resistance to ciprofloxacin is now relatively high at, 10-12% in isolates from urine and blood.

Staphylococcus aureus: Resistance to cefoxitin (which is indicative of MRSA) in isolates from blood and samples from skin and soft tissue was 1.9% and 2.3% respectively. The number of reported MRSA from blood was 96 cases in 2022.

Enterococcus faecalis and *Enterococcus faecium*: Vancomycin resistance in isolates from blood remains low (0.1% and 0.3%, respectively) and high-level aminoglycoside resistance is still on a lower level compared to 2017.

Clostridioides difficile: The incidence has been relatively stable since 2018, but has now increased from 61 cases to 65 cases per 100 000 inhabitants and year. No isolates were tested for antibiotic resistance in 2022.

Animal clinical isolates

Bacteria causing clinical disease in animals are mostly susceptible to antibiotics relevant for treatment. Respiratory pathogens from farm animals and horses are generally susceptible to benzylpenicillin, but resistance occurs, for example in *Pasteurella multocida* from calves. Penicillin resistance is common in *Staphylococcus pseudintermedius* from dogs, *Staphylococcus hyicus* from pigs, and occurs in *S. aureus* from horses and *S. felis* from cats. However, in *S. schleiferi* from dogs penicillin resistance is uncommon. Resistance to commonly used antibiotics in *E. coli* occurs in all animals but is most prominent in enteric isolates from young calves and pigs. Susceptibility testing for guidance in antibiotic therapy is warranted, especially for staphylococci, *E. coli*, and *Brachyspira* spp.

Indicator bacteria from healthy animals

Antibiotic resistance in *E. coli* from the intestinal flora of healthy animals serves as an indicator for the presence of resistance in an animal population. The prevalence of acquired resistance in such commensal bacteria also indirectly indicates the magnitude of the selective pressure from the use of antibiotics in an animal population. The prevalence of resistance in indicator bacteria from animals in Sweden is low, and the situation is favourable in an international perspective. As an example, in the latest investigations of indicator *E. coli* from broilers and pigs, 69% and 64% respectively, were susceptible to all tested substances.

Medicinal shortages – the role of the Swedish Medical Products Agency

A medicinal shortage situation occurs when a pharmaceutical company is temporarily unable to deliver a medicinal product so that supply meets demand. The process of manufacturing and the supply chain is global and complex. The supply chain can be disturbed in many ways and the reasons for a shortage can therefore vary. The role of the Swedish Medical Products Agency (MPA) is to inform about reported shortages and by different means moderate the consequences of critical shortages.

What causes medicinal shortages?

Each step in the process of manufacturing medicinal products, as well as the supply chain as a whole, is streamlined and no more medicinal products than normally needed are produced or stored. Production is often located to a limited number of sites around the world. Therefore, the process is vulnerable to disturbances which can lead to shortages. Examples of such disturbances include problems with manufacturing or transportation, a lack of active substance or an unexpectedly high demand for the product.

The different responsibilities of the Swedish MPA and the pharmaceutical companies

The responsibility of the pharmaceutical company

When a shortage of a medicinal product occurs, or is expected to occur, the market authorisation holder (MAH) has a responsibility according to the Medicinal Products Act (2015:315) to report a shortage notification to the Swedish MPA. The notifications are reported via an e-service provided by the Swedish MPA since 2018. Shortage notifications must be made as soon as possible, no later than two months before the shortage is expected to occur. The MAH is also responsible for updating their shortages, for example to prolong, shorten or report the end of a shortage.

The responsibilities of the Swedish MPA

After receiving the shortage notifications via the e-service, the Swedish MPA investigates, compiles, and publishes a list of shortages based on information provided by the pharmaceutical companies. The list includes when the shortage will start or has started and how long it is expected to last. The Swedish MPA investigates if there are any alternatives, for example alternative package sizes, strengths, or medicines within the same ATC-group. Information about possible alternatives is also provided in the published list of upcoming and current shortages. If there are no suitable alternatives on the Swedish market, a shortage situation can sometimes be resolved with an exemption or special permission (license) application. It is the Swedish MPA that grants exemptions or special permissions (licenses).

Medical products intended for humans often have several substitutable alternatives and can often be replaced directly at the pharmacy. Veterinary medical products have fewer alternatives.

The instruction from the government to the Swedish MPA includes that information about shortages for medical products should be published continuously. The Swedish MPA publishes two lists of shortage notifications in Excel-format on the web page. There is one list with all ongoing and upcoming shortage situations and another list with all past shortage notifications that have been reported since 2018. The lists are updated daily and only provided in Swedish. The lists include, for example, a prognosis for start and end dates and the cause of the shortage (if the MAH has given consent for it to be published). The information in the lists is also available as open data in XML format which can be used in other systems. If a medicinal shortage is not found in the list of shortage notifications, the Swedish MPA welcome such information and aim to follow up on all signals of shortage situations.

The Swedish MPA collaborate with representatives from pharmacies, healthcare professionals and other relevant actors within the supply chain, regarding shortage situations, to contribute to availability of medicinal products. For this purpose the Swedish MPA makes compilations about critical or potentially critical shortage situations.

Please, be aware that the Swedish MPA does not manufacture, order or stock any medicinal products.

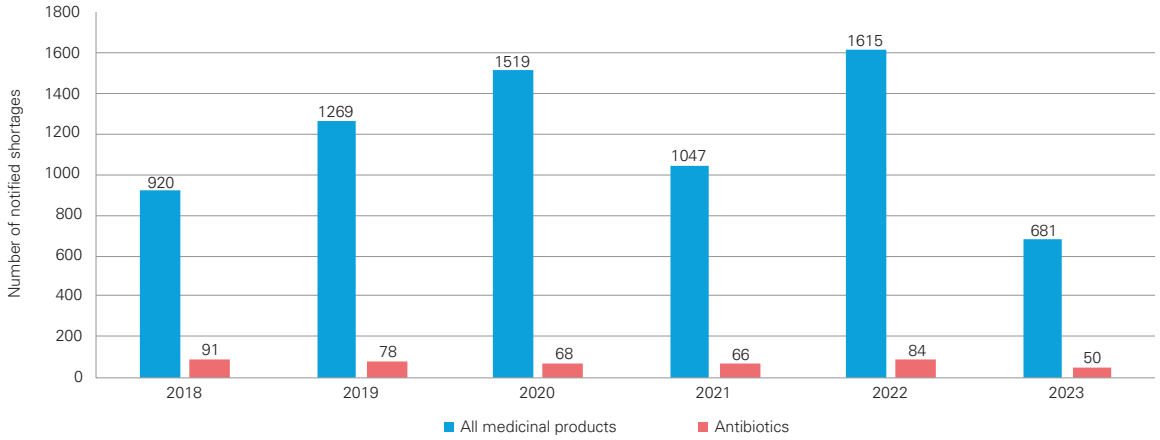
Statistics

The Swedish MPA publishes statistics quarterly concerning the number of reported shortages.

The number of medicinal products with an ongoing shortage situation is relatively small. When the most recent statistics were published (April 18, 2023) the number of notified shortages for medicinal products on a package-size level was only 4.6 % compared to the total number of packages of registered and marketed medicinal products.

Since the start of the e-service and publication of the list of shortage notifications in 2018, the Swedish MPA has seen an increase of the number of reported shortages, except for in 2021. During 2021, there were fewer shortage notifications, potentially related to the COVID-19 pandemic; big stocks of medicinal products were built up during the first pandemic year 2020 combined with a lower demand by then due to the restrictions (Figure 1).

Figure 1. Notified shortages for medicinal products and for antibiotics on a package-size level, per year, February 2018 to March 2023.



Both human and veterinary medicinal products are shown.

Source: Swedish Medical Products Agency

The number of notified shortages during 2022 until the end of the first quarter of 2023 for medicinal products within the ATC-groups J01 and QJ01 Antibacterial drugs for systemic use, both medicinal products for human and veterinary use, is shown in Table 1. Even though the number of notified shortages for medicinal products within these ATC-groups is small compared to the total number of notified shortages for medicinal products, potentially critical shortages for antibiotics can occur and lead to severe consequences for patient groups that are already vulnerable. Additionally, a shortage of an antibiotic might lead to the use of an antibiotic with a wider spectrum than normally needed.

Table 1. The number of notified shortages for medicinal products within the ATC-groups J01 and QJ01 during 2022 and the first quarter of 2023.

ATC group	Veterinary shortages	Human shortages
(Q)J01A Tetracyclines	2	4
(Q)J01C Beta-lactams (penicillins)	8	61
(Q)J01D Other beta-lactams	1	18
(Q)J01E Sulphonamides and trimethoprim	3	0
(Q)J01F Macrolides, lincosamides and streptogramins	3	8
(Q)J01M Quinolones	3	9
(Q)J01X Other antibiotics	0	14

Source: Swedish Medical Products Agency

Continuous improvement and development

There are many ongoing and upcoming development projects in this area. To mention a few, the list of shortage notifications will be published as a web page instead of in Excel-format, the decisions of exemptions will be published and the Swedish MPA will be able to submit penalty fees when shortage notifications are late or absent. The Swedish MPA has also been commissioned by the government to survey, analyse and come with suggestions to prevent and manage shortages of medicinal products in Sweden.

More information

More information can be found on the Swedish MPA's website, both in English and Swedish: www.lakemedelsverket.se

Contact

Questions or signals about shortage situations not being reported? Please contact the Swedish MPA:
Opening hours: Weekdays between 08.00 and 16.30.
Switch board: 018-17 46 00
E-mail address: registrator@lakemedelsverket.se

Guidance for readers

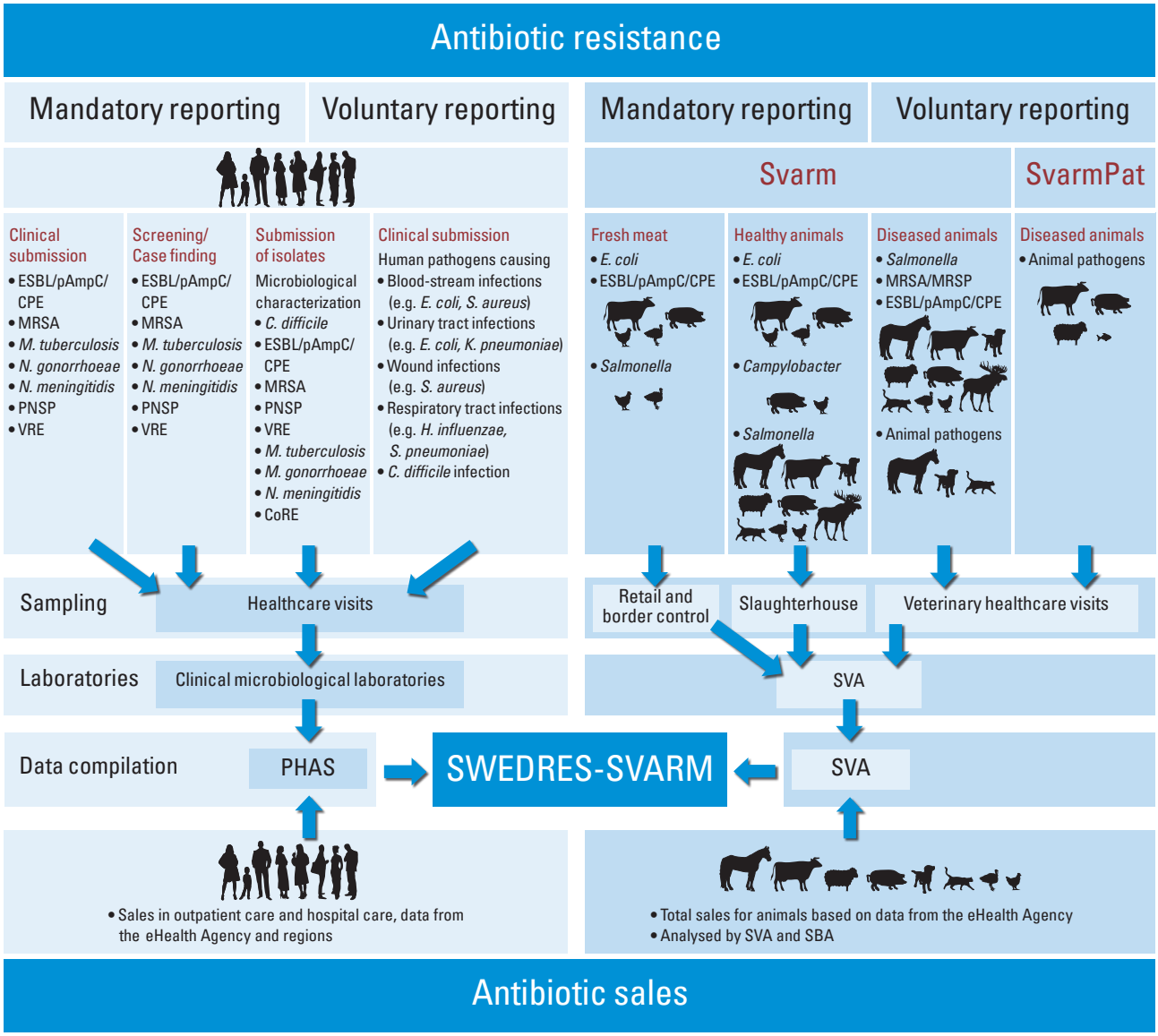
The Swedres-Svarm report is the result of a cooperation between the Public Health Agency of Sweden and the National Veterinary Institute with the aim to present data relating to both humans and animals on the sales of antibiotics and on antibiotic resistance in a joint report.

Data on occurrence of notifiable antibiotic resistance in bacteria as well as data on resistance in zoonotic bacteria and in bacteria from clinical submissions are presented. Additionally, the report includes data on sales of antibiotics and resistance in so called indicator bacteria from healthy animals and from food of animal origin.

Data on resistance in bacteria from humans are mainly obtained from clinical microbiology laboratories and in addition via notifications from clinicians. They are compiled by the Public Health Agency of Sweden in Swedres. In contrast, data on animals and food, compiled by the National Veterinary Institute, are from the national monitoring program in the veterinary field Svarm. This program is specifically designed to monitor resistance in bacteria from animals and food and is organised and run at the National Veterinary Institute. Data in the veterinary field also emanate from other sources, such as the SvarmPat project and specific research projects. For details on data sources see respective bacteria in Antibiotic resistance in animals and Background data, material, methods and references.

Schematic view of antimicrobial sales and resistance monitored in Sweden 2022.

Resistance in bacteria from humans and sales for humans to the left and resistance in bacteria from animals and food and sales for animals to the right.



Embedded files in the PDF-file version of the report

The data from many of the tables and figures in Swedres-Svarm can be accessed from embedded Excel-files. To access the embedded files, indicated with paperclips, we recommend using Adobe Acrobat Reader.

Antibiotic sales

Swedres - Humans

Antibacterials for systemic use in humans are indexed as J01 in the Anatomical Therapeutic Chemical classification system. The J01 group also includes the antiseptic substance methenamine, which is not an antibiotic and is not a driver of antibiotic resistance. Throughout this report, methenamine is excluded whenever antibiotics are referred to or presented as a group. Statistics for dentistry includes oral metronidazole (P01AB01) in addition to antibiotics in the J01 group.

All pharmacies in Sweden are required to provide statistics on sales of all products on a daily basis to the Swedish eHealth Agency (eHälsomyndigheten), which maintains a national database with sales statistics for all drugs. The database includes statistics on prescriptions to individuals issued by healthcare providers from all 21 regions in Sweden and encompasses primary healthcare centres, outpatient specialist clinics, hospitals and dental clinics. In addition, statistics on medicines sold on requisition to hospitals, nursing homes and other health- and social care facilities are also accessible through the database. While prescription data accurately reflects antibiotic use, procurement data based on requisitions are impacted by procurement-related factors that may over- or underestimate antibiotic use. For detailed description of the pharmaceutical system in Sweden, please refer to the *Materials and methods*, *sales of antibiotics* section.

Comparison of sales of antibiotics between regions and to the elderly population over time is complicated by the fact that there are differences in how drugs are distributed to residents in nursing homes. In Sweden, most people living in nursing homes still receive their medication by prescription, whereby data are included in outpatient sales. However, there are also nursing homes where medicines are procured by the facility and then dispensed to the residents. These sales are included in hospital care data. Since routines differ between regions and over time, the estimation of antibiotic use to the elderly population is not entirely reliable.

Wherever sales of antibiotics to a certain population group are displayed (children aged 0-6 years, women aged 15-79 years, inhabitants in a region), the denominator is the total number of individuals in the same population group.

In this report the term 'outpatient care' includes all antibiotic sales on prescription to individuals. 'Hospital care' includes antibiotic sales to hospitals, nursing homes and other health- and social care facilities. Since national data on antibiotic sales to hospitals in Sweden are combined with sales to some nursing homes and other facilities, the figures are not suitable for evaluation of antibiotic use in acute care hospitals. Therefore, data on sales exclusively to acute care hospitals have been provided by pharmacists in local Strama groups from all regions for the purpose of this report.

As data on antibiotic sales to humans are not linked to treatment indications, this report has grouped antibiotics frequently prescribed for treatment of common infections in Sweden in order to estimate the prescription rates for these diagnoses. All figures and tables referring to these treatment indications are based on the following antibiotics:

Per oral antibiotics commonly prescribed for specific therapeutic areas in Sweden

Indication	Antibiotics included
Respiratory tract infections (RTIs)	Doxycycline (J01AA02; excluding packages larger than 50 tablets), penicillin V (J01CE02), amoxicillin (J01CA04), amoxicillin with enzyme inhibitor (J01CR02), cephalosporins (J01DB-DE) and macrolides (J01FA)
Urinary tract infections (UTIs)	Pivmecillinam (J01CA08), trimethoprim (J01EA01), ciprofloxacin (J01MA02), norfloxacin (J01MA06) until 2020 and nitrofurantoin (J01XE01)
Skin and soft tissue infections (SSTIs)	Clindamycin (J01FF01) and flucloxacillin (J01CF05)
Acne vulgaris	Doxycycline (J01AA02; packages over 50 tablets), lymecycline (J01AA04), oxytetracycline (J01AA06) and tetracycline (J01AA07).

Antibiotic resistance

Swedres - Humans

Most of the data on resistance in Swedres is derived from routine diagnostic samples sent for testing at clinical microbiological laboratories. The results are mostly presented as proportion of resistance in tables or graphs. The methods used for antibiotic susceptibility testing, whether MIC determination or disk diffusion method, are standardised by European Committee on Antimicrobial Susceptibility Testing (EUCAST) and available online at www.eucast.org. The methods and breakpoints routinely used in Sweden are available at www.nordicast.org. EUCAST also presents yearly updated interpretative criteria for clinical use in human medicine, i.e. clinical breakpoints, also available at www.eucast.org.

Svarm - Animals and food

Data on resistance in Svarm are from MIC determinations performed at the National Veterinary Institute using broth microdilution following the standards of the Clinical and Laboratory Standards Institute (CLSI, 2018). Results for isolates of zoonotic and indicator bacteria are interpreted according to ECOFFs from EUCAST (www.eucast.org). Clinical isolates from animals are generally classified by ECOFFs when such values are available. Interpretive criteria used are given in the section Materials and methods resistance in bacteria from animals.

ECOFFs classify isolates with acquired reduced susceptibility as non-wild type. In Svarm, non-wild type isolates are called "resistant". This classification is relevant for monitoring purposes, but it should be understood that resistance defined in this manner not always implies clinical resistance.

Since the first report from Svarm, the interpretive criteria for some combinations of bacteria and substance have been changed. To facilitate comparisons when retrospect data are presented, levels of resistance have been recalculated using current interpretive criteria if not otherwise stated.

Indicator bacteria in animals

In Svarm, *Escherichia coli*, *Enterococcus faecalis* and *E. faecium* serve as indicators for presence of antibiotic resistance in the enteric flora of healthy animals and in the flora contaminating food. The prevalence of acquired resistance in such commensal bacteria in animals indicates the magnitude of the selective pressure from use of antibiotics in an animal population. Most bacteria of the enteric flora are unlikely to cause disease, but they can be reservoirs for resistance genes that can spread to bacteria that cause infections in animals or humans. Prevalence of resistance in indicator bacteria contaminating meat indicates the magnitude of the potential human exposure to such reservoirs in food producing animals.

Presentation of MIC distributions in bacteria from animals

Results from MIC determinations in Svarm are presented as distributions of MICs in tables of a uniform design as below. Distributions are given as percentages of isolates tested. In the tables, white fields denote range of dilutions tested for each antibiotic and vertical bold lines indicate cut-off values used to define resistance.

The percentage of isolates with a certain MIC of an antibiotic is given in the corresponding white field. For MICs above the range tested of an antibiotic (>X mg/L) the percentage is given in the field closest to the range, i.e. in the first shaded field to the right of the tested range. For MICs equal to or lower than the lowest concentration tested for an antibiotic (≤Y mg/L) the percentage is given as the lowest tested concentration, i.e. in the first white field of the tested range.

Multidrug resistance

The terms multidrug resistance (MDR), multiresistance and multiresistant are in Svarm generally used for isolates with acquired resistance to three or more antibiotic classes. However, for aminoglycosides every substance is considered separately because of the complexity of the resistance mechanisms against this class. Furthermore, for staphylococci each subclass of beta-lactams is considered separately but for Enterobacterales all beta-lactams are considered as one class.

Presentation of MIC distributions in bacteria from animals

Antibiotic	Resistance (%)	Distribution (%) of MICs (mg/L)											
		≤ 0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ciprofloxacin	21	21.0	52.0	6.0			1.0			20.0			
Erythromycin	0				93.0	4.0	3.0						
Tetracycline	2		75.0	22.0	1.0			1.0	1.0				

Abbreviations of generic antibiotic names

When abbreviations for antibiotics were needed in tables or graphs the following were used.

Amp	Ampicillin	Ery	Erythromycin	Nit	Nitrofurantoin
Azt	Azithromycin	Flf	Florfenicol	Oxa	Oxacillin
Bac	Bacitracin	Fox	Cefoxitin	Pen	Penicillin G
Caz	Ceftazidime	Fus	Fusidic acid	Ptz	Piperacillin-Tazobactam
Cdr	Cefadroxil	Gen	Gentamicin	Rif	Rifampicin
Cer	Ceftiofur	Imp	Imipenem	Str	Streptomycin
Cet	Cephalothin	Kan	Kanamycin	Sul	Sulphonamide
Chl	Chloramphenicol	Lin	Linezolid	Tet	Tetracycline
Cip	Ciprofloxacin	Mec	Mecillinam	Tgc	Tigecycline
Cli	Clindamycin	Mer	Meropenem	Tmp	Trimethoprim
Col	Colistin	Nal	Nalidixic acid	Tsu	Trimethoprim-sulphonamide
Ctx	Cefotaxime	Nar	Narasin	Tob	Tobramycin
Enr	Enrofloxacin	Neo	Neomycin	Van	Vancomycin

Abbreviations

AMEG	Antimicrobial ad hoc expert group of the European medicines agency
AST	Antimicrobial susceptibility testing
ATC	Anatomical therapeutic chemical classification system
BSI	Bloodstream infection
CDI	*Clostridioides difficile* infection
CPE	Carbapenemase producing Enterobacterales (formerly Enterobacteriaceae)
CSF	Cerebrospinal fluid
DDD	Defined daily dose
ECDC	European Centre for Disease Prevention and Control
ECOFF	Epidemiological cut-off value for non-susceptibility
EARS-Net	European antimicrobial resistance surveillance network
EMA	The European Medicines Agency
ESC	Extended spectrum cephalosporin
ESBL	Extended spectrum beta-lactamase
$ESBL_A$	Extended spectrum beta-lactamase, plasmid-mediated, inhibited by clavulanic acid (A = classical)
$ESBL_M$	Extended spectrum beta-lactamase inhibited by cloxacillin, also called plasmid-mediated AmpC (M = miscellaneous)
$ESBL_{CARBA}$	Extended spectrum beta-lactamase with activity against carbapenems
EUCAST	European Committee on Antimicrobial
GBS	*Streptococcus agalactiae* (Group B streptococci)
GLASS	Global Antimicrobial Resistance and Use Surveillance System
HLAR	High-level aminoglycoside resistance (e.g. in *Enterococcus*)
MALDI-TOF MS	Matrix-assisted-laser-desorption/ionization time-of-flight mass spectrometry
MDR	Multidrug resistance, i.e. phenotypic resistance to three or more antibiotic classes
MIC	Minimal inhibitory concentration
MLST	Multilocus sequence typing
MRSA	Methicillin-resistant *Staphylococcus aureus*
MRSP	Methicillin-resistant *Staphylococcus pseudintermedius*
NordicAST	Nordic Committee on Antimicrobial Susceptibility Testing
PHAS	The Public Health Agency of Sweden
PNSP	*Streptococcus pneumoniae* with reduced susceptibillity to penicillin
PVL	Panton-Valentine leukocidin
ResNet	Webb application for Resistance surveillance and quality control programme
RSV	Respiratory syncytial virus
RTI	Respiratory tract infection
spa	*Staphylococcus aureus* protein A gene
SSTI	Skin and soft tissue infection
ST	Sequence type
Strama	Swedish strategic programme against antibiotic resistance
SVA	Statens veterinärmedicinska anstalt (National veterinary institute)
TB	Tuberculosis
UTI	Urinary tract infection
VRE	Vancomycin-resistant enterococci
XDR	Extreme drug resistance (used for *Mycobacterium tuberculosis*)

Sales of antibiotics for humans

Exceptional changes to antibiotic sales in Sweden were observed during 2020 and 2021 due to the COVID-19 pandemic. Recommendations issued to reduce the spread of COVID-19 resulted in changed behaviour in the general population, which in turn led to a reduced spread of communicable diseases in general. Healthcare-seeking behaviour appears to have been affected, and the management of the COVID-19-pandemic forced health care to reprioritise resources, leading to, for example, cancelling or postponing some planned healthcare visits and elective surgeries (National Board of Health and Welfare, 2021). These factors affected the sales of antibiotics during this time. Most notably, considerable decreases were observed in prescriptions to children, especially of antibiotics commonly used to treat respiratory tract infections.

Total sales of antibiotics have increased during 2022, while still remaining lower than before the pandemic. This increase was most noticeable for antibiotics commonly prescribed for respiratory tract infections to children towards the end of 2022, reaching higher sales levels than those seen in 2019. The same factors that contributed to a decline in antibiotic sales during the first years of the pandemic likely explain this increase. More social interactions, made possible by the continued COVID-19 vaccination and consequent phasing out of restrictions, contributed to the increased spread of communicable diseases as evidenced by surveillance data on common viral and bacterial infections; surges in infections with respiratory syncytial virus (RSV), influenza virus and group A streptococci, as well as COVID-19, were reported during especially the fourth quarter of 2022 after a few years of reduced transmission (Public Health Agency, 2023a-d). Additionally, regular seasonal variations of viral infections have been disrupted, leading to a large burden of several respiratory infections towards the end of the year (Public Health Agency, 2023a-c).

An increase in antibiotic prescribing following the removal of COVID-19 restrictions was expected. However, if antibiotic sales will return to the levels observed prior to the pandemic overall remains to be seen. There are lingering effects of the pandemic, and the degree to which the increased antibiotic prescribing observed in outpatient care during the latter part of 2022 was appropriate cannot be elucidated from sales data alone. Continued antimicrobial stewardship efforts are needed to ensure that appropriate prescribing practices are maintained, especially as primary care contacts have increasingly shifted from physical visits towards digital appointments (Cederberg, 2021).

The data sources and methodology underlying the statistics presented in this chapter are described in the *Materials and methods*, *sales of antibiotics* section. Due to regulations regarding the confidentiality of sales data, detailed data for certain substances and groups cannot be shown.

Total sales of antibiotics

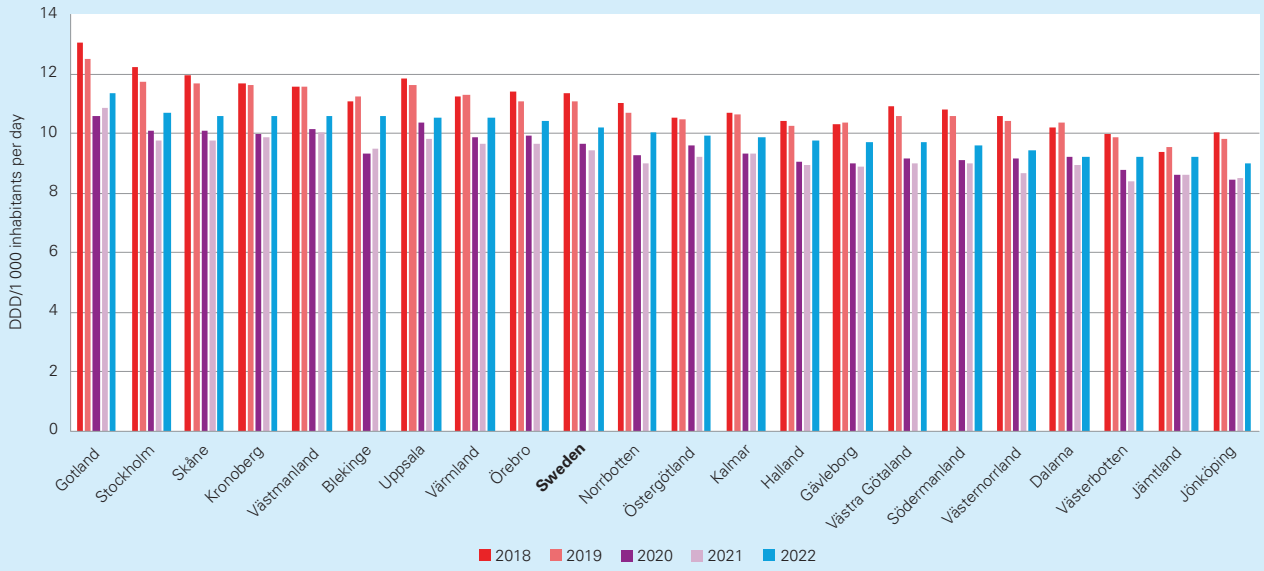
Results

- Total sales of antibiotics (J01 excl. methenamine) increased by 8.2% compared to 2021 (from 9.4 DDD to 10.2 DDD per 1 000 inhabitants per day), Figure 1.1.
- Total sales of antibiotics varied between regions, ranging from 9.0 DDD per 1 000 inhabitants per day in Jönköping region to 11.3 DDD per 1 000 inhabitants per day in Gotland region, Figure 1.1.
- Sales of beta-lactamase sensitive penicillins and combinations of penicillins increased the most, while the sales of carbapenems and trimethoprim decreased, Figure 1.2.
- Beta-lactamase sensitive penicillins and tetracyclines remain the two most sold antibiotic classes in Sweden during 2022, while sales of tetracyclines do not appear to be returning to levels observed in 2019, Figure 1.2.

Comments

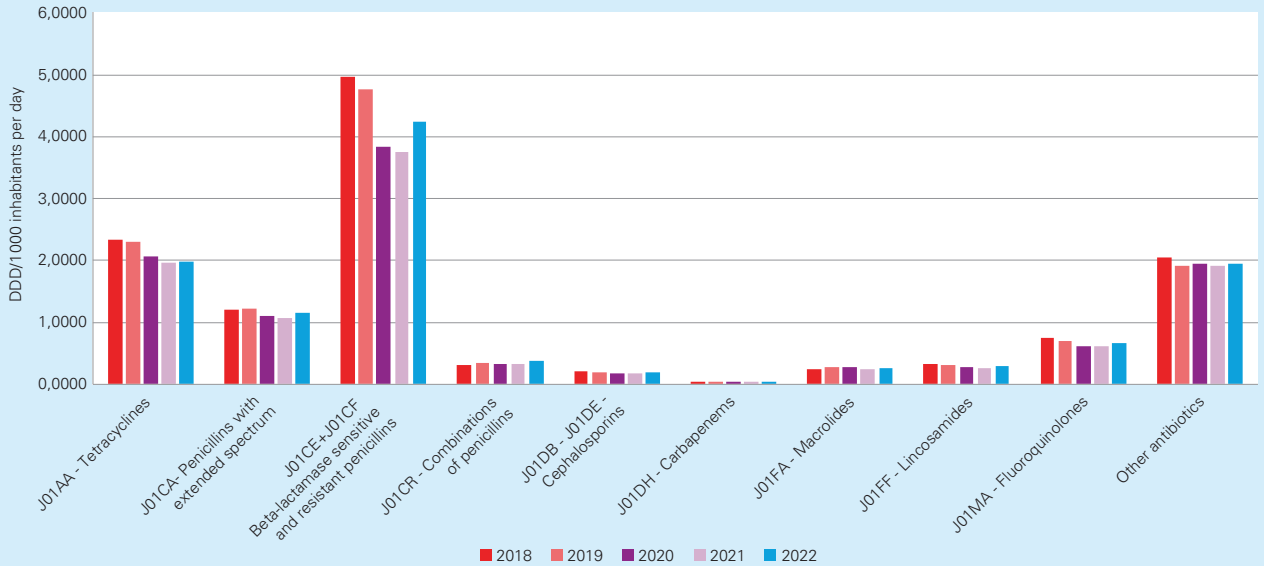
The sales of antibiotics increased in 2022, but remain below the sales volumes observed in 2019, before the COVID-19 pandemic. A comparison with the population-weighted mean of the EU/EEA countries from 2012-2021 (ECDC, 2022) confirms Sweden's restrictive position regarding antibiotic prescribing. Due to regulations regarding the confidentiality of sales data, detailed data for certain substances and groups cannot be shown.

Figure 1.1. Total sales of antibiotics (J01 excl. methenamine) in 2018-2022, by region.



Source: The Public Health Agency of Sweden

Figure 1.2. Total sales of selected[a] antibiotic classes (ATC level 4) between 2018 and 2022.



[a]Other antibiotics includes all remaining antibiotic groups sold in Sweden.

Source: The Public Health Agency of Sweden

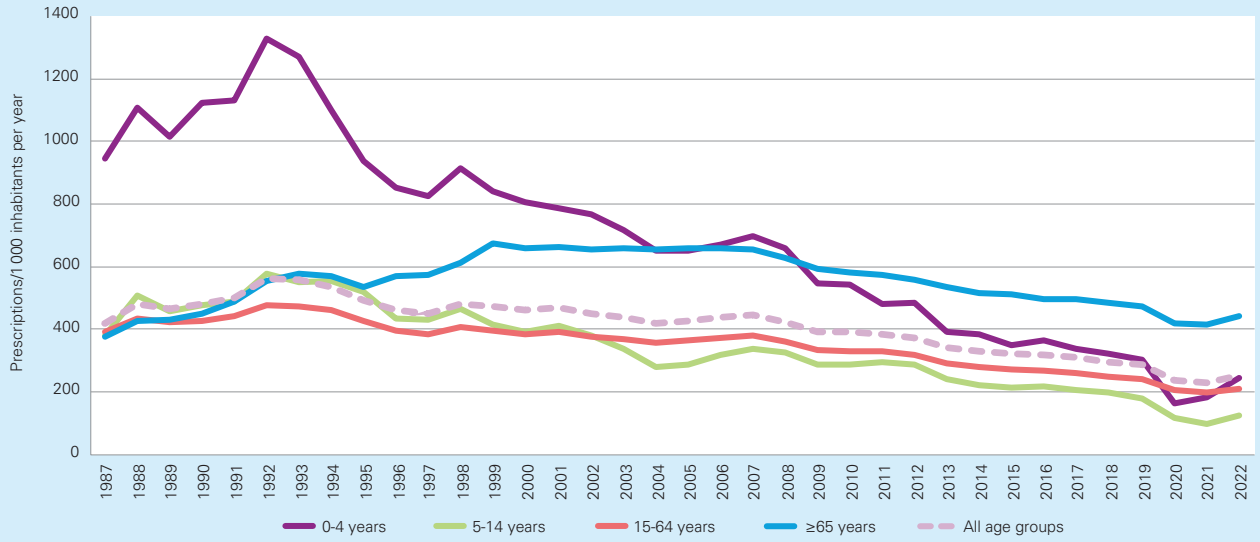
Antibiotics in outpatient care

Total sales in outpatient care

Results

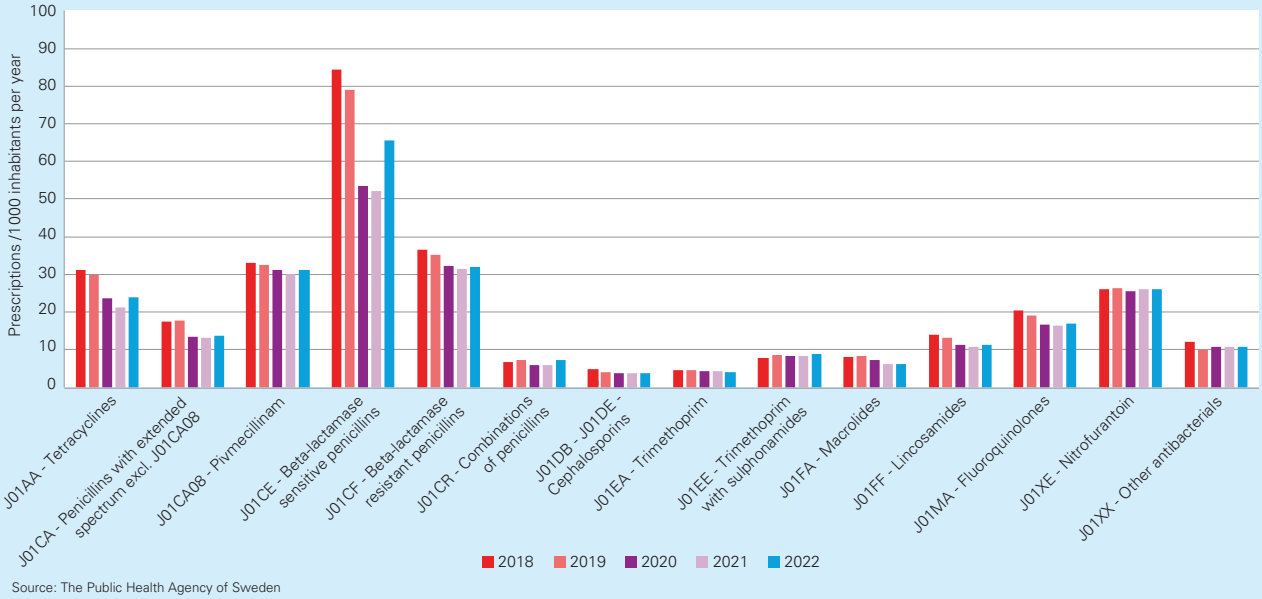
- In 2022, 251 prescriptions per 1000 inhabitants were sold in Sweden – an increase of 9.3% compared to 2021.
- Sales of antibiotics increased for all age groups in 2022, with the largest increase observed for children aged 0-4 years (33.9% increase compared to 2021, Figure 1.3).
- An increase in sales was observed for most antibiotic classes in 2022, but a slight decrease was observed for cephalosporins (J01DB-DE) and trimethoprim (J01EA), Figure 1.4.
- Beta-lactamase sensitive penicillins (J01CE) and beta-lactamase resistant penicillins (J01CF) were the most commonly sold antibiotics in 2022 measured in the number of prescriptions. Measured in DDD, beta-lactamase sensitive penicillins (J01CE) and tetracyclines (J01AA) were the most commonly sold antibiotics (data not shown).
- The number of prescriptions per 1 000 inhabitants varied between 215 in Västerbotten region to 280 in Gotland region in 2022. Antibiotic sales increased in all 21 regions during 2022, Figure 1.5.
- In 2022, 14.5% of the Swedish population was treated with at least one course of antibiotics, ranging from 11.9% in Västerbotten region to 15.9% in Skåne region, Figure 1.6.

Figure 1.3. Sales of antibiotics (J01 excl. methenamine) in outpatient care by age group in 1987-2022.



Source: The Public Health Agency of Sweden

Figure 1.4. Sales of selected antibiotic classes (ATC level 4 and 5) in outpatient care between 2018 and 2022.

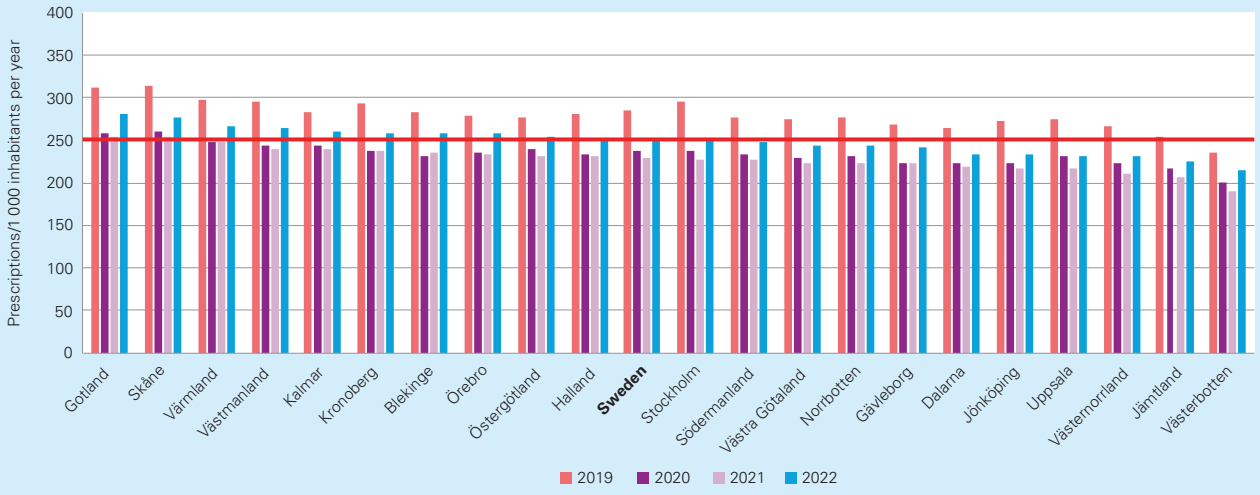


Source: The Public Health Agency of Sweden

Comments

The sales of antibiotics have decreased with 55% since 1992, when the prescription of antibiotics peaked. The greatest decrease during this time period was observed in children aged 0-4 years, dropping from 1 328 prescriptions per 1 000 inhabitants in 1992 to 246 in 2022. The COVID-19 pandemic led to a steep decrease in sales of antibiotics in 2020 and 2021, which was most noticeable for children aged 0-4 years. In 2018, the national annual average sales of antibiotics were below 300 prescriptions per 1 000 inhabitants for the first time since national monitoring started. The trend continued downwards and in 2020 and 2021, and the national long-term target of 250 prescriptions per 1 000 inhabitants per year was achieved nationally (Strama, 2016). This target was also achieved in 10 out of 21 regions in 2022. However, the national annual average of sales has returned to above the target of 250 prescriptions per 1 000 inhabitants. This indicates that this temporary national achievement was a consequence of the COVID-19 pandemic and emphasises the continued need for antibiotic stewardship efforts.

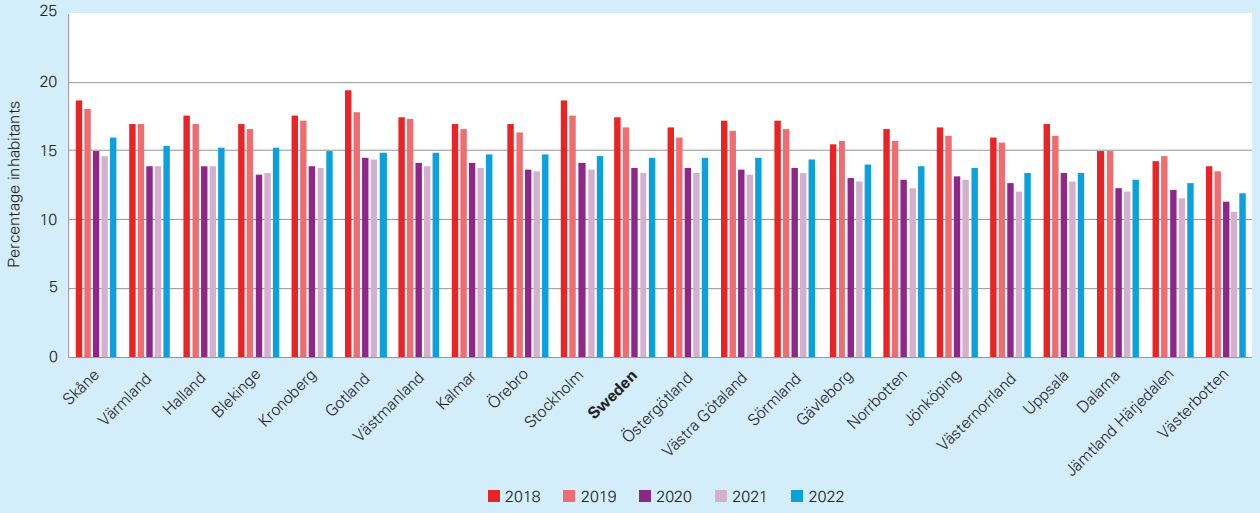
Figure 1.5. Sales of antibiotics (J01 excl. methenamine) in outpatient care in 2019-2022, by region[a].



[a]The red line indicates the national target of 250 prescriptions or less per 1 000 inhabitants per year.

Source: The Public Health Agency of Sweden

Figure 1.6. Percentage (%) of inhabitants treated with at least one course of antibiotics (J01 excl. methenamine) in outpatient care from 2018 to 2022, by region.



Source: The Public Health Agency of Sweden

Antibiotics commonly used to treat certain infections in outpatient care

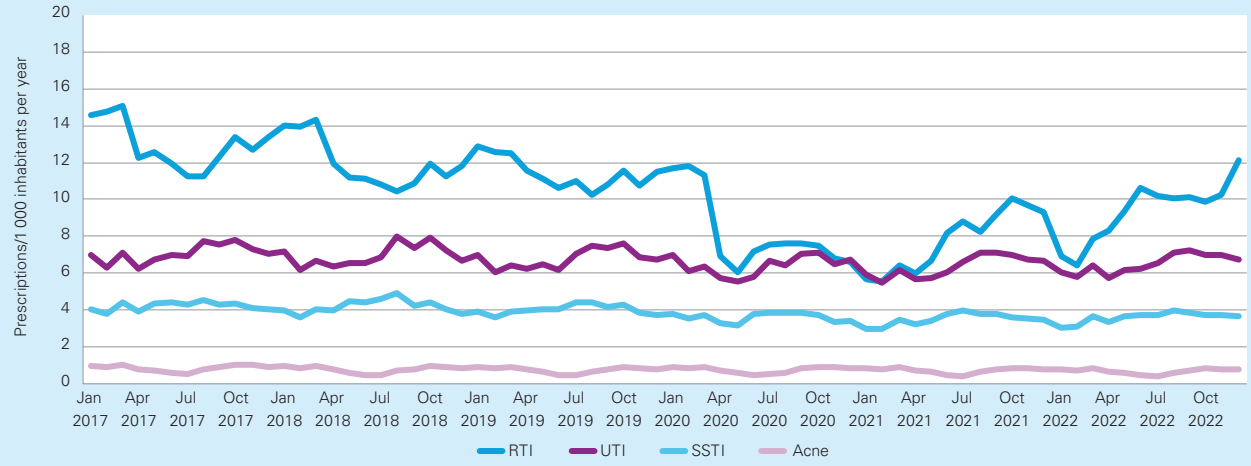
Results

- Starting from the second quarter of 2022, sales of antibiotics commonly used to treat respiratory tract infections (RTIs) increased and peaked in December. Sales of antibiotics commonly used to treat urinary tract infections (UTIs), skin and soft tissue infections (SSTIs) and acne remained relatively stable and followed the expected periodic fluctuations during 2021-2022, Figure 1.7.
- Overall sales of antibiotics commonly prescribed against RTIs increased by 18.9% in 2022 compared to 2021.
- At the national level, the number of prescriptions per 1 000 inhabitants for RTIs varied between 132 in Skåne region to 80 in Västerbotten region in 2022, Figure 1.8.

Comments

The effect of the decrease in sales due to the COVID-19 pandemic, primarily observed for antibiotics commonly used to treat RTIs and to a smaller degree UTIs, diminished during 2022. The pandemic had a small or negligible effect on antibiotics sales commonly used for SSTIs and acne. For all regions, the majority of antibiotic prescriptions during 2022 were for antibiotics commonly used to treat RTIs.

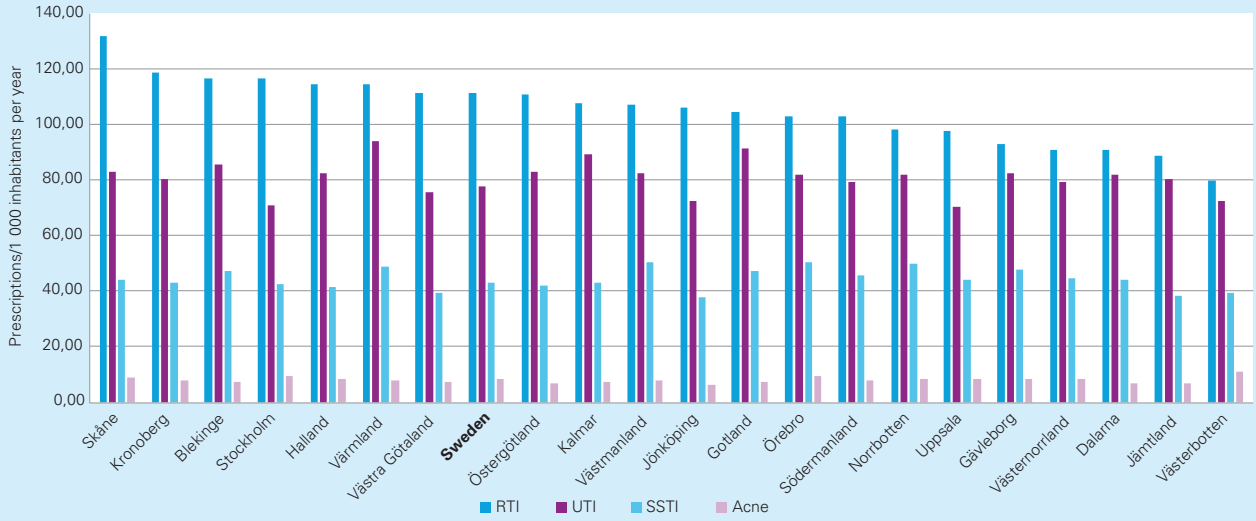
Figure 1.7. Sales of antibiotics commonly used to treat respiratory tract infections (RTI), urinary tract infections (UTI), skin and soft tissue infections (SSTI) and acne vulgaris in outpatient care from 2017 to 2022, by month[a].



[a]RTI:doxycycline (J01AA02); excluding packages larger than 50 tablets, penicillin V (J01CE02), amoxicillin (J01CA04), amoxicillin with enzyme inhibitor (J01CA08), cephalosporins (J01DB-DE) and macrolides (J01FA); UTI: pivmecillinam (J01CA08), trimethoprim (J01EA01), ciprofloxacin (J01MA02), norfloxacin (J01MA06) until 2020 and nitrofurantoin (J01XE01); SSTI: clindamycin (J01FF01) and flucloxacillin (J01CF05); acne vulgaris: doxycycline (J01AA02; packages over 50 tablets), lymecycline (J01AA04), oxytetracycline (J01AA06) and tetracycline (J01AA07).

Source: The Public Health Agency of Sweden

Figure 1.8. Sales of antibiotics commonly used to treat respiratory tract infections (RTI), urinary tract infections (UTI), skin and soft tissue infections (SSTI) and acne vulgaris in outpatient care 2022, by region[a].



[a]RTI:doxycycline (J01AA02); excluding packages larger than 50 tablets), penicillin V (J01CE02), amoxicillin (J01CA04), amoxicillin with enzyme inhibitor (J01CA08), cephalosporins (J01DB-DE, excl ceftibuten J01DD14) and macrolides (J01FA); UTI: pivmecillinam (J01CA08), trimethoprim (J01EA01), ciprofloxacin (J01MA02), norfloxacin (J01MA06) until 2020 and nitrofurantoin (J01XE01); SSTI: clindamycin (J01FF01) and flucloxacillin (J01CF05); acne vulgaris: doxycycline (J01AA02; packages over 50 tablets), lymecycline (J01AA04), oxytetracycline (J01AA06) and tetracycline (J01AA07).

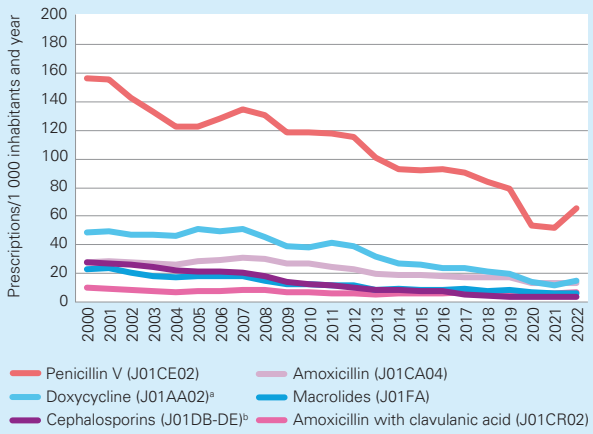
Source: The Public Health Agency of Sweden

Respiratory tract infections (RTIs)

Results

- Beta-lactamase sensitive penicillins (J01CE) were the most frequently prescribed antibiotics in outpatient care in 2022, and increased by 25.9% compared to 2021, Figure 1.9.
- The greatest relative increases in 2022 were observed for doxycycline (J01AA02) and amoxicillin with clavulanic acid (J01CR02), 24.9% and 19.0% respectively compared to 2021, Figure 1.9.
- Sales of antibiotics commonly used to treat RTIs increased the most for children aged 0-6 years, with a 35.6% increase in sales during the fourth quarter of 2022 compared to 2021, approaching pre-pandemic levels, Figure 1.10.

Figure 1.9. Sales of antibiotics commonly used to treat respiratory tract infections in outpatient care between 2000 and 2022.



[a]Doxycycline (J01AA02) excl. packages with more than 50 tablets.
[b]Ceftibuten (J01DD14) excluded.

Source: The Public Health Agency of Sweden

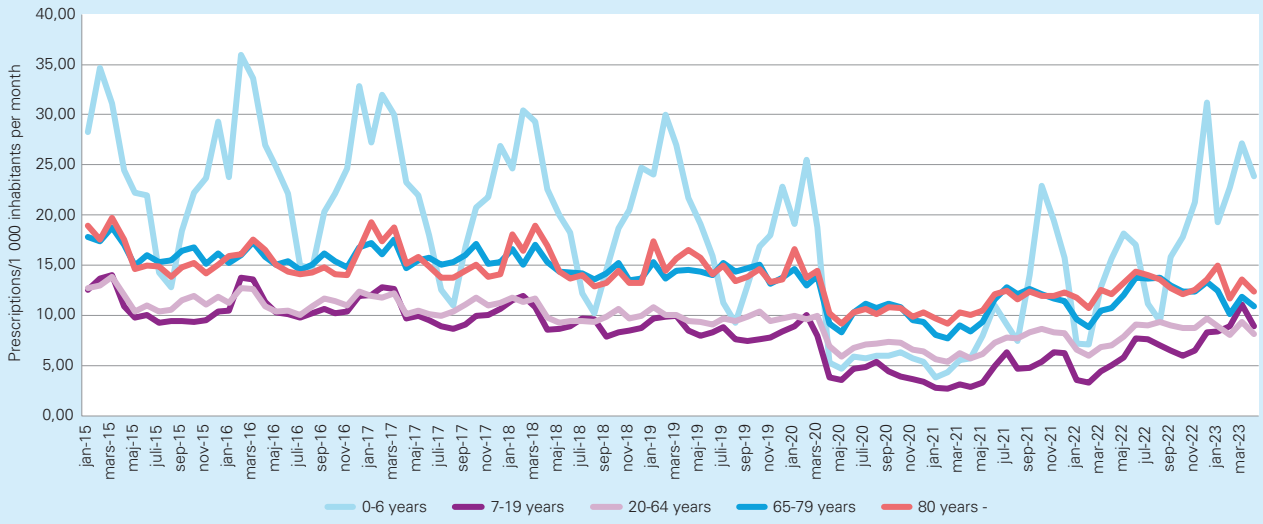
Comments

The recommended first-line treatment for lower RTIs in Sweden is penicillin V (J01CE02) (Medical Products Agency, 2008). In 2022, the sales of antibiotics commonly used to treat RTIs were higher than in 2021 but the total sales did not reach pre-pandemic levels. Trend analysis based on data since the 2000s showed a significant decrease ($p < 0.001$) in the sales of all RTI antibiotics in the recent years, except for amoxicillin with enzyme inhibitor (J01CR02), for which trend analysis showed a marginal increase since 2018.

Shortages of specific antibiotics may impact the patterns of antibiotic sales, possibly resulting in prescription of broader spectrum antibiotics. Especially oral solutions commonly prescribed to children have been particularly exposed to shortages. In 2022, shortages were observed for erythromycin and amoxicillin in Sweden.

Starting from the second quarter of 2022, the sales of antibiotics commonly used to treat RTIs increased and peaked at the end of the year. The increasing number of respiratory infections in society in general during this period likely contributes to this increase. This peak in sales of antibiotics commonly prescribed against RTIs was largely driven by an increase in prescription to children aged 0-6 years. A clear disruption in seasonal patterns can be observed, especially for children, following the COVID-19 pandemic, continuing into the first quarter of 2023.

Figure 1.10. Sales of antibiotics commonly used to treat respiratory tract infections[a] in outpatient care from 2015 to March 2023, per month.



[a]Includes doxycycline (J01AA02), penicillin V (J01CE02), amoxicillin (J01CA04), amoxicillin with enzyme inhibitor (J01CA08), cephalosporins (J01DB-DE) and macrolides (J01FA).

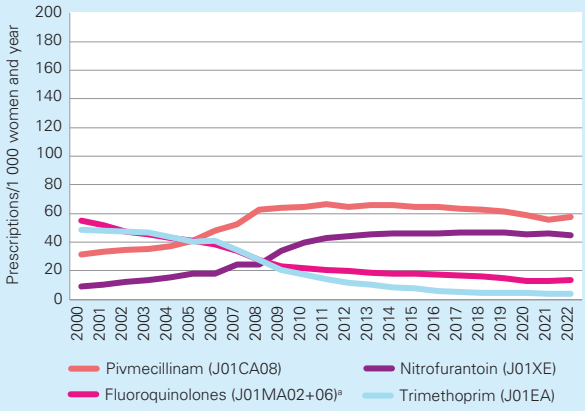
Source: The Public Health Agency of Sweden

Urinary tract infections (UTIs)

Results

- Total sales of antibiotics commonly used to treat UTIs increased by 1.0% in 2022 among women aged 15-79. Sales of nitrofurantoin (J01XE) and trimethoprim (J01EA) decreased by 1.6% and 7.1%, respectively, whereas pivmecillinam (J01CA08) and ciprofloxacin increased by 3.1% and 4.2%, respectively, Figure 1.11.
- In men aged 65 or older, the sales of antibiotics commonly used to treat UTIs increased by 5.4% in 2022 compared to 2021. The greatest relative change was observed for nitrofurantoin (J01XE01), which increased by 9.6%, and for trimethoprim with sulphonamides (J01EE), which increased by 9.4%, Figure 1.12.
- At the national level, 11.3% of the antibiotics commonly prescribed for UTIs in women aged 15-79 consisted of ciprofloxacin in 2022. This proportion ranged from 7.9% in Jönköping region to 14.5% in Västernorrland region, Figure 1.13.

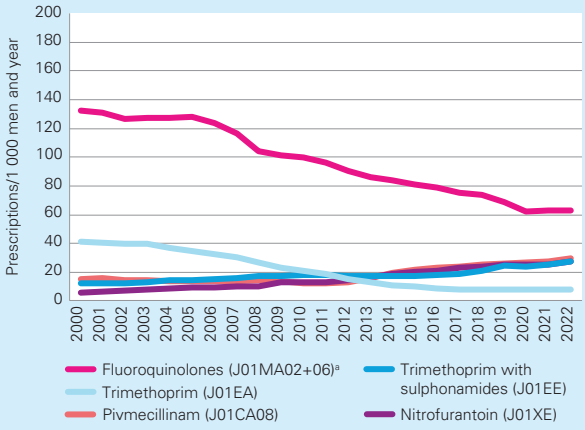
Figure 1.11. Sales of antibiotics commonly used to treat urinary tract infections in women aged 15-79 years in outpatient care between 2000 and 2022.



aFrom 2021, only ciprofloxacin (J01MA02) is represented in the group fluroquinolones.

Source: The Public Health Agency of Sweden

Figure 1.12. Sales of antibiotics commonly used to treat urinary tract infections in men aged 65 years or older in outpatient care between 2000 and 2022.



aFrom 2021, only ciprofloxacin (J01MA02) is represented in the group fluroquinolones.

Source: The Public Health Agency of Sweden

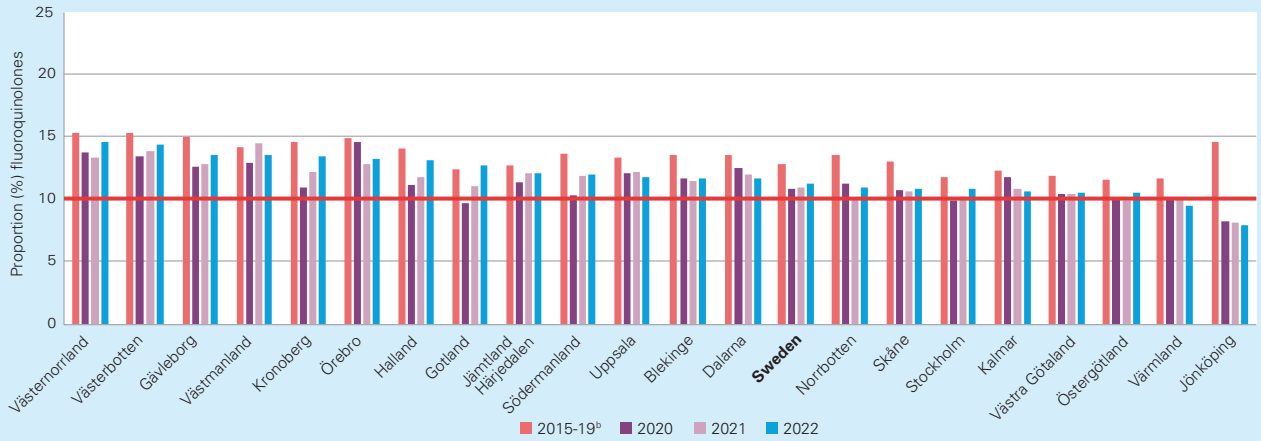
Comments

According to national treatment recommendations, pivmecillinam and nitrofurantoin are first-line treatments for UTIs in women aged 15 or older and in men with afebrile symptomatic UTIs (Medical Products Agency, 2017).

In line with treatment recommendations, 86% of the UTI antibiotics sold to women aged 15-79 in 2022 consisted of these two antibiotics. In men aged 65 or older, fluoroquinolones made up 40% of the UTI antibiotics in 2022, but trend analysis indicates decreasing sales of fluoroquinolones and increasing sales of pivmecillinam and nitrofurantoin in this population since the mid-2000s. Note that since 2021, norfloxacin (J01MA06) has been removed from the market and only ciprofloxacin (J01MA02) is included among the fluoroquinolones.

Strama has proposed a number of quality indicators in outpatient care, including that a maximum of 10% of antibiotics prescribed to treat UTIs in women aged 18-79 years consist of fluoroquinolones (Strama, 2016). This target was achieved by 2 out of 21 regions in 2022, a decrease compared to 2021.

Figure 1.13. Proportion of fluoroquinolones (ciprofloxacin, J01MA02; norfloxacin, J01MA06, until 2020) among antibiotics commonly used to treat urinary tract infections[a] in women aged 18-79 years in outpatient care from 2015 to 2022, by region.



aPivmecillinam (J01CA08), trimethoprim (J01EA01), ciprofloxacin (J01MA02), norfloxacin (J01MA06) until 2020 and nitrofurantoin (J01XE01).
bAverage proportion is presented for the time period 2015-19. The red line indicates Strama's target of maximum 10% fluoroquinolones.

Source: The Public Health Agency of Sweden

Age and gender comparisons

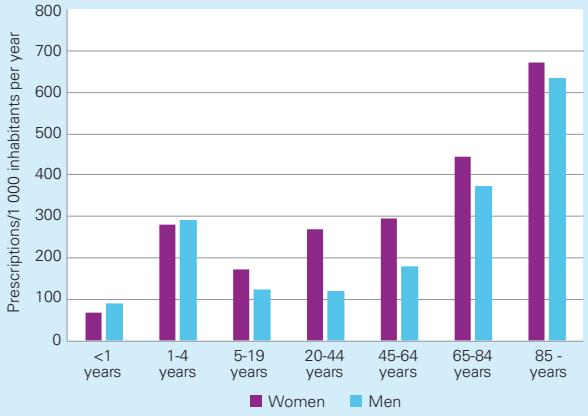
Results

- The rate of antibiotic prescriptions in outpatient care increased during 2022 but followed the same pattern as during 2021 i.e. the highest prescription rates were observed for people aged 85 years or older; 671 prescriptions per 1 000 inhabitants in women and 635 prescriptions per 1 000 inhabitants in men in 2022, Figure 1.14. 61% of all antibiotic prescriptions during 2022 were issued to women, the same as the year before.
- The most frequently prescribed antibiotics to children aged 0-4 were antibiotics commonly used to treat RTIs, representing 83% of the total antibiotic sales in this age group. RTI antibiotics were prescribed more to women than to men, except the youngest and oldest age groups, Figure 1.15.
- Antibiotics commonly used to treat UTIs are mostly prescribed to women, and the prescription rate increases with age, Figure 1.16.
- Sales of antibiotics commonly used to treat SSTIs were highest for the oldest age groups, and prescriptions to men exceed those to women in these age groups, Figure 1.17.
- Antibiotics commonly used to treat acne are mainly used in the age groups 5-44 years and predominately by women, Figure 1.18. In the age group 20-44, most of the prescriptions are found among 20-29 year-olds (data not shown).

Comments

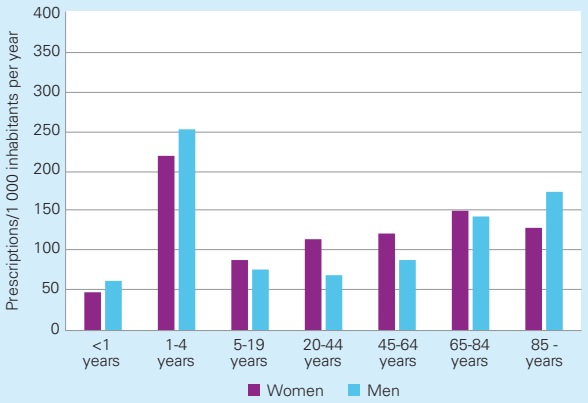
Concerning antibiotics commonly used to treat SSTIs and acne or similar skin conditions, older patients are more often prescribed longer treatments, which impacts the amount of antibiotics used. In general, comparisons across age groups show that antibiotics are used more in the older age groups. As mentioned in the *Guidance for readers*, some of the antibiotics used among the elderly population are not included in the outpatient care statistics as some medicines are sold on requisition and included in hospital care statistics. Therefore a possible underestimation in the oldest age groups cannot be ruled out.

Figure 1.14. Sales of antibiotics (J01 excl. methenamine) in outpatient care in 2022, by age and gender.



Source: The Public Health Agency of Sweden

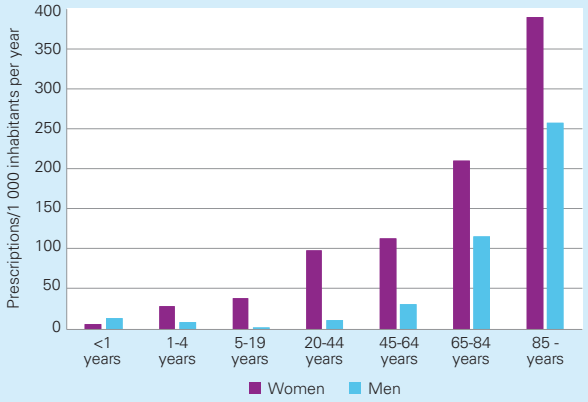
Figure 1.15. Sales of antibiotics commonly used to treat respiratory tract infections (RTIs)[a] in outpatient care in 2022, by age and gender.



[a]Doxycycline (J01AA02; excluding packages larger than 50 tablets), penicillin V (J01CE02), amoxicillin (J01CA04), amoxicillin with enzyme inhibitor (J01CR02), cephalosporins (J01DB-DE; excluding ceftibuten) and macrolides (J01FA).

Source: The Public Health Agency of Sweden

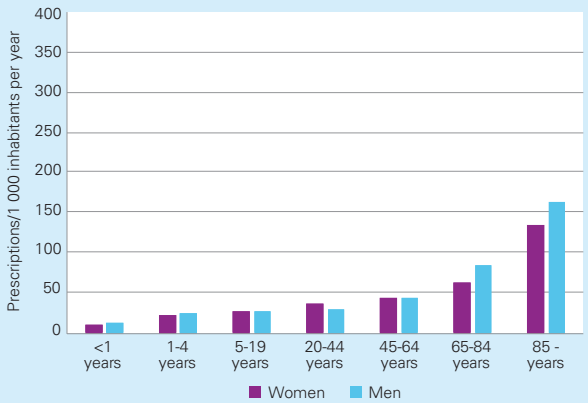
Figure 1.16. Sales of antibiotics commonly used to treat urinary tract infections[a] in outpatient care in 2022, by age and gender.



[a]Pivmecillinam (J01CA08), trimethoprim (J01EA01), ciprofloxacin (J01MA02), norfloxacin (J01MA06) until 2022 and nitrofurantoin (J01XE01).

Source: The Public Health Agency of Sweden

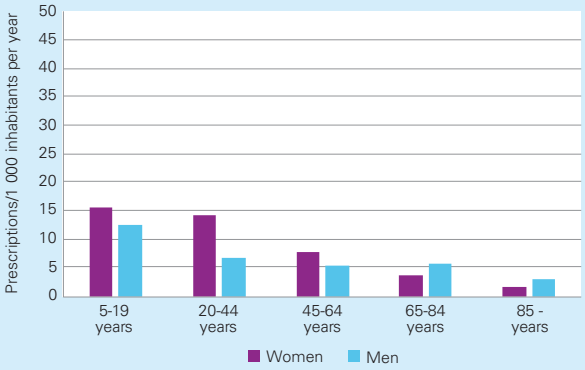
Figure 1.17. Sales of antibiotics commonly used to treat skin and soft tissue infections[a] in outpatient care in 2022, by age and gender.



[a]Clindamycin (J01FF01) and flucloxacillin (J01CF05).

Source: The Public Health Agency of Sweden

Figure 1.18. Sales of antibiotics commonly used to treat acne vulgaris[a] in outpatient care in 2022, by age and gender.



[a]Doxycycline (J01AA02); packages over 50 tablets, lymecycline (J01AA04), oxytetracycline (J01AA07) and tetracycline (J01AA07).

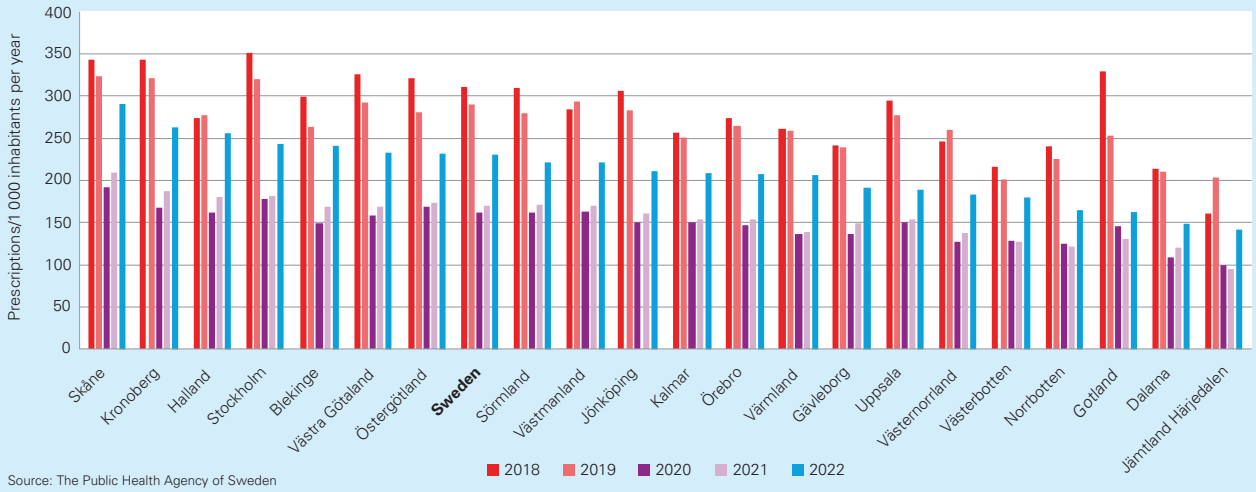
Source: The Public Health Agency of Sweden

Antibiotic sales in children

Results

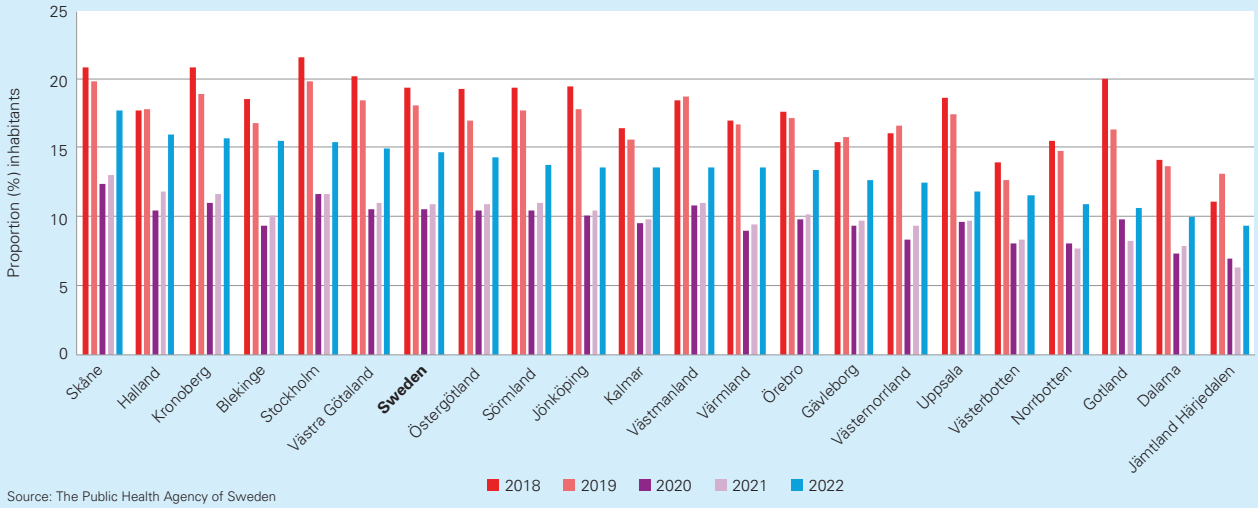
- Sales of antibiotics for children aged 0-6 years were 35.6% higher in 2022 than in 2021.
- The sales of antibiotics for children aged 0-6 years increased in all 21 regions in Sweden. There were large variations between regions, from 290 prescriptions per 1 000 children in Skåne region to 141 in Jämtland Härjedalen region in 2022, Figure 1.19.
- The most sold antibiotics for children aged 0-6 years were beta-lactamase sensitive penicillins (J01CE), which constituted 58% of the sales measured as prescriptions/1 000 inhabitants (data not shown).
- The proportion of children aged 0-6 years treated with at least one course of antibiotics increased in 2022 compared to 2021 and was estimated to 15%, Figure 1.20.

Figure 1.19. Sales of antibiotics (J01 excl. methenamine) to children aged 0-6 years in outpatient care between 2018 and 2022, by region.



Source: The Public Health Agency of Sweden

Figure 1.20. Proportion (%) of children aged 0-6 years treated with at least one course of antibiotics (J01 excl. methenamine) in outpatient care between 2018 and 2022, by region.



Source: The Public Health Agency of Sweden

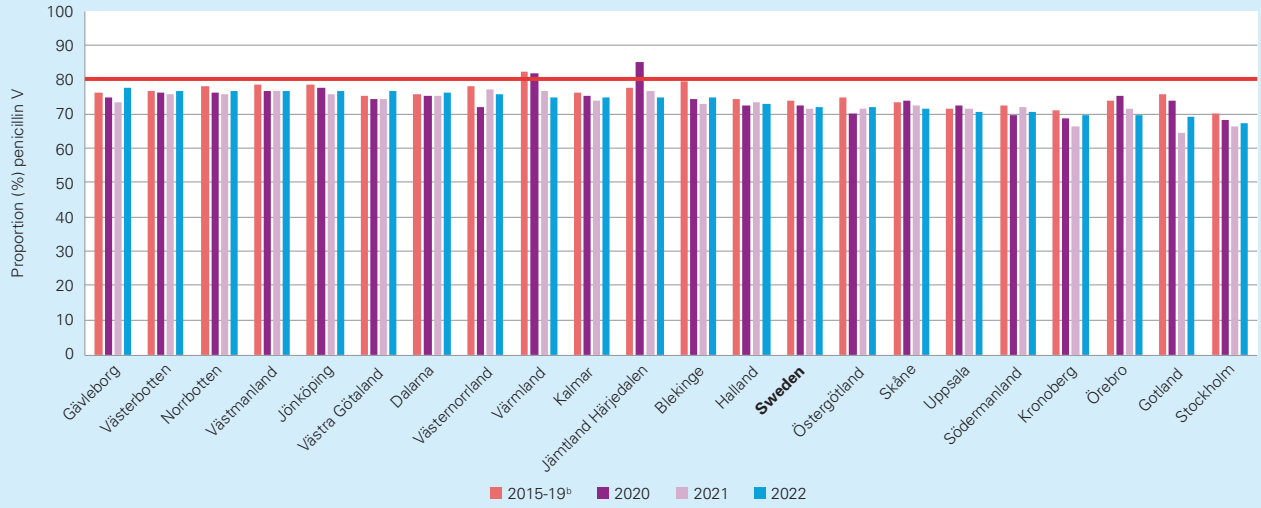
- At the national level, 72% of antibiotics commonly used to treat RTIs in children aged 0-6 consisted of penicillin V. This proportion ranged from 67% in Stockholm region to 78% in Gävleborg region, Figure 1.21.

Comments

While sales of antibiotics to children aged 0-6 years have increased in all of the regions in Sweden during 2022 compared to 2021, the prescriptions rates are well below the levels observed prior to the COVID-19 pandemic.

According to Strama's proposed quality indicator for outpatient care, at least 80% of antibiotics prescribed for RTIs in children aged 0-6 years should consist of penicillin V (Strama, 2016). To calculate this indicator, the following antibiotics are included in the denominator: amoxicillin (J01CA04), penicillin V (J01CE02), amoxicillin with clavulanic acid (J01CR02), cephalosporins (J01DB-DE excl. ceftibuten J01DD14) and macrolides (J01FA). In 2022, none of the 21 regions achieved this target.

Figure 1.21. Proportion (%) penicillin V (J01CE02) of antibiotics commonly used to treat respiratory tract infections[a] in children aged 0-6 years in outpatient care between 2015 and 2022, by region.



[a]Doxycycline (J01AA02; excluding packages larger than 50 tablets), penicillin (J01CE02), amoxicillin (J01CA04), amoxicillin with enzyme inhibitor (J01CR02), cephalosporins (J01DB-DE; excluding ceftibuten) and macrolides (J01FA). b Average proportion is presented for the time period 2015-2019. The red line indicates Strama's target of at least 80% penicillin V.

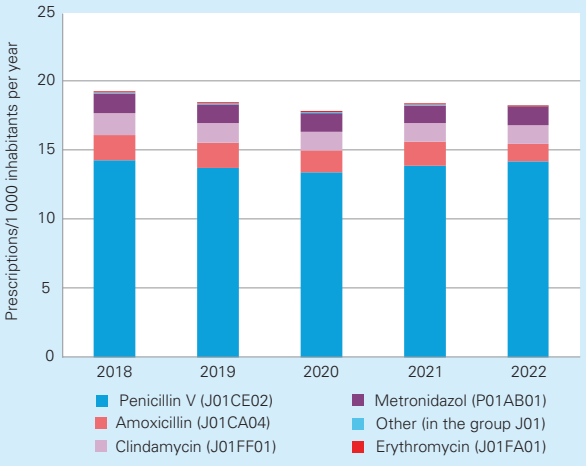
Source: The Public Health Agency of Sweden

Antibiotics in dentistry

Results

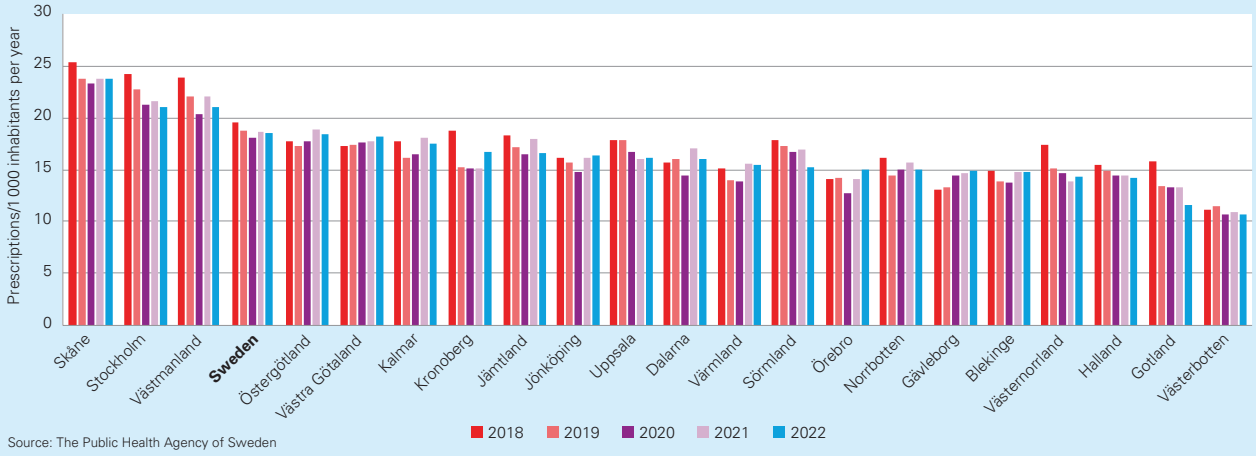
- Dentists accounted for 6.6% of all systemic antibiotics (J01 excl. methenamine) prescribed in Sweden in 2022, a decrease from 7.1% in 2021.
- Antibiotics (J01 excl. methenamine; metronidazole P01AB01) prescribed by dentists in 2022 was estimated to 18.5 prescriptions per 1 000 inhabitants, a decrease by 0.8% compared to the year before, Figure 1.22.
- The most commonly prescribed antibiotic by dentists was penicillin V (76.4% of total sales), Figure 1.22. Compared to 2021, the sales of clindamycin and penicillin V increased by 2.2% and 2.0%, respectively, whereas the sales of other antibiotics decreased.

Figure 1.22. Antibiotics prescribed by dentists in outpatient care between 2018 and 2022.



Source: The Public Health Agency of Sweden

Figure 1.23. Antibiotics (J01 incl. methenamine; metronidazole P01AB01) prescribed by dentists in outpatient care between 2018 and 2022, by region.



Source: The Public Health Agency of Sweden

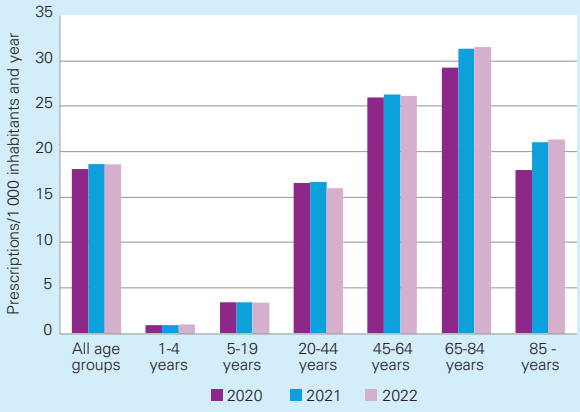
- Sales of antibiotics decreased in 13 of 21 regions during 2022. There were notable regional differences; dentists in Skåne region issued 23.8 prescriptions per 1 000 inhabitants, more than double that of dentists in Västerbotten region (10.6 prescriptions per 1 000 inhabitants), Figure 1.23.
- Prescriptions increased the most for patients aged 1-4 years (7.6%) and decreased 4.0% for patients aged 20-44 years. Most antibiotics were prescribed to those aged 65-84 years, followed by the age group 45-64 years, Figure 1.24.

Comments

The decline in antibiotic prescriptions observed in 2020 may have been the result of fewer dental care visits, especially among the elderly (National Board of Health and Welfare, 2022a). Following this decrease in antibiotic prescribing by dentists, prescription levels appear to have returned to a pre-pandemic level and stabilised during 2021 and 2022 with smaller changes observed, despite a continued reduction dental care visits in 2021 (National Board of Health and Welfare, 2022). This effect of the pandemic was most apparent in antibiotic prescriptions for the two oldest age groups. However, for patients older than 85 years of age, antibiotic prescribing by dentists remained higher than levels observed in 2019. Prescriptions to patients below the age of 1 are not shown, as no antibiotics were prescribed to patients in this age group during 2022.

Penicillin V was the most commonly prescribed antibiotic by dentists and made up 76.4% of the total sales, which is in line with treatment recommendations (Medical Products Agency, 2014). Metronidazole is also recommended as first-line treatment in combination with or without penicillin V to attain a broader anaerobic spectrum and is therefore included in the measure of sales. The low levels of erythromycin prescription continue to decrease. Shortages were observed for both erythromycin and amoxicillin in Sweden during 2022.

Figure 1.24. Antibiotics (J01 incl. methenamine; metronidazole P01AB01) prescribed by dentists in outpatient care between 2020 and 2022, by age group.



Source: The Public Health Agency of Sweden

Antibiotics in hospital care

Data in this section include sales to all Swedish hospitals, some but not all nursing homes, and other institutions within health- and social care that procure antibiotics for dispensing to patients or residents. Out of the total sales in hospital care, the proportion of antibiotics dispensed to acute care hospitals varies from region to region. Some challenges associated with this procurement data are further described in *Guidance to readers*. Due to regulations regarding confidentiality of sales data, detailed data for certain substances and groups cannot be shown.

To present statistics on antibiotic consumption in acute care hospitals only, data have been requested directly from Strama pharmacists in the regions and are presented under the subsection *Antibiotic sales in acute care hospitals*. Not all acute care hospitals are included. For this publication, proportions of antibiotic consumption in acute care hospitals are shown.

Antibiotic sales in hospitals and other health- and social care facilities

Results

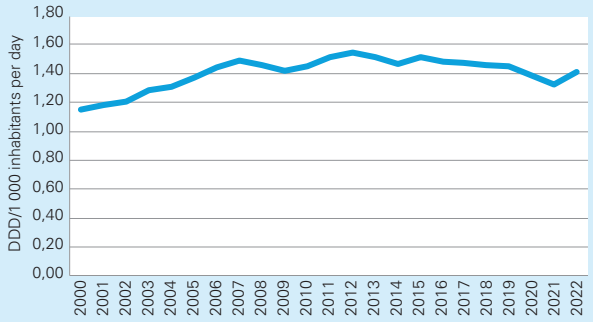
- Total sales of antibiotics (J01 excl. methenamine) to hospitals and other health- and social care facilities were 1.4 DDD/1 000 inhabitants per day in 2022, a 6.7% increase compared to 2021, Figure 1.25.

Comments

The increase in antibiotic sales to hospitals and other health- and social care facilities observed in 2022 could be due in part to effects of the COVID-19 pandemic during 2020 and 2021. Substances such as penicillins (J01CE and J01CF) are often used as prophylaxis (Skoog et al., 2016) and a decreased number of surgeries during the COVID-19 pandemic may have reduced the use of these substances (National Board of Health and Welfare, 2021). However, a similar decrease in sales to hospitals and other health- and social care facilities during 2020 and 2021 was not observed for all antibiotics. For example, sales of combinations of penicillins (J01CR), specifically piperacillin-tazobactam, increased steadily through the years 2018-2022 (data not shown).

Since 2021, hospitals have started to prescribe cefiderocol (J01DI04). As there is currently no DDD assigned to this antibiotic, the use of cefiderocol is not included in the figures and tables displayed in this report. Based on the number of packages sold and a self-assigned DDD of 6 grams, the use of cefiderocol did not have any impact on the estimates in this report.

Figure 1.25. Sales of antibiotics (J01 excl. methenamine) to hospitals and other health- and social care facilities between 2000 and 2022.



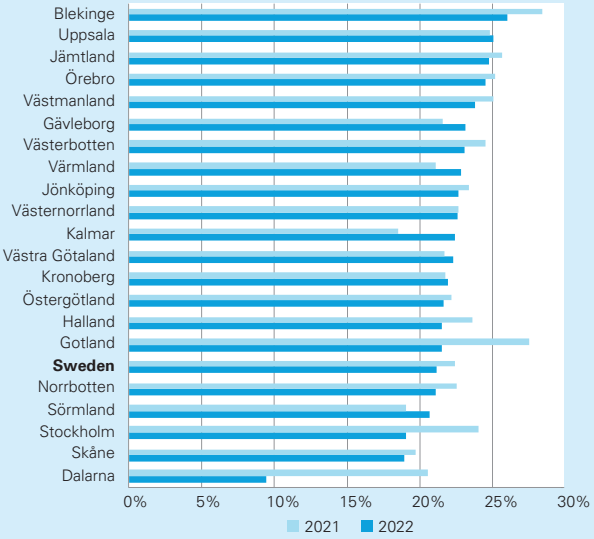
Source: The Public Health Agency of Sweden

Antibiotic sales in acute care hospitals

Results

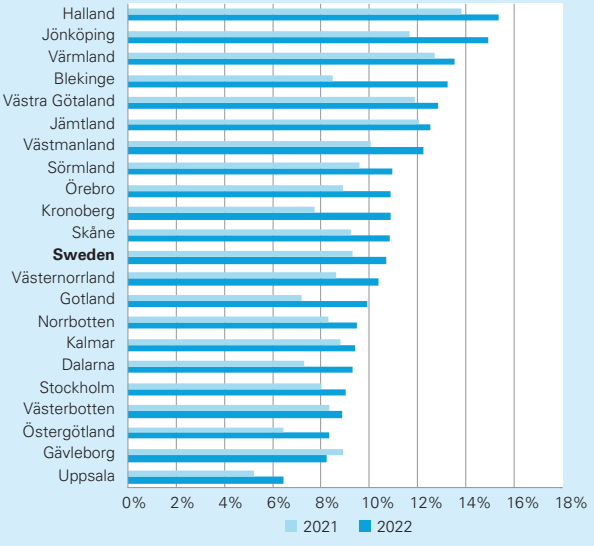
- Beta-lactamase resistant penicillins (J01CF) are the most commonly prescribed antibiotics in Swedish acute care hospitals, making up 23% of the sales, Figure 1.26.
- The proportion of beta-lactamase sensitive antibiotics (penicillin V and G J01CE01-02) sold during 2022 increased in 20 of 21 regions compared to 2021, Figure 1.27.
- Broad-spectrum antibiotics (cephalosporins J01DB-DE, carbapenems J01DH, fluoroquinolones J01MA, and piperacillin-tazobactam J01CR05) made up 36% of antibiotic sales to acute care hospitals in 2022 – a negligable difference compared to 2021 (36%). The proportions ranged from 29% in Jönköping region to 46% in Dalarna region, Figure 1.28.
- Notable regional variations were also observed for the individual classes of broad-spectrum antibiotics; 4% to 15% for cephalosporins, 5% to 14% for fluoroquinolones, 8% to 14% for piperacillin-tazobactam, and 2% to 5% for carbapenems, Figure 1.28.
- The proportion of piperacillin-tazobactam (J01CR05) sold during 2022 decreased in 13 of 21 regions compared to 2021, Figure 1.29.

Figure 1.26. Proportion (%) of beta-lactamase resistant penicillins (J01CF) out of all antibiotics sold to Swedish acute care hospitals in 2021 and 2022, by region.



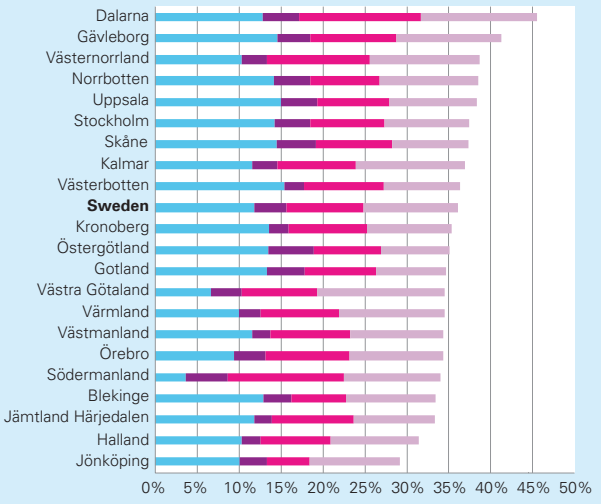
Source: The Public Health Agency of Sweden

Figure 1.27. Proportion (%) of beta-lactamase sensitive penicillins (penicillin V and G, J01CE01-02) out of all antibiotics sold to Swedish acute care hospitals in 2021 and 2022, by region.



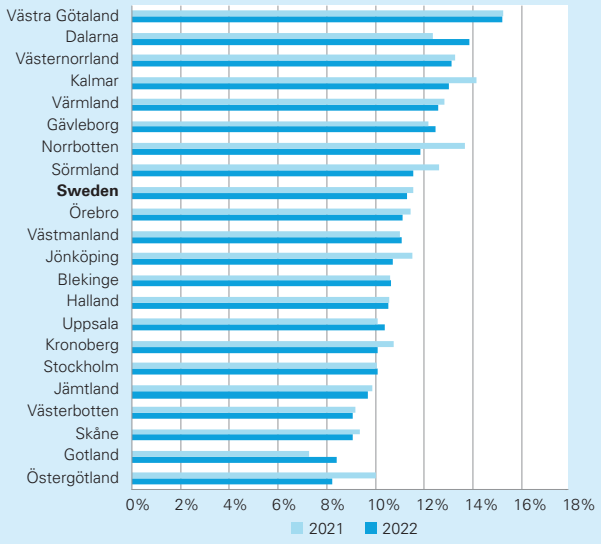
Source: The Public Health Agency of Sweden

Figure 1.28. Proportion (%) of selected broad-spectrum antibiotics out of all antibiotics sold to Swedish acute care hospitals in 2022, by region.



Source: The Public Health Agency of Sweden

Figure 1.29. Proportion (%) of piperacillin-tazobactam (J01CR05) out of all antibiotics sold to Swedish acute care hospitals in 2021 and 2022, by region.



Source: The Public Health Agency of Sweden

Comments

The main antibiotic classes used in acute care hospitals are beta-lactamase resistant penicillins (J01CF), penicillin combinations (J01CR, primarily piperacillin-tazobactam), cephalosporins (J01DB-DE), beta-lactamase sensitive penicillins (J01CE), and fluoroquinolones (J01MA). Accounting for hospital activity (admissions and patient days), the consumption of piperacillin-tazobactam and carbapenems has increased during the past five years despite the COVID-19 pandemic. Notably, despite a steady increase in sales to acute care hospitals, the proportion of piperacillin-tazobactam sales has decreased in a majority of regions over the past year.

There are substantial regional variations in the proportion and distribution of the different antibiotic classes in sales of antibiotics to Swedish acute care hospitals, Figures 1.27-1.30. These differences can be partially attributed to the type of hospitals, case mix and patient demographics in the region, and these factors should be taken into account when comparisons are made. For example, the regions Uppsala, Stockholm, Västerbotten, Västra Götaland, Skåne, Östergötland and Örebro all have tertiary referral hospitals with more advanced care, which affects the amount and type of antibiotics used.

Adverse reactions related to antibiotic use

Reported drug-related adverse reactions are continuously entered into BiSi, a national database administered by the Swedish Medical Products Agency. The reports originate both from healthcare professionals and patients. Adverse reactions related to antibiotics between 2017 and 2022 were analysed for various classes of agents.

There were 2 937 reports of side effects caused by the use of antibiotics during this period. The following organ system groups received most reports related to the use of systemic antibiotic drugs: skin- and subcutaneous tissue disorders (n=1,265), gastrointestinal disorders (n=703), nervous system disorders (n=419), general disorders (n=416), respiratory disorders (n=205), musculoskeletal disorders (n=202), investigations (n=135), immune system disorders (n=132), hepatobiliary disorders (n=129), renal and urinary disorders (n=123), psychiatric disorders (n=100), infections and infestations (n=90) and reproductive system and breast disorders (n=88). The majority of the reports (65%) concern female patients, which corresponds to the gender difference seen in sales of antibiotics. The ten antibiotic substances most commonly associated with adverse reactions in the last six years, unadjusted for sold substances and regardless of the cause of the report, are presented in Table 1.1.

Table 1.1. Substances most commonly associated with adverse reactions reported to the Swedish Medical Products Agency 2017-2022.

Antibiotic	Total number of adverse drug reaction reports 2017-2022	Number of 'serious' reports	Number of fatal cases
Penicillin V (J01CE02)	375	108	0
Flucloxacillin (J01CF05)	278	141	4
Ciprofloxacin (J01MA02)	269	181	6
Nitrofurantoin (J01XE01)	232	81	2
Clindamycin (J01FF01)	217	89	4
Trimethoprim and sulphamethoxazole (J01EE01)	222	138	3
Amoxicillin (J01CA04)	147	61	0
Doxycycline (J01AA02)	126	32	0
Piperacillin-tazobactam (J01CR05)	107	63	2
Metronidazole (P01AB01)	83	42	0

Swedish antibiotic prescribing according to the WHO AWaRe classification

WHO AWaRe classification

The World Health Organization (WHO) introduced the AWaRe Classification of Antibiotics in 2017 as a tool to support antibiotic stewardship efforts locally and globally. Since then, it has been updated twice, most recently in 2021.

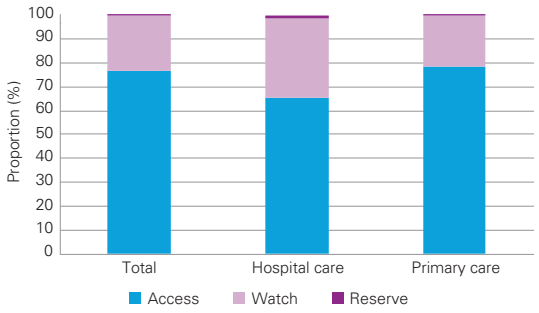
AWaRe classifies antibiotics into three groups based on their impact on antibiotic resistance, i.e. Access, Watch and Reserve. The Access group includes first- and second-line treatments for common infections, and should be made widely accessible. The Watch group consists of broad-spectrum antibiotics that are used for specific, limited indications. This group includes most of the "highest priority" antibiotics on the WHO list of critically important antimicrobials for human medicine and veterinary use. Finally, the Reserve group includes last-resort antibiotics that should only be used for life-threatening infections caused by multi-drug resistant bacteria when other treatments have failed (WHO 2021).

Watch and Reserve group antibiotics are recommended as targets for monitoring and stewardship programs, and the overall goal is to reduce their use. According to a target set by the WHO, at least 60% of all antibiotics consumed in each country should belong to the Access group by 2023. There are no separate targets for consumption in hospital and primary care based on the AWaRe classification.

Consumption of Access, Watch, and Reserve antibiotics in Sweden from 2000-2022

Based on data from electronic prescribing (primary care) and requisitions (hospital care), 76.9% of antibiotics sold in 2022 were Access antibiotics according to the most recent version of the AWaRe classification. Watch group antibiotics made up 22.9% of all antibiotics sold, and the remaining 0.26% consisted of Reserve group antibiotics. As expected, the proportion of Watch antibiotics was higher in hospitals than in primary care, i.e. 33.7% versus 21.1% (Figure 1). Most Reserve antibiotics were sold to hospitals, but a small proportion was also prescribed in primary care and consisted mainly of parenteral colistin, linezolid, aztreonam and daptomycin. The sector classified as "hospital care" also includes antibiotics supplied to other care providers than hospitals, such as some elderly homes and dental care. Thus, it is reasonable to assume that the proportions of Watch and Reserve antibiotics used in hospitals may be higher in reality than the estimates presented here. In addition, due to the inability to include certain antibiotics prescribed on license (see Methods section), it is reasonable to assume that the overall proportions of prescription for these antibiotics may be somewhat underestimated.

Figure 1. Relative consumption of Access, Watch and Reserve antibiotics in Sweden in 2022, total and divided by healthcare sector.



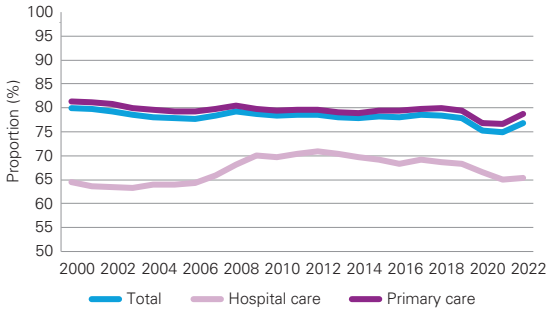
Source: the Public Health Agency of Sweden

Over the last 20 years, the proportion of Access antibiotics has stayed stable between 77-80%, but a drop was observed during 2020 and 2021 in both primary and hospital care as an effect of the COVID-19 pandemic (Figure 2a). Simultaneously, the proportion of Watch antibiotics increased, while the prescribing of Reserve antibiotics has gradually increased since the early 2000s (Figures 2b and 2c). Therefore, while the total consumption of antibiotics decreased during the COVID-19 pandemic, there seems to have been a shift towards broader spectrum antibiotics. In 2022, as the effects of the COVID-19 pandemic gradually receded, there was an increase in the proportion of Access antibiotics prescribed, as well as a decrease in the proportion of Watch and, to a degree, Reserve antibiotic prescription. Notably, only a marginal decrease was observed for the proportion of Watch antibiotics prescribed in hospital care, and prescription proportions overall have not completely returned to levels observed before the pandemic. Further analysis over the following years is required to fully observe the effects of the COVID-19 pandemic on antibiotic prescribing according the AWaRe classification.

A breakdown of antibiotic prescription according to the AWaRe classification system is published in the annual ESAC-Net report of Antimicrobial consumption in the EU/EEA (ECDC 2022). However, a direct comparison between the data presented here and the data shown in the ESAC-Net annual report is not appropriate due to potential differences in methods of DDD calculation and the difficulty including some antibiotics sold on license in this report, described above. Generally, the proportion of prescription of Access antibiotics in Sweden is above the mean proportion observed in the EU/EEA in 2021 (60.7%).

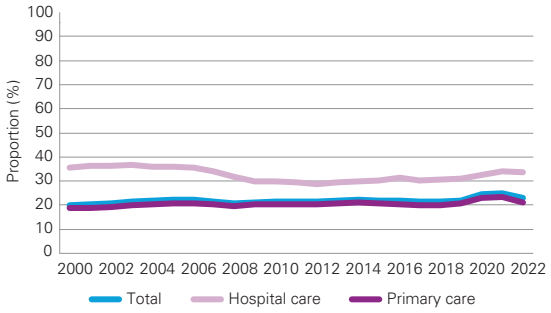
In conclusion, Sweden exceeds the WHO minimum target for Access antibiotics of 60%. Although the consumption of Reserve group antibiotics seems to be low, the increased prescribing of these substances, especially in primary care, merits further review.

Figure 2A. Relative consumption of Access antibiotics in Sweden between 2000-2022, total and divided by healthcare sector.



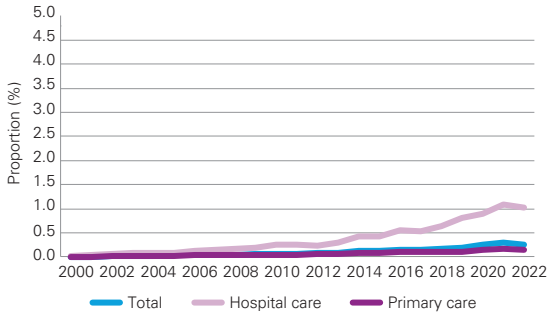
Source: the Public Health Agency of Sweden

Figure 2B. Relative consumption of Watch antibiotics in Sweden between 2000-2022, total and divided by healthcare sector.



Source: the Public Health Agency of Sweden

Figure 2C. Relative consumption of Reserve antibiotics in Sweden between 2000-2022, total and divided by healthcare sector.



Source: the Public Health Agency of Sweden

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WHO 2021 AWaRe classification. World Health Organization: Geneva, 2021. https://www.who.int/publications/i/item/2021-aware-classification

ECDC (European Centre for Disease Prevention and Control). Antimicrobial consumption in the EU/EEA (ESAC-Net) - Annual Epidemiological Report 2021. Stockholm: ECDC; 2022

Antibiotics in digital health

In this report, the digital health concept refers to medical consultations provided through telecommunication technologies, such as various digital health platforms and health apps.

The digital healthcare sector in Sweden has grown in recent years, and developed rapidly during the COVID-19 pandemic (Cederberg, 2021). A large proportion of the primary care centres that previously only offered face-to-face consultations have also developed platforms for digital consultations. Simultaneously, several healthcare providers that used to only offer digital care have also opened facilities for physical visits.

In Sweden, unique prescription codes are issued to all healthcare providers and provide the opportunity to monitor prescriptions. Prescriptions issued by healthcare centres that provide both physical and digital healthcare services use the same prescription code, regardless of the kind of visit. Consequently, it has become more complicated to separate prescriptions issued during digital consultations from those issued during physical visits. Therefore, providing a comprehensive picture of prescribing patterns in digital health is not possible at this point in time.

In 2019 the Swedish strategic programme against antibiotic resistance (Strama) published treatment guidelines for diagnosis-linked antibiotic prescribing in digital health (Strama, 2022). The guideline functions as a handbook for prescribers in the diagnosis and treatment of a range of common infections in digital health. To evaluate adherence to Strama's treatment guidelines, linkages between the prescriptions and diagnoses are required, which are complicated or impossible to establish for the most regions in Sweden. Due to all of challenges described above, data presented in this section is limited to Stockholm region. For the purpose of this report, data was collected from Stockholm region, which was able to extract prescriptions linked to diagnoses from digital consultations in primary care. However, not all prescriptions are included due to the inability to collect data from healthcare centres that do not have an agreement with the region to provide primary care. Thus, the numbers reflect a proportion of the digital consultations and are likely underestimated.

Prescriptions of antibiotics in digital primary care in Stockholm region 2022

The total number of prescriptions in digital primary care during 2022 from the Stockholm region was 71 247 prescriptions, a slight increase compared to year 2021 where the total number of prescriptions was 63 490. These data do not include healthcare providers that only provide digital primary care. The slight increase in prescriptions from digital primary care correlates with the increase of total prescriptions in outpatient care.

This increase was mostly seen in the group aged 0-6 years were the number of prescriptions in digital health increased by 52% compared to 2021 (10 259 prescriptions vs 6750 prescriptions).

During 2022, antibiotics were prescribed in 12% of the digital consultations, indicating no change compared to the year before. Similar to the year before, most antibiotic prescriptions were issued to patients aged 15-64 years, while among patients aged 65+, only 3% received an antibiotic prescription. This might indicate that the age group 15-64 seeks digital primary care to a higher extent compared to the patients 65+, which might be due to the reason for seeking digital care (Table 1).

Out of the 71 247 antibiotic prescriptions issued through digital primary care in Stockholm region in 2022, almost half of them were linked to common infection diagnoses (Table 2). As in 2021, the most common diagnosis for antibiotic prescribing in digital care was acute cystitis followed by lyme borreliosis, upper respiratory tract infection and tonsillitis. According to Strama guidelines, only four types of infections can be diagnosed and prescribed antibiotics through digital consultations, i.e. acne, acute cystitis, impetigo and lyme borreliosis. A review of the antibiotics prescribed per diagnosis indicate that the recommended first-hand treatment was commonly prescribed for most, but not all, diagnoses. For cough and upper respiratory tract infections, where no antibiotics should be prescribed, beta-lactamase sensitive penicillins and tetracyclines were the most commonly prescribed antibiotics. The same pattern was observed during 2021.

This sample of data from Stockholm region suggests that the prescribing of antibiotics in digital primary care is increasing and that adherence to Strama guidelines can be improved. It is therefore important to be able to collect and analyse data from digital primary care in the same manner as outpatient care, dentistry, and hospital care. Prescription data from digital primary care helps identify the gaps and the interventions needed to promote responsible use of antibiotics.

Table 1. The number of prescriptions in Stockholm's outpatient care and digital primary care, per age group, 2022.

Age	Total digital	Total outpatient	Proportion digital
0-6	10 259	49 065	21%
7-14	3 766	26 149	14%
15-64	52 300	338 276	15%
65+	4 922	177 849	3%
Total	**71 247**	**591 339**	**12%**

Table 2. Diagnostic groups connected to the number of prescriptions in Stockholm's digital primary care, per age group, 2022.

Diagnostic group	All ages	0-6	7-14	15-64	65+
Acute bronchitis	250	20	5	187	38
Acute cystitis	13 439	164	109	11 812	1 354
Acute otitis media	555	373	43	132	7
Acute sinusitis	1 667	9	14	1 545	99
Lyme borreliosis	5 679	668	425	3 939	647
Erysipelas	245	7	8	174	56
Tonsillitis	3 934	282	346	3 274	32
Cough	1 114	259	35	676	144
Imeptigo	1 393	712	285	392	4
Carbuncle, furuncle, abscess, atheroma	280	20	21	229	10
Ingrown toenail	537	89	91	349	8
Nonspecific skin infections	1 639	239	210	1 168	76
Pneumonia	155	28	5	94	28
Upper respiratory tract infections	4 433	1 139	215	2 850	229
Total	**35 374**	**4 009**	**1 812**	**26 821**	**2 732**

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Cederberg J. 2021, Flerfaldig ökning av digital vård [Multiple increase in digital healthcare]. *Läkartidningen*, 13-14/2021.

Strama. 2022, Rekommendationer för kvalitetsindikatorer vid digitala vårdmöten [Recommendations for quality indicators in digital health]. https://strama.se/wp-content/uploads/2022/04/Kvalitetsindikatorer-for-digitala-vardmoten-2022.pdf

Sales of antibiotics for animals

Brief on data sources, methodology and confidentiality

In Sweden, all veterinary medicinal products are sold by pharmacies. All pharmacies are obliged to report all sales of medicinal and veterinary medicinal products to the eHealth Agency who maintains a database of sales from pharmacies to animal owners (prescriptions dispensed) or to veterinarians (requisition for use in practice).

For confidentiality reasons, sales of classes with less than three products on the market have been aggregated as "others" in Table 2.1.

The sales of veterinary medicinal products for mixing into feed for aquaculture for food production are not included in the data referred to above, as such feed is traded from other countries. Data on prescriptions for fish are collected through a separate system, see Comments by animal species, Fish.

The protocol for the European surveillance of veterinary antimicrobial consumption (ESVAC) has been updated regarding conversion factors for certain benzylpenicillins (EMA, 2021). Data for procaine benzylpenicillin from 1980 and onwards were recalculated with the new conversion factor (0.57 compared to previously 0.6) and previously published data has been updated as from Svarm 2020.

Further details on data sources and inclusion criteria are given in Materials and methods, sales of antibiotics.

Trends in animal populations

Changes in the numbers of animals may affect trends in statistics on sales of antibiotics. Compared to 2013, the number of pigs slaughtered in 2022 was 5% higher, while the number of broilers has increased by 36%. The number of dairy cows decreased by 13% during the same period. The number of horses was estimated to 355 500 in 2016. The number of dogs was estimated to 784 000 in 2012 and 881 000 in 2017.

Further details on animal numbers and data sources are found in the subchapter Demographics and denominator data in this report.

Completeness of data

Until 2009, pharmacies in Sweden were run by a state-owned co-operation (a monopoly). In July 2009, the Swedish pharmacy market was reregulated and today, there are many pharmacies competing on the market. A few of those have niched in veterinary medicinal products.

At the time of the reregulation, the responsibility to collect sales data from pharmacies was transferred from the monopoly to a state-owned infrastructure company, and a few years later (2014) to the newly formed eHealth Agency. All pharmacies are obliged to report all sales of medicinal and veterinary medicinal product to the eHealth Agency, and are supervised by the Medical products agency.

Between 2010 and 2015, there were two different problems resulting in lack of completeness of data. Sales of products sold on special license were incomplete between 2011 and 2013 due to system change. In 2013, concerns were also raised about a more general lack of completeness in the sales reported by pharmacies. The overall lack of completeness was estimated by SVA in collaboration with Marketing authorization holders and was in the range of 5 to 10%. The problem persisted until 2015.

When SVA retrieved data on sales for animals for the year 2022 from the eHealth Agency, the overall sales (in kg active substance) in 2022 was more than 10% lower than in 2021, and a lack of completeness was suspected. The eHealth Agency initiated an investigation in collaboration with SVA and the Swedish Board of Agriculture. A number of reports from some pharmacies had been rejected from the receiving database, and this problem affected 2017 – 2022. The rejected reports have now been corrected by the pharmacies and their system-provider, and successfully transferred to the main database.

Data for the period 2017 – 2021 (measured as kg active substance) resulted in updates for all years. The problem mainly affected data for 2020 and 2021, for which the corrected figures on overall sales in kg active substance were 9 and 10% higher, respectively.

The difference between 2021 and 2022 was still inexplicably large (-12%). A thorough search for yet undiscovered errors was undertaken but none was identified. No indication of a corresponding decrease in sales of non-antibiotic veterinary medicinal products could be identified.

Further description of the difference between sales 2022 and previous years

As noted above, the overall sales of antibiotics for animals from Swedish pharmacies (as kg active substance) was conspicuously lower in 2022 compared to previous years (Table 2.1). When analysing data by yearly quarters, a decrease in sales from the fourth quarter in 2021 and onwards is apparent.

All analyses are impeded by shorter and longer shortages of veterinary antibiotics on the market, sometimes affecting all products of a certain type (e.g. sulfonamide-trimethoprim for injection). Products with longer shortages are generally replaced by sales of similar products sold with special license, but some replacement by products with other substances is likely.

Major decreases are seen for all classes or aggregated classes, except for aminoglycosides and "macrolides and lincosamides". In the case of aminoglycosides, there is instead a major increase that is explained by increased sales of products for

treatment of weaning diarrhoea (see "effects of phasing out products with zinc-oxide). For some classes, there has been a downward trend over several years but for others, like penicillin (QJ01CE), sales have been relatively stable over time until 2022.

Sales of antibiotics for animals on requisition (for use in veterinary practice) was 16% lower in 2022 compared to 2021. The corresponding figure for sales on prescription was 8%. Requisition represented 40-42% of the overall sales during 2020-2021.

Products formulated for injection and oral medication of individual animals were 12 and 18% lower in 2022 compared to 2021. Products formulated for medication of groups of animals increased by 10%, mainly explained by increased sales of products for treatment of weaning diarrhoea in piglets (see "effects of phasing out products with zinc-oxide").

Analysis of data by animal species given on prescriptions (as recorded by the pharmacies at dispensing), showed major decreases in sales for horses and cattle (-19 and -18%, respectively). In contrast, sales for pigs were relatively stable over the past years. Horses and cattle are also the two species that are assumed to dominate the use of products sold on requisition and used in veterinary practice, at least when the unit of measurement is kg active substance.

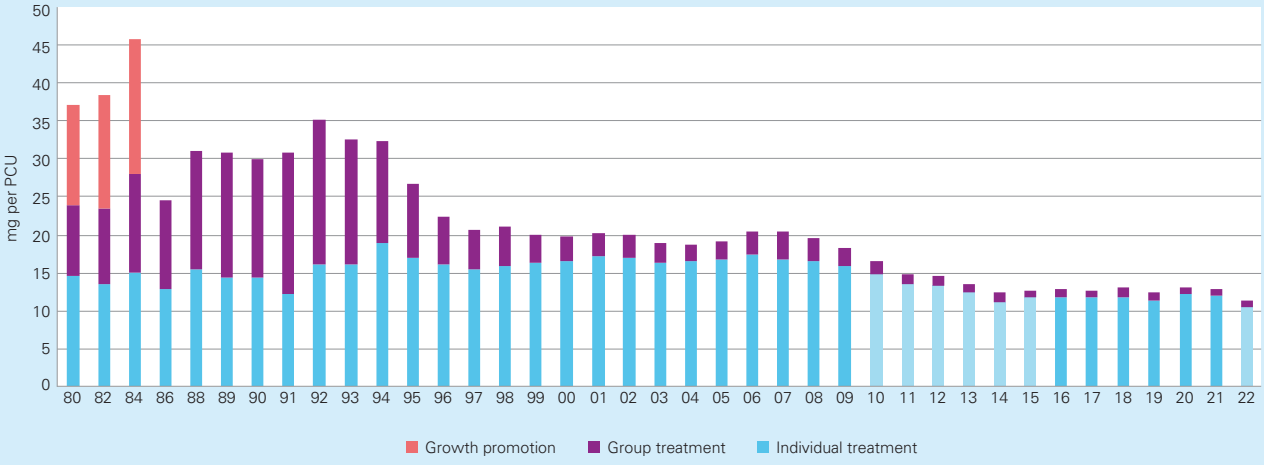
Decreases of more than 10% from one year to another has only been recorded on three previous occasions, and in all these cases the explanation is known. Despite in depth analysis of data and interviews of different experts outside SVA, no clear explanations of the overall drop in sales of antibiotics for animals between 2021 and 2022 could be drawn. Data should therefore be interpreted with caution, and no conclusions drawn regarding 2022. At the time of publication of Swedres-Svarm 2022, existing evidence indicated that the data presented below represents all sales of included antibiotics for animals from Swedish pharmacies to animal owners and veterinarians. If, at a later stage some yet unidentified error causing a lack of completeness is discovered, data will be updated and published online on the SVA web page (www.sva.se/svarm).

Comments on overall sales

To correct for changes in the numbers of animals over time, the population correction unit (PCU) described in a publication from the European Medicines Agency was applied (EMA, 2011). The PCU is a purely technical term representing an approximation of the summed live weight of the major animal populations, excluding companion animals. In Figure 2.1, the total sales of antimicrobials for animals (including sales for companion animals) from 1980 and onward are presented as mg active substance per PCU, using figures for 2021 as a proxy for PCU in 2022. As sales for use in aquaculture are not included in the data presented, fish have been excluded from the PCU given in the reports from the ESVAC. Another difference from data published in the ESVAC-reports is that in Figure 2.1, data on products for use in companion animals are included.

Measured as mg per PCU, the overall sales were around 70% lower in 2022 compared to the average figures for 1980-1984 (i.e. before the Swedish ban on growth promoting antimicrobials in 1986). This is explained first by the removal of growth promoting antimicrobials in 1986, followed by a major gradual decrease from the mid-90s of the sales of veterinary products for medication via feed or water (group medication). A decrease of sales of products for individual medication is also noted in the past decade.

Figure 2.1. Yearly sales of veterinary medicines with antibiotics expressed as mg per population correction unit (PCU)[a]. Uncertain figures are indicated with a lighter shade.



[a]Data for 2022 may be subject to change. Data from 2010-2015 are uncertain because of a lack of completeness mainly affecting injectable products. Data for 2022 are also uncertain as a full explanation is lacking. This is indicated by a paler colour for antibiotics for individual treatment. In the present figure, all products (including tablets) are included while in data presented in the European surveillance of veterinary antimicrobial consumption tablets are excluded when calculating mg/PCU.

Table 2.1. Yearly sales of veterinary medicines with antibiotics, expressed as kg active substance per class[a].

ATCvet code		2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
QJ01AA, QG01A	Tetracyclines	935	787	685	515	529	516	524	638	748	573
QJ01CE,-R, QJ51	Benzylpenicillin[b]	5 592	5 148	5 479	5 620	5 591	5 597	5 525	5 795	5 872	5 130
QJ01CA, QJ01CR	Aminopenicillins	645	635	642	677	638	670	643	759	664	612
QJ01D	Cephalosporins	330	299	267	242	210	187	161	163	164	150
QA07AA, QJ01G,-R, QJ51R	Aminoglycosides	264	300	322	312	302	376	343	404	366	506
QA07AB, QJ01E	Sulphonamides	1 707	1 699	1 634	1 643	1 682	1 542	1 457	1 509	1436	1 180
QJ01E	Trimethoprim	320	314	313	318	326	297	283	294	279	237
QJ01F	Macrolides & lincosamides	564	484	485	472	527	581	486	449	419	400
QJ01MA	Fluoroquinolones	52	45	34	30	25	30	21	28	22	16
QA07AA,QJ01BA, QJ01XQ	Others[c]	205	201	224	337	149	220	114	137	69	60
Total sales		**10 614**	**9 912**	**10 086**	**10 165**	**9 981**	**10 016**	**9 557**	**10 175**	**10 039**	**8 865**

[a]Data from 2010-2015 are uncertain because of a lack of completeness mainly affecting injectable products. Data for 2022 are also uncertain as a full explanation of the decrease is lacking. [b]Also includes small amounts of phenoxymethylpenicillin and penicillinase stable penicillins. [c]Others include: amphenicols, pleuromutilins and polymyxins, aggregated for confidentiality reasons.

Comment on data by animal species

Pigs – initial effects of the phasing out of products with zinc-oxide

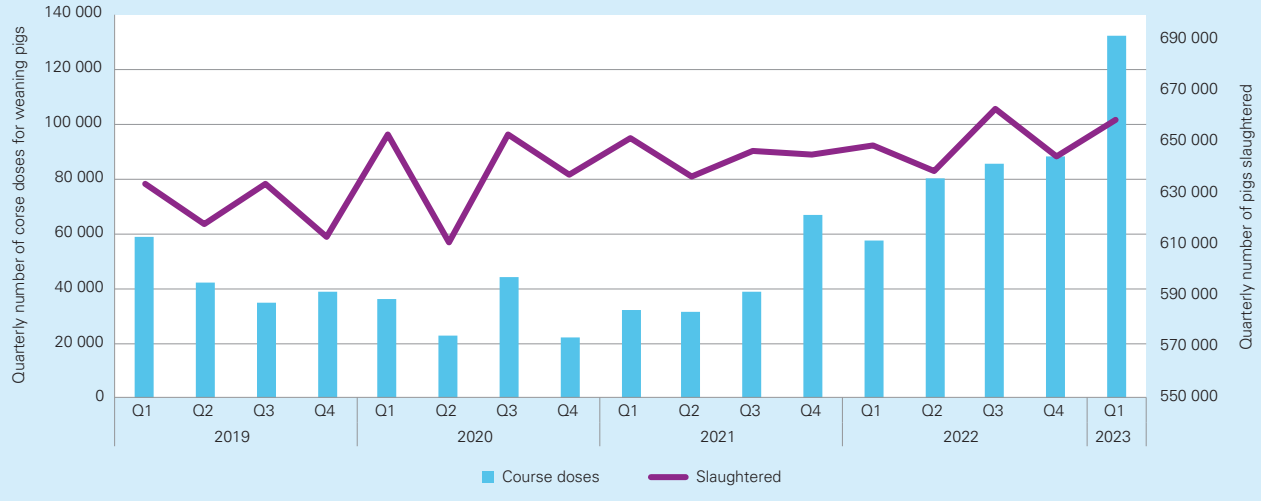
In June 2017, the European Commission decided that in the EU, the authorisations of all veterinary medicinal products with zinc-oxide in high dosage should be withdrawn at the latest by June 26, 2022. Sweden opted for using the full phasing out period.

Products with zinc-oxide were authorised for prevention of weaning diarrhoea in piglets, and a potential consequence of the withdrawal is an increased need to treat diarrhoeic weaners with antibiotics. A collaborative group with representatives from pig production, organisations providing animal health services, the feed-industry and authorities was formed to discuss and implement actions to support the phasing out, and to share experiences. For example, freely available educational materials (printed and films) were developed and distributed in various meetings.

As an early follow-up of potential consequences, data on sales for pigs of antibiotic products indicated for group-medication were explored on a quarterly level for 2019-first quarter 2023. The dosage indicated in the specific product characteristics and a standard weight per pig (12 kg) were used to calculate kg active substance sold to course doses for weaners. The selected products all had ATCvet-code QA07AA, contained colistin, neomycin or paromomycin and were all sold on special license.

In Figure 2.2 quarterly sales of selected products are shown together with quarterly figures on numbers of slaughtered pigs. When interpreting the data, it is important to note that

Figure 2.2. Quarterly sales of products for group-medication of diarrhoea in weaning pigs, expressed as course doses for pigs (bars, left Y-axis) and quarterly number of pigs slaughtered (line, right Y-axis) [a, b]



[a]Number of pigs slaughtered are from the statistical database of the Swedish board of agriculture. [b]Q in the legend of the X-axis stands for quarter.

the actual use takes place later than the date of sales. Also, the pigs are treated at weaning but will be slaughtered a couple of months later. Therefore, treatment incidence was not calculated.

Sales of selected products increased from the fourth quarter 2021 and onwards, and this is not matched by a corresponding increase in slaughter volumes. The high sales during the first quarter 2023 should be interpreted with caution, as there may be a compensatory decrease in the following months. The increase in sales of selected products is not matched by a corresponding decrease in sales of injectable products with sulfonamides and trimethoprim (data not shown).

Taken together, initial data show that the need for group medication of weaning diarrhoea has increased during and after the phasing out of products with zinc-oxide. It is still early days, and data for one or two years ahead will show if this is simply an adaptation phase, or if the situation remains for a longer period.

Poultry

From 2011, the Swedish poultry meat association requests all treatments of broilers, parents, and grandparents to be reported as part of the Poultry health control programme. The programme covers more than 98% of the broilers reared in commercial production. The reported figures are shown in Table 2.2.

Antibiotics are rarely used for treatment of bacterial diseases in commercially reared *Gallus gallus*. Localised outbreaks can therefore have a major influence on the sales in a specific year. Over the last ten years, the yearly sales of fluoroquinolones for slaughter chickens and hens have been below or much below 0.25 kg. Cephalosporins or colistin are never used.

The 10 flocks reported as treated were administered phenoxymethylpenicillin for necrotic enteritis. In addition, three parent flocks were treated on six occasions, in all cases with phenoxymethylpenicillin. No grand-parent flocks were treated.

Coccidiostats of the ionophore group are used as feed additives to control coccidiosis in the production of chickens for slaughter and for turkeys. Since the late 80s, narasin is by far the most widely applied substance for broilers.

Fish

Medicated feed for fish is always traded from other Nordic countries. Therefore, the quantities sold are not captured by the national pharmacy sales collected by the eHealth Agency. Records of prescription of veterinary medicines for fish are collected annually by the veterinarian co-ordinating the limited number of veterinarians that are dealing with farmed fish and results are reported annually to the Board of Agriculture.

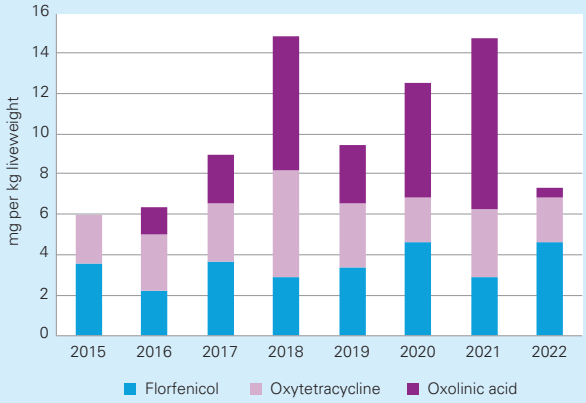
The occurrence of bacterial disease in farmed fish is influenced by water temperatures in summer, and the amounts prescribed may therefore vary between the years. Antibiotics prescribed in 2022 were florfenicol, oxolinic acid and oxytetracycline.

In Figure 2.3, the prescription of antibiotics for farmed fish is shown as mg per kg biomass produced (liveweight fish slaughtered). Florfenicol is primarily used for treatment of flavobacteriosis (*Flavobacterium psychrophilum*), a disease mainly affecting juvenils (with a very low weight). Oxolinic acid and oxytetracycline are used to treat diseases caused by *Aeromonas salmonicida* and *F. columnare*. These are diseases affecting production fish, i.e. of a higher weight. Therefore, the relations between the antibiotics shown in Figure 2.3 do not translate to treatment frequencies or actual exposure of individual fishes.

Table 2.2. Number of broiler flocks treated with antibiotics, and total number of flocks slaughtered per year.

Year	Number of flocks produced	Number of flocks treated
2013	3 133	4
2014	3 138	4
2015	3 191	28
2016	3 300	14
2017	3 300	1
2018	3 223	4
2019	3 368	54
2020	3 557	11
2021	3 684	13
2022	3 470	10

Figure 2.3. Prescription of antibiotics for fish as mg per kg live weight of slaughtered fish.



Antibiotic resistance in humans

Overview of surveillance systems and methods for antibiotic susceptibility testing

All surveillance of antibiotic resistance in Sweden relies on results from the clinical microbiology laboratories. The laboratories use the methods and breakpoints recommended by NordicAST for susceptibility testing. This Nordic organisation support the implementation of EUCAST recommendations in the Nordic countries. The national resistance surveillance is based on data from different sources and collections (Table 3.1).

Table 3.1. Summary of species and types of resistance included in national surveillance of antibiotic resistance.

Species, group or type	Sampling
Mandatory reporting (SmiNet)	
Enterobacterales with ESBL Enterobacterales with $ESBL_{CARBA}$ *Staphylococcus aureus* resistant to methicillin *Streptococcus pneumoniae* with reduced susceptibility to penicillin G *Enterococcus faecium* or *Enterococcus faecalis* resistant to vancomycin *Mycobacterium tuberculosis*[a] *Neisseria gonorrhoeae*[a]	Samples of all types for clinical, screening or case finding purposes.
Neisseria meningitidis[a]	Invasive disease (blood, CSF, or other normally sterile sample).
Voluntary surveillance (Svebar)	
Escherichia coli	Clinical sampling from blood and urine.
Klebsiella pneumonia	Clinical sampling from blood and urine.
Staphylococcus aureus	Clinical sampling from blood and skin and soft tissue infections.
Streptococcus pneumoniae	Clinical sampling from blood.
Enterococcus faecalis *Enterococcus faecium*	Clinical sampling from blood.
Pseudomonas aeruginosa	Clinical sampling from blood and non respiratory infections.
Acinetobacter spp.	Clinical sampling from blood.
Haemophilus influenza	Clinical sampling from blood and nasopharynx.
Streptococcus pyogenes *Streptococcus agalacticae*	Clinical sampling from blood.
Clostridioides difficile[b]	Clinical sampling from faeces.
Salmonella spp[c]	Clinical sampling from blood, faeces and urine.
Campylobacter jejuni[c]	Clinical sampling from faeces.
Shigella spp[c]	Clinical sampling from faeces
Microbiological characterisation programme	
Colistin resistance in Enterobacterales	All isolates from clinical, screening or case finding samples with reduced susceptibility to colistin.
Enterobacterales with $ESBL_{CARBA}$	All isolates from clinical, screening or case finding samples with reduced susceptibility to meropenem.
Acinetobacter spp. with $ESBL_{CARBA}$	All isolates from clinical, screening or case finding samples with reduced susceptibility to meropenem.
Staphylococcus aureus resistant to methicillin	All isolates from clinical samples.
Streptococcus pneumoniae with reduced susceptible to penicillin G (MIC ≥ 0.5)	All isolates from clinical, screening or case finding samples.
Enterococcus faecium or *Enterococcus faecalis* resistant to vancomycin or linezolid	All isolates from clinical, screening or case finding samples.
Clostridioides difficile	All isolates from clinical samples during weeks 39-40.
Haemophilus influenzae with cephalosporin resistance	All isolates from clinical, screening or case finding samples.

[a]All infections with these bacteria are mandatory to report. Antibiotic resistance data are acquired from these surveillance programs. bA separate voluntary surveillance programme based on reports from laboratories. cAll infections with these bacteria are mandatory to report. However, the antibiotic resistance data are acquired through voluntary reporting in Svebar.

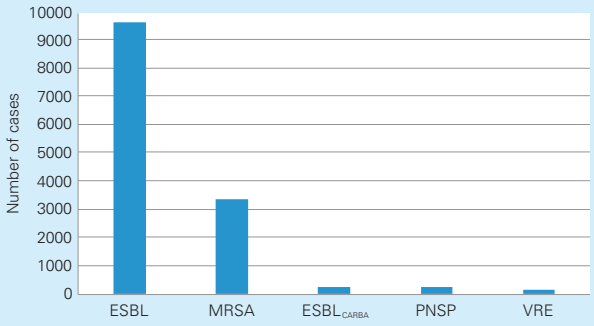
Indicators of antibiotic resistance

Since 2020 resistance to cefotaxime in *E. coli* isolated from blood from women and men and the proportion of MRSA among *S. aureus* isolated from blood from women and men has been used as indicators for antibiotic resistance in Sweden. The results for these are presented under their respective section.

Notifiable diseases

Four types of antibiotic resistance in bacteria are included in the Swedish Communicable Diseases Act. These are *Staphylococcus aureus* resistant to methicillin (MRSA), *Streptococcus pneumoniae* with reduced susceptibility or resistance to penicillin (PNSP), *Enterococcus faecalis* and *Enterococcus faecium* resistant to vancomycin (*van*A or *van*B, VRE), and Enterobacterales with ESBL (including AmpC) or $ESBL_{CARBA}$. However, ESBL and $ESBL_{CARBA}$ are reported separately. As in previous years, the notifications of ESBL have greatly exceeded the other three (Figure 3.1 and Table 3.2).

Figure 3.1. Number of mandatory reported cases during 2022.



Source: The Public Health Agency of Sweden

Table 3.2. Summary of results for mandatory reported antibiotic resistance 2022

	ESBL	$ESBL_{CARBA}$	MRSA	PNSP	VRE
Number of cases (incidence)	9 611 (91)	240 (2.3)	3 340 (32)	146 (1.4)	236 (2.2)
Proportion clinical infection	70%	32%	47%	45%	10%
Gender	67% women	57% men	53% women	57% men	55% men
Median-age (range)	57 year (0-100+)	56 year (0-93)	33 year (0-100+)	49 year (0-98)	63 year (0-98)
Proportion of domestic cases	No information	28% (6% no data)	60% (11% no data)	61% (35% no data)	58% (5% no data)
Short epidemiological information	Community and healthcare	Hospital abroad	Community	Community	Hospital, domestic spread
Bloodstream infections	818 (599 new cases 2022, 219 cases known from previous years)	14 (12 new cases 2022, 2 cases known from previous year)	96 (75 new cases 2022, 21 cases known from previous years)	9	5

Voluntary surveillance based on clinical samples

This surveillance uses results collected from the regional clinical microbiology laboratories. From 2015 and onwards, all data on clinical isolates from humans have been collected through Svebar. This is a system that automatically collects all culture results from participating clinical microbiology laboratories. Currently 22 laboratories deliver data to Svebar (May 2023). It is not possible to deduplicate data from Svebar since patient identification is not permitted in the system. Consequently, duplicate findings from blood and other samples will be included. Patients with highly resistant isolates tend to be sampled more frequently which can result in overestimation of the resistance. Data analysed from the voluntary surveillance system (Svebar) are collected from laboratories with validated data (Table 3.3). Most antibiotic resistance levels presented in this report are based on non-selective susceptibility testing from at least five laboratories, thus avoiding bias from hierarchical testing and regional differences. When data presented is based on selective testing, this will be indicatied in the graphs and tables. The number of AST isolates for each species and antibiotic combination is given in the attached file. The 95% confidence intervals are presented in figures showing resistance. The confidence intervals are given from 2015 and onwards.

Data from Svebar is used for reporting both to EARS-Net (an ECDC surveillance system) and to GLASS (a WHO surveillance system). Prior to 2015, ResNet, a national surveillance programme on antibiotic resistance, was used to collect data. From 2015 and onwards, this yearly data is based on SIR reported by the clinical microbiology laboratories to Svebar.

Microbiological characterisation program

The Public Health Agency of Sweden provide microbiological characterisation programs for verification and characterisation of isolates that participating laboratories send in. An overwiev is given in Table 3.1.

Table 3.3. Number of laboratories used for antibiotic resistance calculations among clinical cases during 2015-2022.

	2015	2016	2017	2018	2019	2020	2021	2022
Number of clinical microbiology laboratories	9	9	10	9	20	21	22	22
Coverage of population (%)	52	52	55	52	78	86	89	89

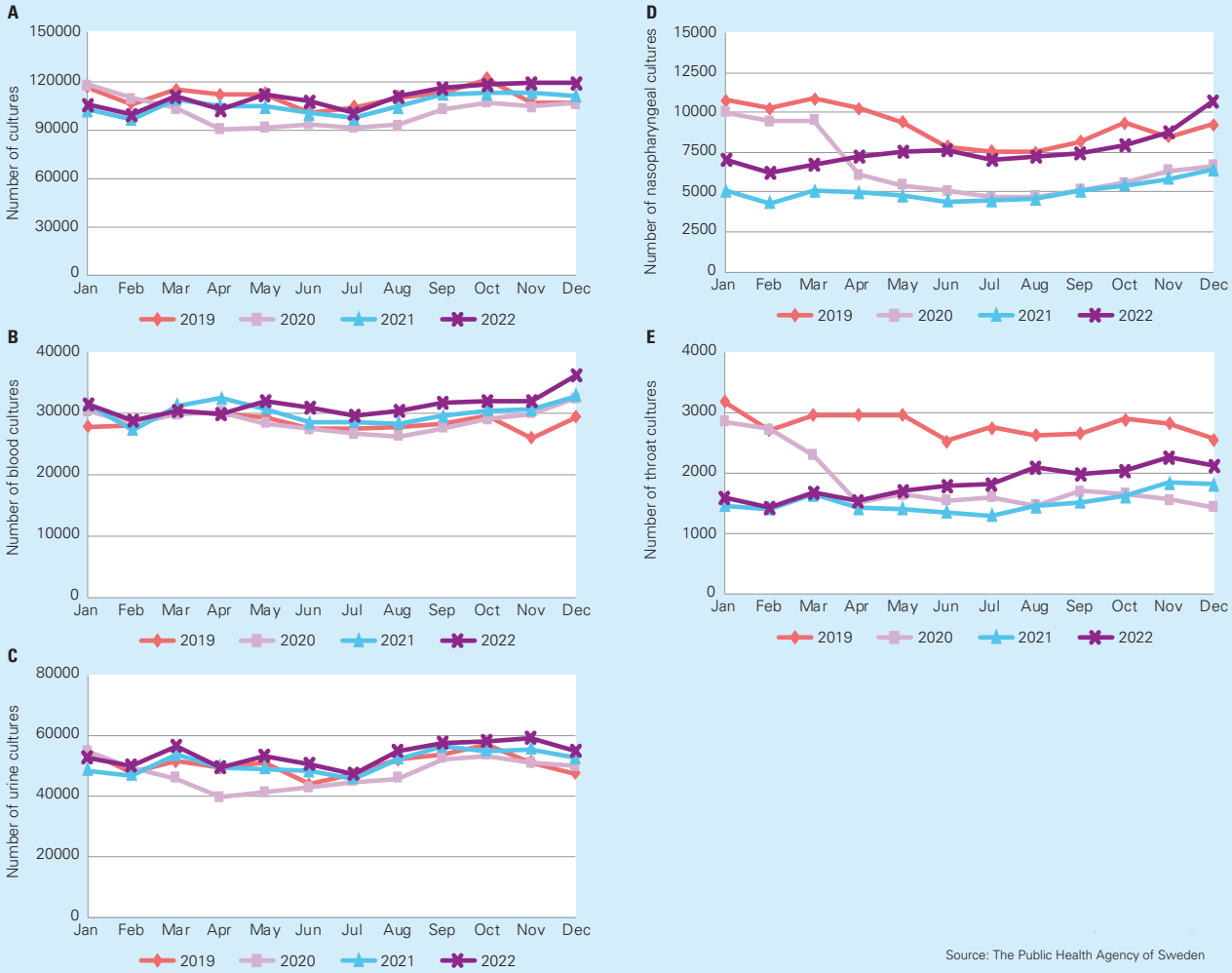
Overview of sampling and culture results

Denominator data is derived from Svebar. The last four years denominator data from twelve clinical laboratories covering around 60% of the population in Sweden were included. In Figure 3.2 the annual numbers of analyses are presented for: total number of cultures (A), blood cultures (B), urine cultures (C), nasopharyngeal cultures (D) and throat cultures (E).

The total number of cultures increased by 4% compared to 2021, for blood cultures the increase was 4%, and for urine cultures 5%. The number of these cultures are now at the same level or at a higher level than in 2019. Although an increase was seen for the number of nasopharyngeal cultures (52%) and for throat cultures (21%), the number is still lower than in 2019.

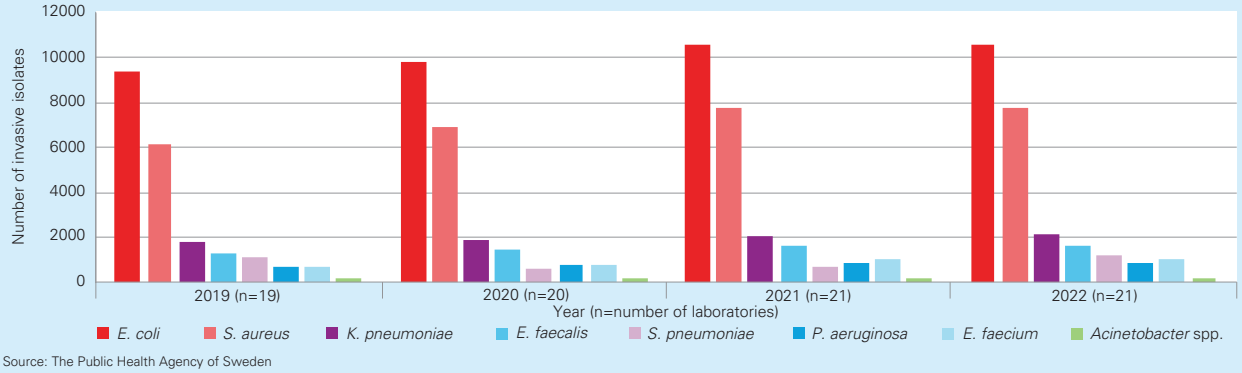
The number of bacteria reported to EARS-Net yearly is shown in Figure 3.3.

Figure 3.2 A to E. Number of analyses are presented for different and total number of cultures, year 2019-2022. Data from one laboratory is excluded in the calculation for number of all cultures and blood cultures due to a change in laboratory information system in 2021.



Source: The Public Health Agency of Sweden

Figure 3.3. Number of isolates, collected from blood during 2019-2022, reported to EARS-Net.



Source: The Public Health Agency of Sweden

Escherichia coli, Klebsiella pneumoniae, and other Enterobacterales with ESBL and ESBL$_{CARBA}$

Mandatory reporting of ESBL-producing Enterobacterales

Results from 2022

- Number of reported cases: 9 611 (previous year 7 860), relative change +22%
- Number of bloodstream infections: 818 (previous year 719)

Trends

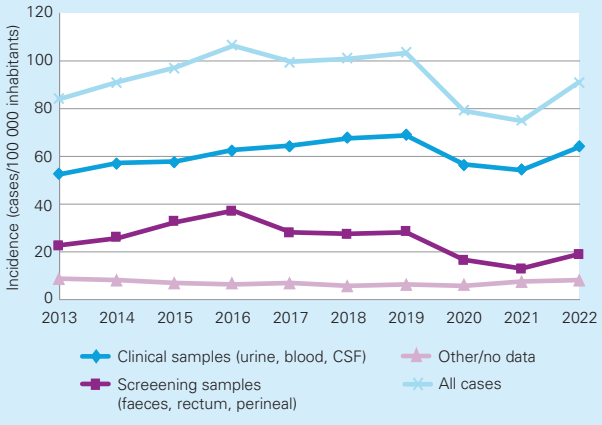
The ESBL incidence increased in 2022, to 91 new cases per 100 000 inhabitants, see Figure 3.4. The increase was seen in clinical samples (urine, blood and cerebrospinal fluid (CSF)) and in samples taken for screening purposes (faeces, rectum and perineal).

The number of bloodstream infections (BSI) with ESBL-producing Enterobacterales has increased steadily since it became notifiable and after a decrease in 2020 the numbers are back to nearly the same level as in 2019 (Figure 3.5). *E. coli* was the most common cause of BSI, 73% followed by *K. pneumoniae* 15%.

The gender and age distribution has not changed much since the surveillance started and reflects the expected occurrence of urinary tract infections in the different groups. Elderly, 85 years and older (n=979, incidence 357) followed by children under one year (n=331 incidence 315) had the highest incidence. The high incidence in neonates is probably a result of screening and contact tracing at neonatal units. Among the elderly urinary tract infection is a common bacterial infection explaining the high incidence in this group.

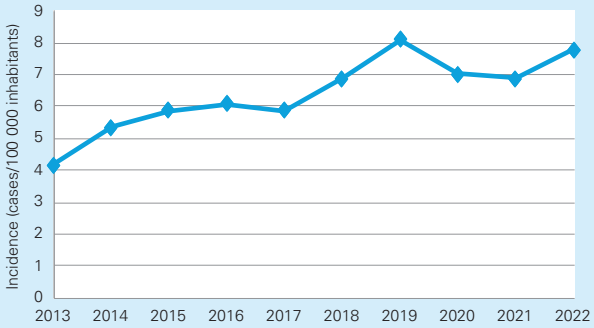
As in previous years, the most commonly reported species was *E. coli* found in 82% of all cases followed by *K. pneumoniae* with 10%. The remaining cases comprised of several other species of Enterobacterales (for detailed information see attached file Figure 3.4).

Figure 3.4. The incidence (cases/100 000 inhabitants) of cases with ESBL-producing Enterobacterales in relation to type of infection, year 2013–2022.



Source: The Public Health Agency of Sweden

Figure 3.5. The incidence (cases/100 000 inhabitants) of invasive cases with ESBL-producing Enterobacterales, reported during year 2013–2022.



Source: The Public Health Agency of Sweden

Clusters and outbreaks

In 2022, seven clusters with ESBL were confirmed based on SNP-analysis (n=2-5 cases per cluster). One cluster started in 2018 and now has five cases with the latest reported in 2022. Five clusters were caused by ESBL-producing *E. coli* and two cluster were caused by ESBL-producing *K. pneumoniae*. All but two of these clusters were healthcare related. However, outbreaks with ESBL-producing Enterobacterales are not consistently reported.

Comments

In 2022, the number of cases with ESBL-producing Enterobacterales increased. The increase is probably linked to a rise in international travel.

Mandatory reporting of ESBL$_{CARBA}$-producing Enterobacterales

Results from 2022

- Number of reported cases: 240 (previous year 137), relative change 75%
- Number of bloodstream infections: 14 (previous year 7)

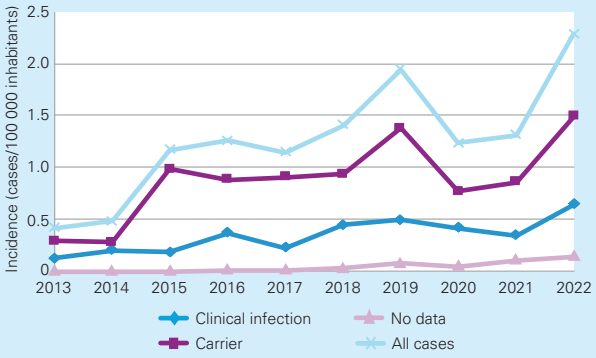
Trends

In 2022, the incidence for ESBL$_{CARBA}$ producing Enterobacterales was 2.3 cases per 100 000 inhabitants, a large increase with 75% (103 cases) compared to 2021. A majority, 65% of the cases, were carriers (Figure 3.6). Most cases reported as acquired abroad (65%, n=157) were identified in targeted screening (n=102) after hospitalisation abroad (n=70). Out of the 68 domestic cases, 44 were identified by investigation of clinical infection. The proportion of domestic cases with healthcare-acquired ESBL$_{CARBA}$ remained at the same level as previous year (32%, n=22). For 32 domestic cases, information of acquisition was missing. The median age was 56 years and 57% of the cases were men. The most common countries of infection in the notifications, were Sweden (n=68), Ukraine (n=24), Turkey (n=14), Greece (n=10) and Spain (n=9).

Epidemiological typing of ESBL$_{CARBA}$

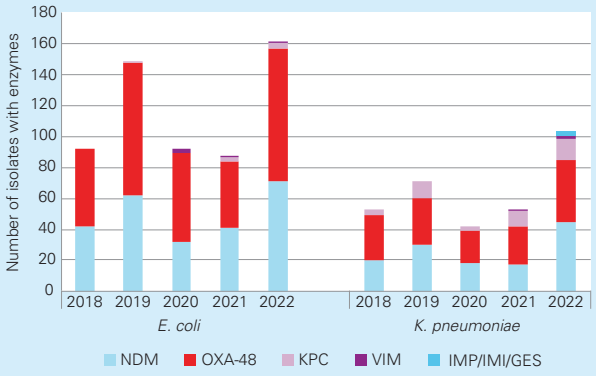
ESBL$_{CARBA}$ isolates from notified cases in 2022 have been characterised using whole genome sequencing (WGS). The most common carbapenemase-producing Enterobacterales was *E. coli*, accounting for 56% of all cases, followed by *K. pneumoniae* (31%). Genes encoding for carbapenem resistance have also been detected in several other species of Enterobacterales. Multiple species, resistance genes and/or sequence types could be identified in several cases. The most abundant carbapenemase genes in these isolates were variants of NDM and OXA-48. In addition to these genes, KPC, VIM, IMP and IMI were also detected, but to a lesser extent (Figure 3.7). Apart from the genotypic analysis, isolates have been tested for antibiotic susceptibility using broth microdilution (BMD) (since June 2020). The phenotypic resistance shows a high degree of carbapenem resistance in metallo beta-lactamase (MBL)-producing isolates. But in OXA-48-producing *E. coli*, meropenem and imipenem resistance is low, just under 100% are sensitive, in contrast to *Klebsiella* species where meropenem and imipenem resistance is higher, only about 20% are sensitive (Figure 3.8).

Figure 3.6. The incidence (cases/100 000 inhabitants) of cases with ESBL$_{CARBA}$ producing Enterobacterales in relation to type of infection, year 2013-2022.



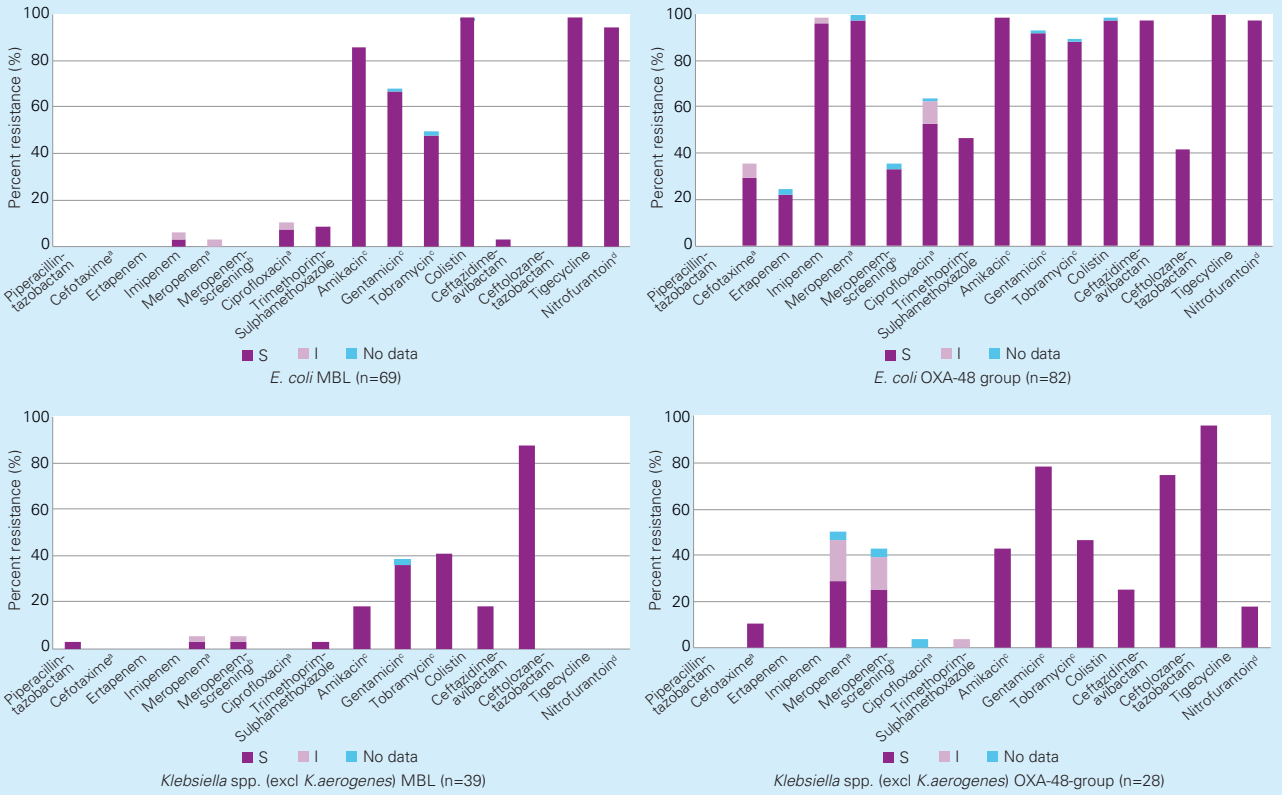
Source: The Public Health Agency of Sweden

Figure 3.7. Number of isolates and enzyme types of ESBL$_{CARBA}$ in Enterobacterales in Sweden 2013-2022.



Source: The Public Health Agency of Sweden

Figure 3.8 A to E. AST results from ESBL$_{CARBA}$ producing *E. coli* and *Klebsiella* spp. (excluding *K. aerogenes*) collected among notified cases in 2022.



[a]Indications other than meningitis. [b]MIC >0.125 mg/L. [c]Urinary tract infections (UTI). [d]Uncomplicated UTI

Source: The Public Health Agency of Sweden

Table 3.4. Number of clusters with $ESBL_{CARBA}$ in Sweden identified by "single nucleotide polymorphism" SNPs based analysis during 2022

Resistance gene	Species	No of isolates	Year of isolation (number of cases)	Possible country of infection	Way of acquisition
NDM-1/OXA-48	*K. pneumoniae*	7	2022 (7)	Ukraine	Healtcare
OXA-48	*E. coli*	7	2023 (3), 2022 (2), 2021 (1), 2020 (2)	Sweden	Unknown
NDM-7	*K. pneumoniae*	3	2022 (3)	Sweden	Healtcare
NDM-5	*K. pneumoniae*	2	2022 (2)	Ukraine	Healtcare
KPC	*K. pneumoniae*	2	2022 (2)	Ukraine	Healtcare
NDM-1	*K. pneumoniae*	2	2022(2)	Ukraine	Healtcare
NDM-1	*P. mirabilis*	2	2022 (2)	Ukraine	Healtcare
OXA-48	*K. pneumoniae*	2	2022 (2)	Spain	Healtcare
NDM-5	*E. coli*	2	2022 (2)	Pakistan/Sweden	Healtcare
Five pairwise linked clusters	Four *E. coli* One *K. pneumoniae*	5 * 2	2022 (10)	Country outside Sweden/Sweden	Family

Clusters and outbreaks

In 2022, fourteen clusters or pairwise linked cases of $ESBL_{CARBA}$ were confirmed based on SNP analysis (Table 3.4). Fifteen of the 24 cases with Ukraine as possible country of infection belonged to five cluster with 2-7 cases each. In the largest cluster, cases came from three different regions and were *K. pneumoniae* isolates with NDM-1+OXA-48 with sequence type (ST) 147. This combination and ST were also found in Germany with cases linked to Ukraine (Sandfort et al., 2022). One domestic cluster with $ESBL_{CARBA}$-producing *E. coli* with OXA-48 has been ongoing since 2020 with three additional cases early in 2023. Information on way of acquisition for these cases is still missing.

Comments

The number of $ESBL_{CARBA}$ cases is still low in Sweden. Increased travel abroad and further care in Sweden by Ukrainian patients partly explains the increase in 2022. The lack of information on the way of acquisition for nearly 50% of the domestic cases is worrisome. However, clusters can still be detected in the national surveillance program.

Escherichia coli, from blood and urine cultures

Results from 2022

- Number of reported cases with $ESBL_{CARBA}$-producing *E. coli*: 154
- Number of reported cases with bloodstream infections caused by $ESBL_{CARBA}$-producing *E. coli*: 10
- Number of reported cases with ESBL-producing *E. coli*: 8 110
- Number of reported cases with bloodstream infections caused by ESBL-producing *E. coli*: 605

Trends

The proportion of ESBL producing *E. coli* among invasive isolates, one of two AMR indicators, has increased continually over the years to the current 7% (Figure 3.9 and Figure 3.10). The proportion of resistance is in general higher among men while the resistance to carbapenems is still very low. Combined resistance to cefotaxime/ceftazidime and gentamicin/tobramycin or the combination piperacillin-tazobactam and gentamicin/tobramycin was 2.2% and 1.3% respectively (Table 3.5). The resistance levels remained stable among isolates from urine. Cefadroxil resistance, which can be used as an indicator for production of ESBL, remained at 6% (Figure 3.11)

Table 3.5. Proportion (%) of antibiotic resistant *E. coli* from blood or urine 2022. NA: Not Applicable.

Antibiotic	Blood isolates, % R (n=10 554)	Urine isolates, % R (n=223 039)
Ampicillin	NA	28.8
Cefadroxil	NA	6.2
Cefotaxime	7.3	NA
Ceftazidime	6.3	NA
Ciprofloxacin	13.8	10.5
Gentamicin	6.0	NA
Tobramycin	5.2	NA
Mecillinam	NA	4.2
Meropenem	0.0	NA
Nitrofurantoin	NA	1.2
Piperacillin-tazobactam	6.0[a]	NA
Trimethoprim	NA	18.6
Trimethoprim-sulphamethoxazole	18.7	NA
Combined resistance to Cefotaxime/ceftazidime + Gentamicin/tobramycin	2.2	NA
Combined resistance to both Piperacillin-tazobactam + Gentamicin/tobramycin	1.3	NA

[a]The resistance to piperacillin-tazobactam is presented based on the current breakpoints and historical data has been recalcutaled (NordicAST breakpoint table v 12.0).

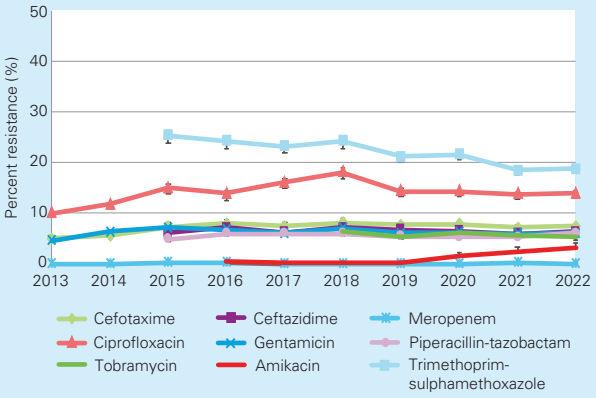
Comments

Among invasive isolates, the resistance to piperacillin-tazobactam is presented based on the current breakpoints and historical data has been recalcutaled (NordicAST breakpoint table v 12.0). Resistance to commonly prescribed oral antibiotics for treatment of urinary tract infections (UTI) caused by *E. coli* remained stable (Figure 3.11).

Resistance to ciprofloxacin is still high, and is now at approximately 14% and 10% for blood and urine isolates respectively (Table 3.5, Figure 3.10 and Figure 3.11). The increasing ciprofloxacin resistance seen during 2016-2017 can mostly be explained by a breakpoint change for ciprofloxacin. The age and gender distributions among patients with *E. coli* isolated from urine reflects the expected occurrence of UTI in the different groups. The high level of ciprofloxacin resistance must be considered when choosing empirical treatment for febrile UTI, especially among men in ages over 20 years (Figure 3.12).

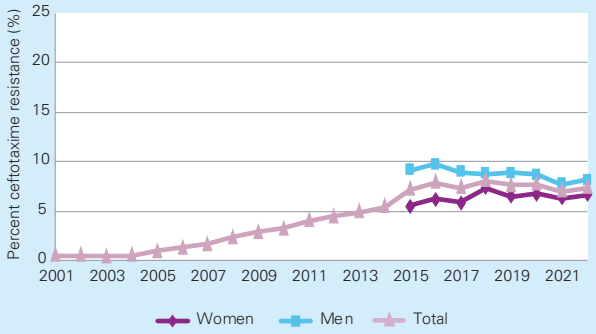
Colistin resistance is occasionally seen in *E. coli* as well as in *K. pneumoniae*, *P. aeruginosa* and *Acinetobacter*. This is mainly tested in multiresistant isolates most of which have a connection with healthcare abroad. It is important to determine colistin susceptibility with broth microdilution as recommended by EUCAST.

Figure 3.10. Antibiotic resistance in *E. coli* isolated from blood during the years 2013-2022. The numbers of AST isolates for all years and antibiotics ranges from 5 183 to 10 629. The exact numbers are given in the attached file.



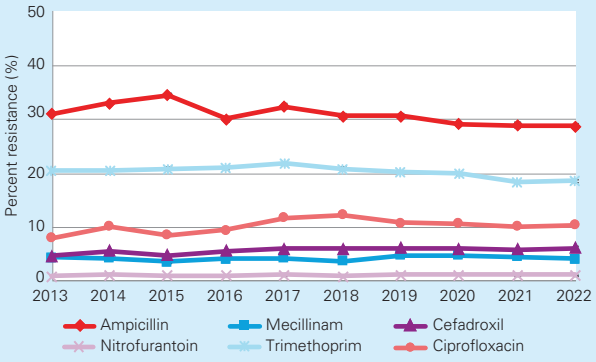
Source: The Public Health Agency of Sweden

Figure 3.9. Antibiotic resistance indicator displaying resistance to cefotaxime in *E. coli* (ESBL) isolated from blood from women and men during 2015-2022.



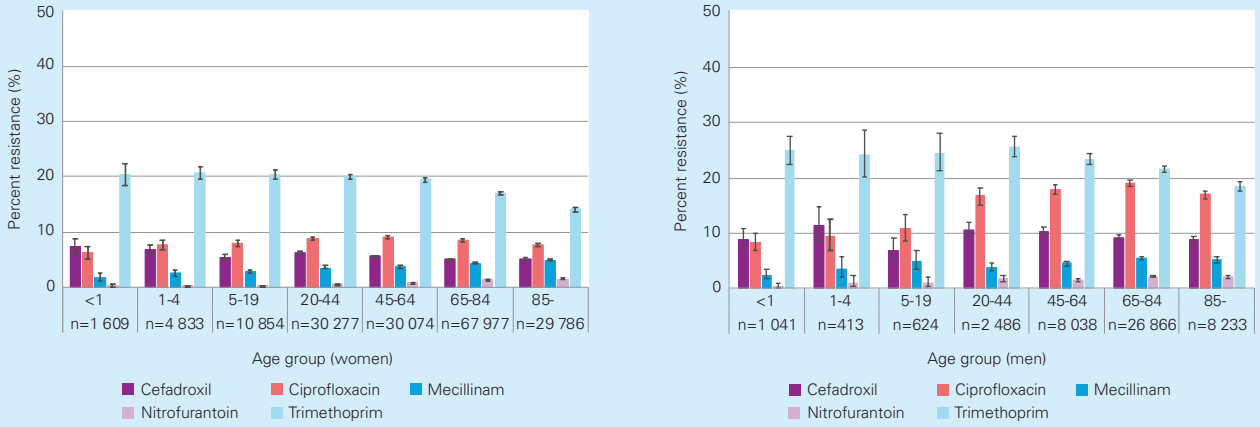
Source: The Public Health Agency of Sweden

Figure 3.11. Antibiotic resistance in *E. coli* isolates from urine during the years 2013-2022. The numbers of AST isolates for all years and antibiotics ranges from 6 417 to 223 039. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Figure 3.12. Antibiotic resistance in *E. coli* from urine in women and men divided in age groups during 2022.



Source: The Public Health Agency of Sweden

Klebsiella pneumoniae, from blood and urine cultures

Results from 2022

- Number of reported cases with $ESBL_{CARBA}$-producing *K. pneumoniae*: 85
- Number of reported cases with bloodstream infections caused by $ESBL_{CARBA}$-producing *K. pneumoniae*: 4
- Number of reported cases with ESBL-producing *K. pneumoniae*: 1030
- Number of reported cases with bloodstream infections caused by ESBL-producing *K. pneumoniae*: 122

Table 3.6. Proportion (%) of antibiotic resistant *K. pneumoniae* from blood or urine 2022. NA: Not Applicable.

Antibiotic	Blood isolates, % R (n=2 161)	Urine isolates, % R (n=24 477)
Cefadroxil	NA	6.3
Cefotaxime	6.7	NA
Ceftazidime	7.3	NA
Ciprofloxacin	12.3	9.6
Gentamicin	3.1	NA
Tobramycin	2.6	NA
Mecillinam	NA	8.3
Meropenem	0.2	NA
Piperacillin-tazobactam[a]	13.2	NA
Trimethoprim	NA	18.0
Trimethoprim-sulphamethoxazole	14.4	NA
Combined resistance to Cefotaxime/ceftazidime + Gentamicin/tobramycin	1.9	NA
Combined resistance to Piperacillin-tazobactam + Gentamicin/tobramycin	2.0	NA

[a]The resistance to piperacillin-tazobactam is presented based on the current breakpoints and historical data has been recalcutaled (NordicAST breakpoint table v 12.0).

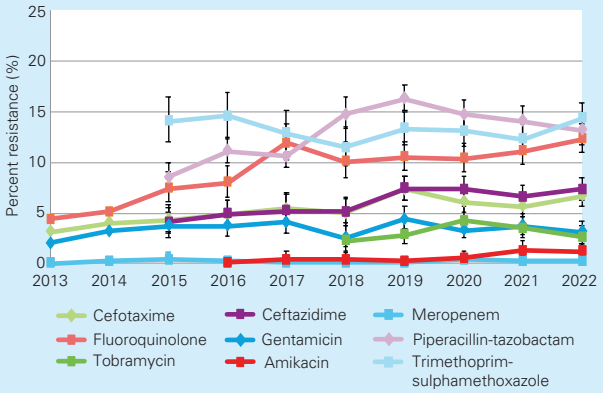
Comments

Among invasive isolates, the resistance levels remained stable for almost all antibiotics tested as well as for carbapenems where the resistance remains low. The resistance to piperacillin-tazobactam is presented based on the current breakpoints and historical data has been recalcutaled (NordicAST breakpoint table v 12.0). The resistance to cefotaxime was 6.7% and the combined resistance to cefotaxime/ceftazidime and gentamicin/tobramycin or the combination piperacillin-tazobactam and gentamicin/tobramycin was 1.9% and 2.0% respectively (Table 3.6 and Figure 3.13).

Resistance to commonly prescribed oral antibiotics for treatment of urinary tract infections caused by *K. pneumoniae* has remained relative stable during the last years (Figure 3.14). Cefadroxil resistance, which can be used as an indicator for production of ESBL, was 6.3%. The high increase in ciprofloxacin resistance seen during 2016-2017 can mostly be explained by a breakpoint change for ciprofloxacin. As for *E. coli*, the high levels of resistance to ciprofloxacin must be taken into account when choosing empiric treatment for febrile UTI.

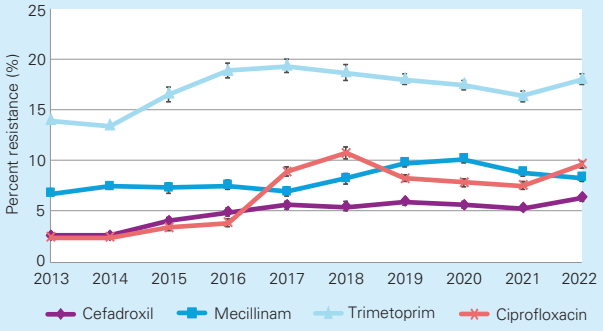
Colistin resistance is occasionally seen in *E. coli* as well as in *K. pneumoniae*, *P. aeruginosa* and *Acinetobacter*. This is mainly tested in multiresistant isolates most of which have a connection with healthcare abroad. It is important to determine colistin susceptibility with broth microdilution as recommended by EUCAST.

Figure 3.13. Antibiotic resistance in *K. pneumoniae* isolated from blood during the years 2013-2022. The numbers of AST isolates for all years and antibiotics ranges from 973 to 2 161. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Figure 3.14. Antibiotic resistance in *K. pneumoniae* isolates from urine during the years 2013-2022. The numbers of AST isolates for all years and antibiotics ranges from 2 499 to 24 477. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Staphylococcus aureus including MRSA

Mandatory reporting of methicillin-resistant *Staphylococcus aureus*

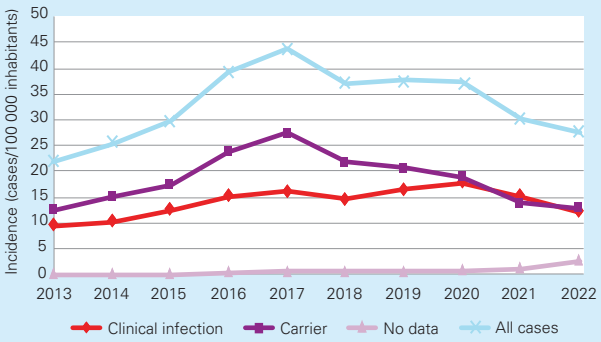
Results from 2022

- Number of reported cases: 3 340 (previous year 2 895), relative change +15%
- Number of bloodstream infections: 96 (previous year 97)

Trends

In 2022, the incidence of MRSA was 32 cases per 100 000 inhabitants compared to 28 cases per 100 000 inhabitants in 2021 (Figure 3.15). The number of cases reported with clinical infections were 1 566 (47%) while 1 575 cases (47%) were listed as carriers.

Figure 3.15. The incidence (cases/100 000 inhabitants) of cases with MRSA in relation to type of infection, year 2013-2022.



Source: The Public Health Agency of Sweden

There was almost equal distribution between women and men, with a median age of 33 for all cases. Among the domestic MRSA cases (n=2 008, 60%), the incidence was highest for children below one year of age (n=183, 174 cases/100 000 inhabitants) followed by the elderly, 85 years or older (n=185, 68 cases/100 000 inhabitants). The high incidence of MRSA among the young children is likely due to screening practices at neonatal- and maternal care units in combination with contact tracing around new cases.

Community-acquired infections continue to be the most prominent route of acquiring MRSA. Among MRSA cases acquired in Sweden, 28% (n=571) were reported as acquired from family/household contacts and 19% as community-acquired (n=380). The proportion of domestic cases with MRSA acquired in hospital as well as healthcare/care outside hospital was 5% and 10% respectively (n=100 and n=193) which is nearly the same as in year 2020 and 2021. A third (n=727) of the domestic cases lacked information on acquisition.

Epidemiological typing of MRSA

Epidemiological typing of MRSA has since 2006 included *spa*-typing and analysis of PVL-status. Since January 2018, the national microbiological surveillance of MRSA only includes isolates from clinical cases. In addition to the surveillance program, typing data is also obtained from regional microbiological laboratories. Typing data were available for isolates from 1 129 (72%) of the clinical cases and for 713 isolates (45%) sampled from asymptomatic carriers. The ten most common *spa*-types were found in 49% of the clinical cases. The top five *spa*-types in 2022, t304, t002, t127, t008 and t223 have been in top five since 2018 although the order has varied.

Clusters and outbreaks

During the year, the Public Health Agency commissioned whole-genome sequencing of around thirty MRSA isolates in fourteen different investigations where spa-typing did not provide a sufficiently high resolution. With the help of the results, probable spread of infection could be established for nine of the investigations, one of which concerned two additional isolates/patients in a cluster originating in 2019.

Comments

The incidence of MRSA in Sweden increased in 2022 compared to 2021 but is still lower than the period before the pandemic. The number of cases with MRSA in blood increased at the beginning of the pandemic but has since been stable.

Staphylococcus aureus from blood and skin and soft tissue cultures

Results from 2022

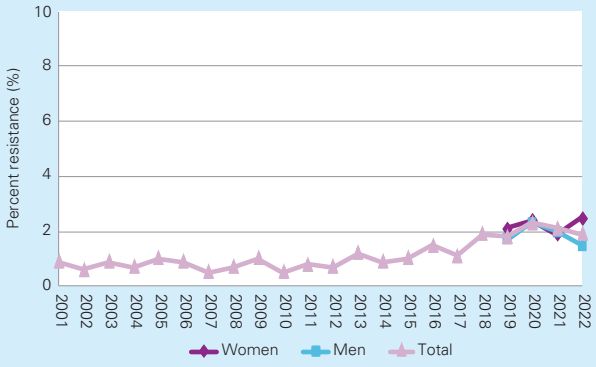
- Number of cases with MRSA reported: 3 340
- Number of cases with bloodstream infections caused by MRSA: 96
- The proportion of MRSA among *S. aureus* isolated from blood has decreased to 1.9%, compared to 2.0% 2021.

Table 3.7. Proportion (%) of antibiotic resistant isolates in *S. aureus* from blood and skin and soft tissue infections 2022.
NA: Not Applicable.

Antibiotic	Blood isolates, % R (n=7 797)	Skin and soft tissue isolates % R (n=79 439)
Cefoxitin	1.9	2.3
Clindamycin	4.8	5.7
Erythromycin	5.1	6.0
Gentamicin	0.8	NA
Tobramycin	1.8	NA
Fluoroquinolone[a]	3.0	NA
Fusidic acid	NA	2.9
Linezolid	0.04	NA
Rifampicin	0.7	NA
Trimetoprim-sulphamethoxazole	0.2	NA

[a]Based on norfloxacin.

Figure 3.16. One of the indicators for antibiotic resistance that shows the proportion of MRSA among *S. aureus* isolated from blood from women, men and in total.



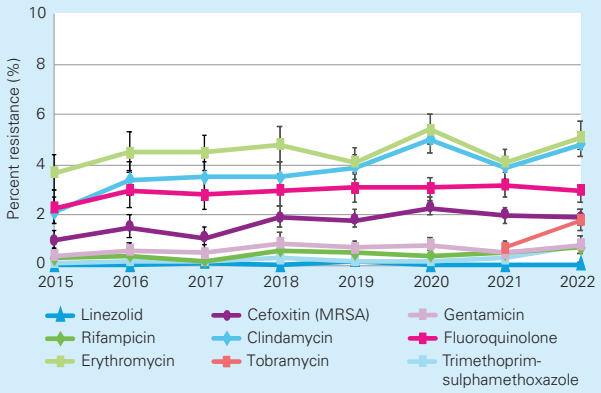
Source: The Public Health Agency of Sweden

Comments

MRSA in bloodstream infections, one of two AMR indicators, has slowly increased and is now 1.9% of isolated *S. aureus* (indicated by cefoxitin resistance) the proportion of resistance (%) was 2.1% among men and 2.5% among women (Figure 3.16 and Figure 3.17) and the same proportion is seen for

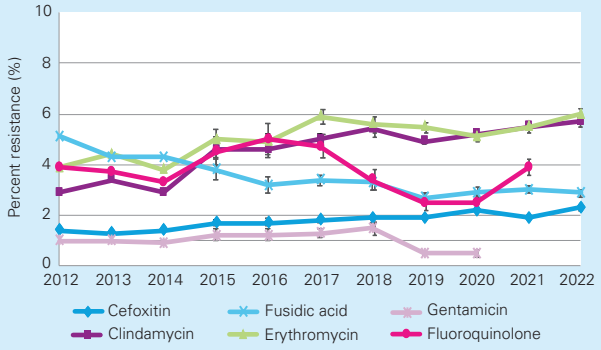
skin and soft tissue infections (Table 3.7 and Figure 3.18). For MRSA susceptibility testing to vancomycin is not routinely performed on cefoxitin-susceptible *S. aureus* and in 2022, 199 out of 7 797 (2.5%) isolates from blood were tested for vancomycin resistance with no resistance detected.

Figure 3.17. Antibiotic resistance in *S. aureus* from blood during the years 2013-2022. The numbers of AST isolates for all years and antibiotics ranges from 3 028 to 7 797. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Figure 3.18. Antibiotic resistance for *S. aureus* from skin and soft tissue samples 2013-2022. The resistance for norfloxacin is based on results from less than five laboratories in 2018-2020 and for gentamicin in 2020. In 2022, data for aminoglycosides and fluoroquinolone may be found in the attached file (not shown in graph) since the resistance rates are based on less than five laboratories. The numbers of AST isolates for all years and antibiotics ranges from 5 343 to 79 904. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Enterococcus faecalis and *Enterococcus faecium* including VRE

Mandatory reporting of vancomycin-resistant enterococci

Results from 2022

- Total number of reported cases: 236 (previous year: 209), relative change +13%.
- Number of reported cases of *E. faecium* with vancomycin resistance: 227 (previous year: 204), relative change +11%
- Number of reported cases of *E. faecalis* with vancomycin resistance: 4 (previous year: 1)
- There were five cases infected with both *E. faecium* and *E. faecalis*.
- Number of bloodstream infections: 5 (previous year: 2)

Trends

The national incidence of VRE increased from 2.0 to 2.2 cases per 100 000 inhabitants between 2021 and 2022. Seventeen out of twenty-one regions reported cases of VRE during 2022. Out of these cases, 186 (79%) were healthcare related. A majority of the isolates (n=164, 69%) were from faeces, and only 7% from urine, wound or other clinical samples (Figure 3.19). Five invasive VRE infections were reported in 2022. More than half of the cases were reported as acquired in Sweden (58%) and among the domestic cases 42% were found through contact tracing and 43% through screening. Cases acquired abroad were detected mostly through screening (84%). The median age for VRE was 63 years and it is still most common among men, 55%. In 2022, 227 *E. faecium* cases and 4 *E. faecalis* cases were reported. The *vanA* genotype was most commonly found (n=181) (Figure 3.20). In some cases, different genotypes of VRE were detected in the same patient and therefore a few more isolates than cases were epidemiologically typed.

Clusters and outbreaks

Whole genome sequencing (WGS) with "single nucleotide polymorphism" (SNP) based analysis and multilocus sequence typing (MLST) is used for epidemiological typing of VRE. The national VRE cluster nomenclature is accordingly: species (Efm = *E. faecium*, Efs = *E. faecalis*) followed by *van*-gene (A or B), year of detection and a consecutive number for respective type found each year, e.g. SE-EfmB-1707. Isolates with no relation to other VRE isolates in the national database are denoted as unique (EfmA unique).

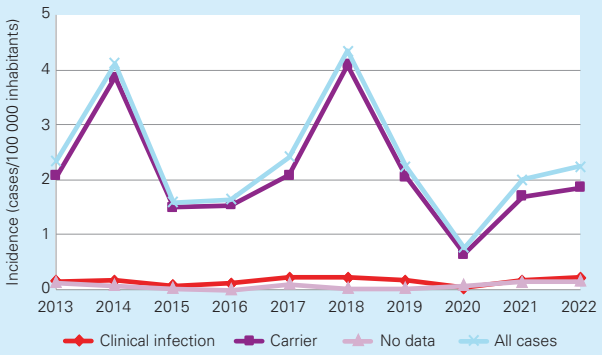
In 2022, six large hospital-related outbreaks with 8-28 cases each and ten smaller clusters with 2-8 cases each were identified, all *E. faecium* (Figure 3.21). Two of the large outbreaks were reported from region Gävleborg (SE-EfmA-2110 and SE-EfmA-2204) of which one was identified in April 2022 and still ongoing at the turn of the year 2022/2023. The remaining four outbreaks were reported from region Blekinge (SE-EfmA-2211), region Kalmar (SE-EfmB-2212), region Västra Götaland (SE-EfmA-2214) and region Östergötland (SE-EfmA-2108).

The five invasive cases were all caused by *E. faecium*, three carrying *vanA*, of which one was vancomycin-variable enterococci (VVE), and two carrying *vanB*. All isolates were determined as unique. Genes connected to linezolid-resistance were detected in five isolates, none of them from invasive cases.

Comments

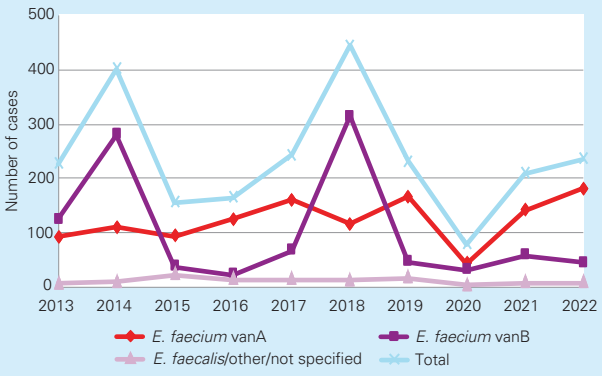
The number of VRE cases increased with 13% during 2022. This increase was mainly due to several hospital related outbreaks. This stresses the importance of preventing spread of VRE in hospitals. The number of invasive cases increased to five compared to two cases last year. None of the invasive cases were part of hospital clusters. Epidemiological typing of VRE is an important tool to monitor and investigate the spread of VRE. Culture and typing results are often necessary to initiate and motivate the extensive work needed to stop outbreaks of VRE.

Figure 3.19. The incidence (cases/100 000 inhabitants) of VRE in relation to type of infection, year 2013-2022.



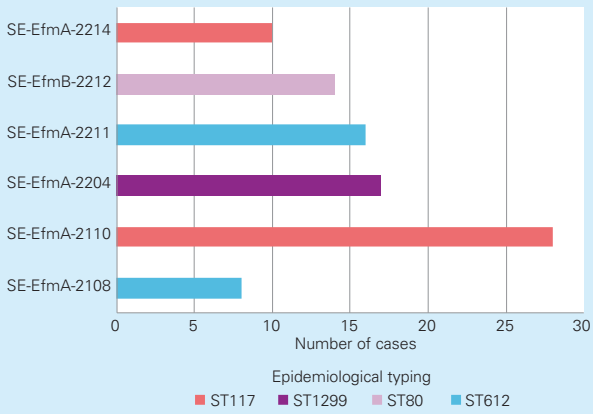
Source: The Public Health Agency of Sweden

Figure 3.20. Number of VRE cases and their corresponding van-type, year 2013-2022.



Source: The Public Health Agency of Sweden

Figure 3.21. Number of VRE cases within the six largest hospital-related outbreaks in 2022 and their respective sequence type.



Source: The Public Health Agency of Sweden

Enterococcus faecalis and *Enterococcus faecium*, from blood cultures

Results from 2022

- Total number of reported cases: 236 (previous year: 209), relative change +13%.
- Number of reported cases of *E. faecium* with vancomycin resistance: 227 (previous year: 204), relative change +11%
- Number of reported cases of *E. faecalis* with vancomycin resistance: 4 (previous year: 1)
- There were five cases infected with both *E. faecium* and *E. faecalis*.
- Number of bloodstream infections: 5 (previous year: 2)

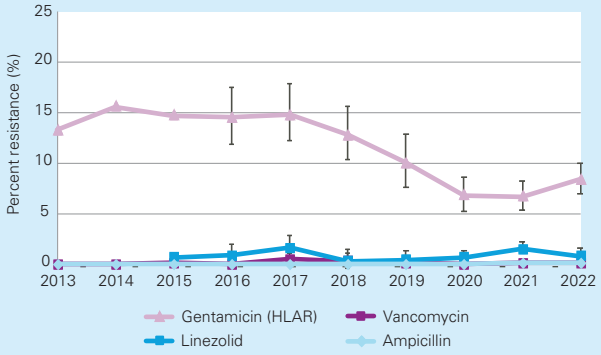
Table 3.8. Proportion (%) of antibiotic resistant *E. faecalis* and *E. faecium* isolated from blood 2022.

Antibiotic	Blood isolates *E. faecalis*, % R (n = 1 571)	Blood isolates *E. faecium*, % R (n = 1 021)
Ampicillin	0.1	84.3
Gentamicin (HLAR)	8.4	8.3
Linezolid	0.8	1.2
Vancomycin	0.1	0.3

Comments

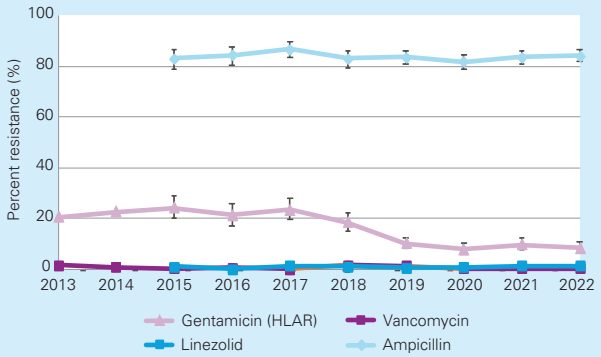
The vancomycin resistance among invasive isolates remains low and was 0.1% for *E. faecalis* and 0.3% for *E. faecium* in 2022. High-level aminoglycoside resistance (HLAR) has decreased since 2017 and seems to have reached a plateau (Table 3.8 and Figures 3.22 and 3.23).

Figure 3.22. Antibiotic resistance in *E. faecalis* isolated from blood during the years 2013-2022. The numbers of AST isolates for all years and antibiotics ranges from 685 to 1 633. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Figure 3.23. Antibiotic resistance in *E. faecium* isolated from blood during the years 2013-2022. The numbers of AST isolates for all years and antibiotics ranges from 368 to 1 021. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Streptococcus pneumoniae including PNSP

Mandatory reporting of *Streptococcus pneumoniae* with reduced susceptibility to penicillin (PNSP)

Results from 2022

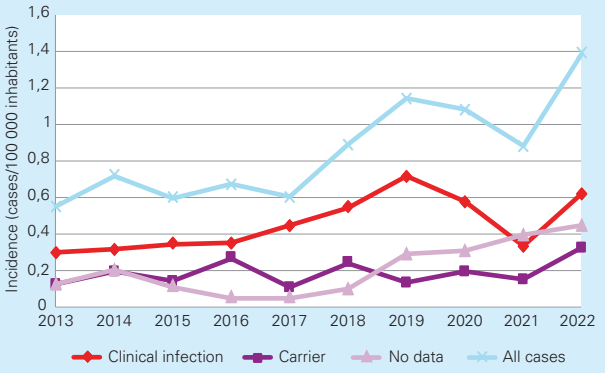
- Number of reported cases: 146 (previous year 92), relative change +59%
- Number of bloodstream infections: 9 (previous year 3)

In November 2019, EUCAST posted a warning against the use of gradient tests for benzylpenicillin MIC in *S. pneumoniae*. Gradient tests were found to frequently underestimate MIC especially in the area around the R breakpoint (0.5 – 4 mg/L). Laboratories using gradient tests must be aware of this and MIC of 0.5 – 2 mg/L should be verified with broth microdilution. This can possibly lead to some underreporting of PNSP cases since *S. pneumoniae* with benzylpenicillin MIC over 1 mg/L is mandatory to report in Sweden.

Trends

The national incidence of PNSP (MIC PcG> 1mg/L) increased from 0.9 to 1.4 cases per 100 000 inhabitants between 2021 and 2022. The incidence for PNSP acquisition was highest among children under five years of age (7.5 cases per 100 000 inhabitants) representing 29% of all cases. Of all cases, 57% were men and 43% women. PNSP was most often found in cultures from the nasopharynx (47%). Nineteen isolates were found in sputum/ bronchoalveolar lavage (25%). Sixty-five cases were reported with clinical infections (45%, incidence 0.6) and 23% (n=34, incidence 0.3) as carriers (Figure 3.24). A majority of the cases had been acquired in Sweden (61%, n=89) and four percent of the cases were acquired abroad. For the remaining cases, no country of acquisition was given (35%).

Figure 3.24. The incidence (cases/100 000 inhabitants) of cases with PNSP in relation to type of infection, year 2013-2022.



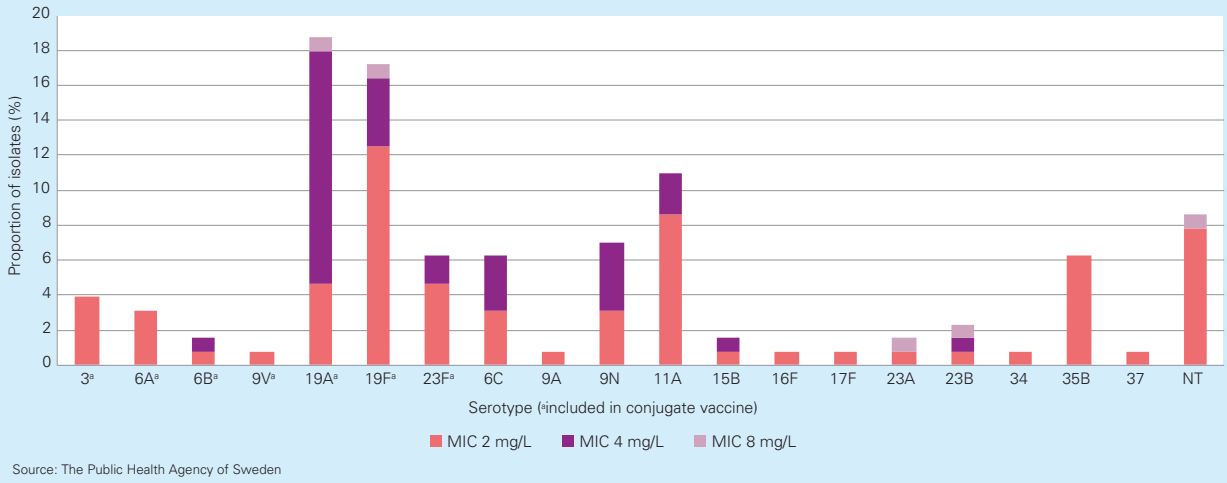
Source: The Public Health Agency of Sweden

Epidemiological typing of PNSP

A total of 128 isolates with PcG MIC > 1 mg/L were sent to PHAS for serotyping during 2022 (88% of notified cases). Of these isolates, 52% (n=66) belonged to serotypes included in the conjugate vaccines (PCV10 and/or PCV13); Figure 3.25. The corresponding figures for 2021 and 2020 were 45% and 44% respectively. Five of the nine isolates from invasive cases typed in 2022 were of vaccine type: 3 (n=1), 19A (n=3) and 19F (n=1). The remaining four cases were of type 9N (n=3) and 11A (n=1), i.e. not included in the vaccines.

To follow and evaluate the effect of vaccination against pneumococcal disease and to identify spread of antibiotic resistant clones, PHAS collects isolates of *S. pneumoniae* with PcG MIC ≥ 0.5 mg/L for serotyping. In 2022, 257 isolates were collected (including the 128 isolates from cases of PNSP). The serotype distribution were, in decending order: 19A (17%), 19F (15%), NT (13%), 11A (8%), 35B (7%), 9N

Figure 3.25. Distribution of serotype MICs among PNSP with PcG MIC > 1 mg/L (n=128).



Source: The Public Health Agency of Sweden

(6%) 23B (5%), 23F (4%), 6C (3%), and 3 (3%). Of the 257 isolates, 45% constituted of types included in the conjugate vaccines (PCV10 and/or PCV13).

Clusters and outbreaks

During 2022, a small spread (n=11) with a *S. pneumoniae* of serotype 19A was found through contact tracing connected to a childrens day care center.

Comments

The number of PNSP cases increased with 59% during 2022. The number of invasive cases increased to nine compared to three cases last year. Overall, the incidence of PNSP has remained fairly stable up to 2017 after the case definition was changed in May 2012 (Figure 3.24). The increase from 2017 could partly be due to changes in diagnostics, as more laboratories have switched to reporting data based on broth microdilution.

Streptococcus pneumoniae, from blood

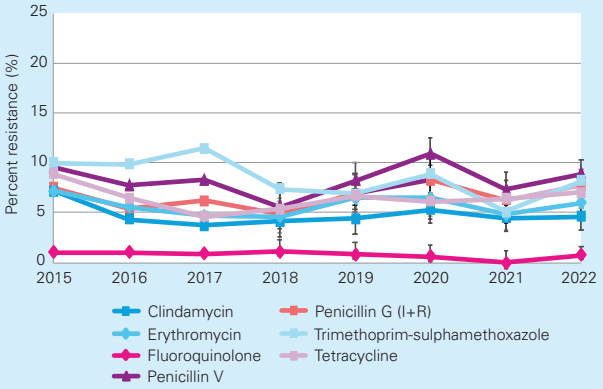
Results from 2022

- Number of reported cases of PNSP: 146 cases
- Cases with bloodstream infections caused by PNSP: 9
- Number of reported cases of invasive pneumococcal disease: 1 270

Comments

The methodological problem with underestimation of benzylpenicillin (PcG) MIC when using gradient tests does not influence the resistance proportions since I and R are reported together. Among invasive infections, the proportion of PcG non-susceptible isolates was 7.7% in 2022 (Figure 3.26).

Figure 3.26. Antibiotic resistance in *S. pneumoniae* isolated from blood during the years 2015-2022. Penicillin V resistance is based on susceptibility testing using oxacillin. The numbers of AST isolates for all years and antibiotics ranges from 550 to 1 153. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Haemophilus influenzae, from blood and nasopharynx cultures

Results from 2022

- Number of reported cases of invasive *H. influenzae*: 224

Table 3.9. Proportion (%) of antibiotic resistant *H. influenzae* from blood or nasopharynx 2022.

Antibiotic	Blood isolates, % R (n = 183)	Nasopharynx isolates, % R (n =11 086)
Ampicillin/ Amoxicillin	28.2	28.2
Cefotaxime	3.1	1.7
Fluoroquinolone[a]	0.7	0.9
Screen betalactam-resistance (PcG 1)	32.3	36.6
Tetracycline	1.4	0.4
Trimethoprim-sulphamethoxazole	21.3	29.5

[a]Nalidixic acid was used for detection of fluoroquinolone resistance.

Trends

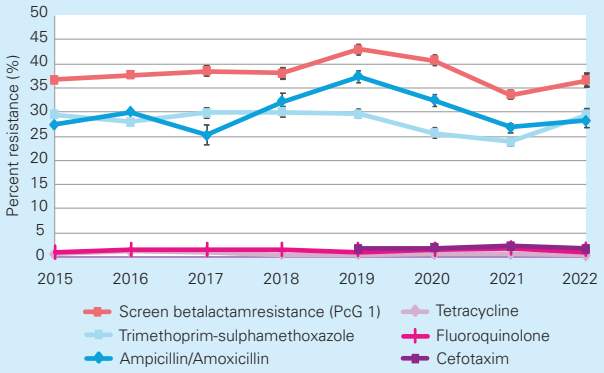
During 2022, 43 isolates were received within the microbiological characterisation program for cephalosporin resistance in *H. influenzae* at PHAS. The majority of these (n=35) showed high-level resistance to extended-spectrum cephalosporins, caused by alterations in penicillin-binding protein 3 (PBP3). Seven of these isolates also carried the betalactamase $bla_{\text{TEM-1}}$ gene which is the most prevalent gene of the acquired betalactamases. The remaining eight isolates showed lower level resistance to cephalosporins. One of the isolates also had genetic mutations in known genes that can give rise to fluoroquinolone resistance.

Five smaller clusters were detected during 2022.

Comments

Invasive isolates of *H. influenzae* are notifiable according to the Communicable Disease Act regardless of antibiotic resistance. The cefotaxime resistance among invasive isolates is still low (Table 3.9 and Table 3.10). Among respiratory isolates, the resistance levels were decreasing during the pandemic but are now starting to increase again (Figure 3.27).

Figure 3.27. Antibiotic resistance in *H. influenzae* isolated from nasopharynx during the years 2015-2022. The numbers of AST isolates for all years and antibiotics ranges from 2 460 to 13 332. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Table 3.10. Antibiotic resistance in *H. influenzae* isolated from blood during the years 2015-2022. The numbers of AST isolates for all years and antibiotics ranges from 73 to 209. The exact numbers are given in the attached file.

Species *Haemophilus influenzae*	2015			2016			2017			2018			2019			2020			2021			2022		
Sample: Blood	**n**	**% R[a]**	**95% CI**	**n**	**% R[a]**	**95% CI**	**n**	**% R[a]**	**95% CI**	**n**	**% R[a]**	**95% CI**	**n**	**% R[a]**	**95% CI**	**n**	**% R[a]**	**95% CI**	**n**	**% R[a]**	**95% CI**	**n**	**% R[a]**	**95% CI**
Number of AST isolates	**109**			**78**			**122**			**111**			**209**			**74**			**73**			**183**		
Screen betalactam-resistance (PcG 1)	109	36.7	(28.2-46.1)	78	33.3	(23.9-44.4)	120	26.7	(19.6-35.2)	111	36	(27.7-45.3)	208	34.1	(28.0-40.8)	60	50.0	(37.7-62.3)	67	26.9	(17.7-38.5)	164	32.3	(25.6-39.8)
Trimetoprim-sulphamethoxazole	109	19.3	(13.0-27.7)	78	21.8	(14.1-32.2)	121	14	(9.0-21.4)	111	12.6	(7.7-20.1)	209	23.9	(18.6-30.1)	74	12.2	(6.5-21.5)	72	13.9	(7.7-23.7)	183	21.3	(16.0-27.8)
Tetracycline	109	0.9	(0.2-5.0)	78	1.3	(0.2-6.9)	122	0.8	(0.1-4.5)	109	0.0	(0.0-3.4)	181	0.6	(0.1-3.1)	58	3.4	(1.0-11.7)	59	0.0	(0.0-6.1)	144	1.4	(0.4-4.9)
Ampicillin	83	22.9	(15.2-33.0)	56	26.8	(17.0-39.6)	40	20	(10.5-34.8)	34	29.4	(16.8-46.2)	157	34.4	(27.4-42.1)	64	43.8	(32.3-55.9)	55	25.5	(15.8-38.3)	142	28.2	(21.4-36.1)
Cefotaxime	91	3.3	(1.1-9.2)	69	0.0	(0.0-5.3)	103	1.0	(0.2-5.3)	90	2.2	(0.6-7.7)	178	2.8	(1.2-6.4)	67	3.0	(0.8-10.2)	53	1.9	(0.3-9.9)	159	3.1	(1.3-7.1)
Fluoroquinolone	88	1.1	(0.2-6.2)	55	1.8	(0.3-9.6)	89	1.1	(0.2-6.1)	75	0.0	(0.0-4.9)	160	0.0	(0.0-2.3)	44	2.3	(0.4-11.8)	73	5.5	(2.2-13.3)	134	0.7	(0.1-4.1)
Cefaclor													98	30.6	(22.4-40.3)	35	28.6	(16.3-45.1)	NA	NA	NA	NA	NA	NA

[a]From 2014 the resistance is expressed as % of isolates tested

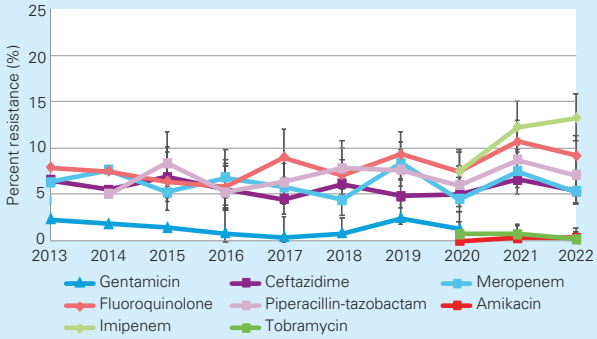
Pseudomonas aeruginosa, from blood and non-respiratory cultures

Results from 2022

Table 3.11. Proportion (%) of antibiotic resistant *P. aeruginosa* isolated from blood and non-respiratory specimens 2022. NA: not applicable.

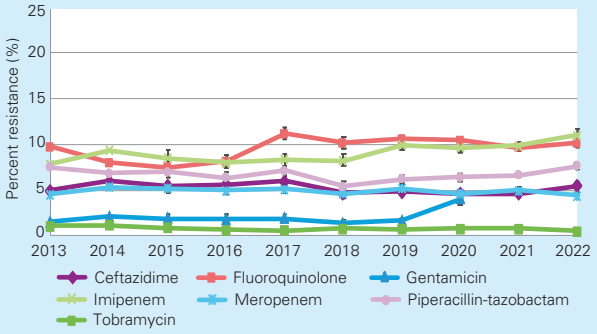
Antibiotic	Blood isolates, % R (n = 852)	Non-respiratory isolates, % R (n=18 832)
Ceftazidime	5.4	4.6
Ciprofloxacin	9.2	9.6
Gentamicin	NA	NA
Tobramycin	0.2	0.8
Meropenem	5.3	5.0
Piperacillin-tazobactam	7.1	6.6

Figure 3.28. Antibiotic resistance in *P. aeruginosa* isolated from blood during the years 2013-2022. The numbers of AST isolates for all years and antibiotics ranges from 348 to 852. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Figure 3.29. Antibiotic resistance in *P. aeruginosa* from non-respiratory isolates 2013-2022. Results for gentamicin are only available until 2020. The numbers of AST isolates for all years and antibiotics ranges from 1 980 to 18 832. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Comments

Resistance to ceftazidime is most often due to efflux pumps and porin loss, not ESBL production. The resistance for most antibiotics is stable for both blood isolates and non-respiratory isolates (Table 3.11, Figure 3.28 and Figure 3.29). Tobramycin has replaced gentamicin as recommended aminoglycoside. Colistin resistance is occasionally seen in *E. coli* as well as in *K. pneumoniae*, *P. aeruginosa* and *Acinetobacter*. This is mainly tested in multiresistant isolates most of which have a connection with healthcare abroad. It is important to determine colistin susceptibility with broth microdilution as recommended by EUCAST.

Acinetobacter spp., from blood cultures

Results from 2022

Table 3.12. Antibiotic resistance in *Acinetobacter* species isolated from blood.

Species *Acinetobacter*	2014		2015		2016			2017			2018			2019			2020			2021			2022		
Sample: Blood	n	% R	n	% R	n	% R	95% CI	n	% R	95% CI	n	% R	95% CI	n	% R	95% CI	n	% R	95% CI	n	% R	95% CI	n	% R	95% CI
Number of AST isolates	**59**		**84**		**54**			**54**			**55**			**113**			**126**			**138**			**151**		
Meropenem	59	3.4	85	2.4	53	1.9	(0.3-9.9)	53	0.0	(0.0-6.8)	54	3.7	(1.0-12.5)	113	3.5	(0.9-7.5)	125	7.2	(3.8-13.1)	133	0.8	(0.1-4.1)	151	1.3	(1.8-8.4)
Ciprofloxacin			84	4.8	54	5.6	(1.9-15.1)	54	0.0	(0.0-6.6)	55	7.3	(2.9-17.3)	113	8.0	(4.2-14.4)	126	7.1	(3.8-13.0)	137	1.5	(0.4-5.2)	149	2.0	(0.7-5.8)
Trimethoprim-sulphamethoxazole			83	6.0	53	5.7	(1.9-15.4)	54	0.0	(0.0-6.6)	55	3.6	(1.0-12.3)	112	4.5	(1.9-10.0)	126	9.5	(5.5-15.9)	138	7.3	(4.0-12.8)	149	4.0	(1.9-8.5)
Gentamicin			66	3.0	43	7.0	(2.4-18.6)	51	0.0	(0.0-7.0)	49	6.1	(2.1-16.5)	72	6.9	(3.9-17.0)	90	11.1	(6.1-19.3)	111	5.4	(2.5-11.3)	94	2.3	(0.6-8.0)
Tobramycin														67	0.0	(0.0-5.4)	65	12.3	(6.4-22.5)	75	2.7	(0.7-9.2)	79	1.3	(0.2-6.8)
Amikacin														65	7.7	(3.3-16.8)	61	11.5	(5.7-21.8)	66	1.5	(0.3-8.1)	78	3.8	(1.3-10.7)

Comments

During 2022, a total of 151 isolates of *Acinetobacter* spp. from blood was reported to Svebar. The carbapenem resistance was 1.3% (Table 3.12). Bloodstream infections caused by *Acinetobacter* spp. are still rare in Sweden compared to other countries in Europe where multiresistant *Acinetobacter* spp. is a problematic pathogen in hospitals. Colistin resistance is occasionally seen in *E. coli* as well as in *K. pneumoniae*, *P. aeruginosa* and *Acinetobacter*. This is mainly tested in multiresistant isolates most of which have a connection with healthcare abroad. It is important to determine colistin susceptibility with broth microdilution as recommended by EUCAST.

Streptococcus pyogenes, from blood cultures

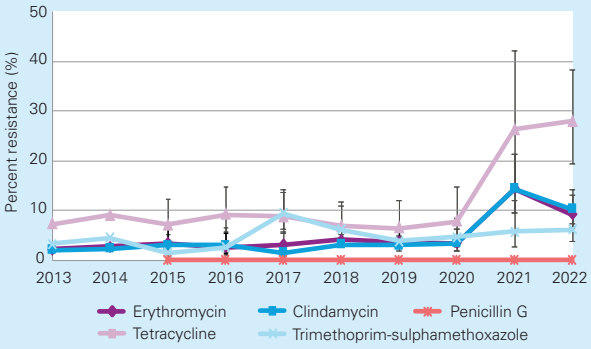
Results from 2022

- Number of reported cases of invasive *S. pyogenes*: 157

Comments

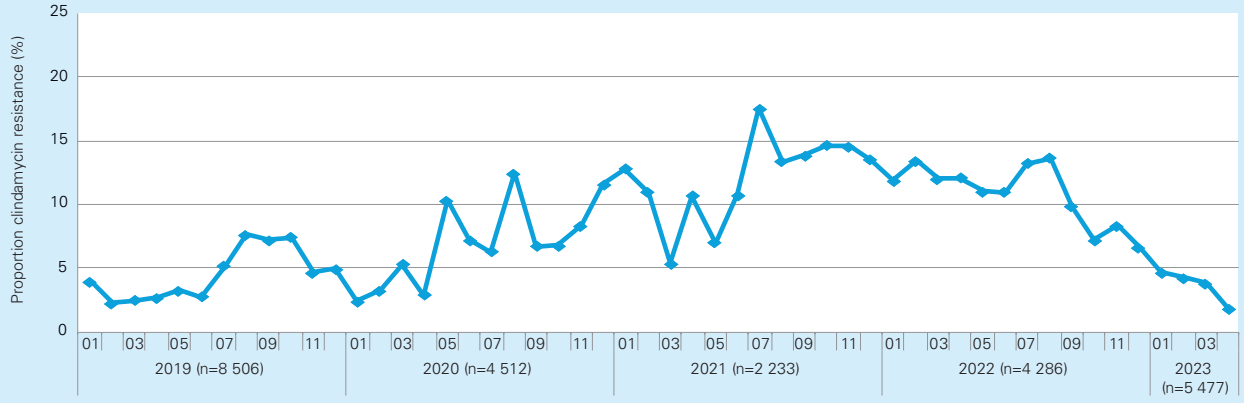
Invasive cases of *S. pyogenes* are notifiable according to the Communicable Disease Act and in 2022, 369 cases were reported. This is a large increase compared with previous year (n=157) and the number of cases increased during the second half of 2022. AST results from 294 isolates were available from Svebar (Figure 3.30). Some laboratories did not test susceptibility for trimethoprim-sulphamethoxazole and tetracycline. The variation in resistance during 2021 should be interpreted with caution since there is a small number of tested isolates. An increase in resistance to clindamycin starting in the spring of 2020 has been noted (Figure 3.31), during the fall 2022 the resistance returned to previous levels, below 5%.

Figure 3.30. Antibiotic resistance in *S. pyogenes* (GAS) from bloodstream isolates during the years 2013-2022. The numbers of AST isolates for all years and antibiotics ranges from 139 to 539. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Figure 3.31. Antibiotic resistance in *S. pyogenes* (GAS) in isolates from total number of cultures during the years 2019 to April 2023. The numbers of AST isolates for all years ranges from 2 233 to 8 506.



Source: The Public Health Agency of Sweden

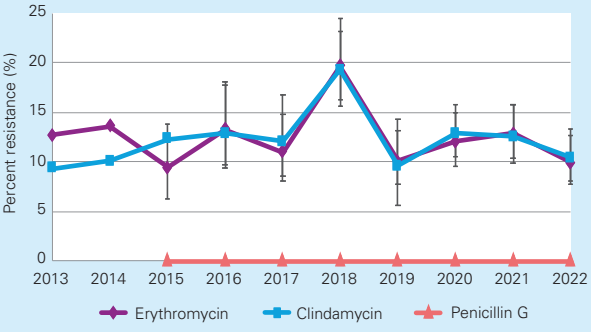
Streptococcus agalactiae, from blood cultures

Results from 2022

Comments

S. agalactiae is not included in the Communicable Disease Act. It is an important pathogen in the context of pregnancy and childbirth and can cause serious infections among others as well, mainly elderly with predisposing disease. Resistance to erythromycin and clindamycin is is now 10% (Figure 3.32).

Figure 3.32. Antibiotic resistance in *S. agalactiae* (GBS) from bloodstream isolates during the years 2013-2022. The numbers of AST isolates for all years and antibiotics ranges from 184 to 607. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Shigella species

Mandatory reporting of *Shigella*

Results from 2022

- Total number of reported cases: 434 (previous year: 187)
- Number of bloodstream infections: 1 (previous year: 5)

The increased number of reported cases during 2022 are mainly due to cases infected abroad. In 72 percent of the cases, the infection were reported as acquired abroad, and in 20 percent reported as acquired in Sweden. The number of reported cases have otherwise increased during the previous years before 2020, partly explained by a shift in the microbiological method of detection used, where nucleic acid amplification tests are more utilised.

In 2022, 52 cases with *Shigella* were also mandatory notified as ESBL-producing Enterobacterales. Of the 35 cases with known ESBL-type, 34 had $ESBL_A$ and one $ESBL_M$. No case with *Shigella* carrying $ESBL_{CARBA}$ were reported during 2022.

Table 3.13. Antibiotic resistance in *Shigella* spp. from faecal samples 2017-2022. Data for azithromycin is not shown for 2021-2022 due to the low number of tested samples. The numbers of AST isolates for all years and antibiotics ranges from 40 to 242.

Species *Shigella* spp.	2017			2018			2019			2020			2021			2022		
Sample: Faeces	**n**	**% R**	**95% CI**	**n**	**% R**	**95% CI**	**n**	**% R**	**95% CI**	**n**	**% R**	**95% CI**	**n**	**% R**	**95% CI**	**n**	**% R**	**95% CI**
Number of AST isolates	**112**			**179**			**242**			**63**			**65**			**151**		
Ciprofloxacin	111	11.7	(7.0-19.0)	174	25.3	(19.4-32.2)	242	14.5	(10.6-19.4)	63	22.2	(13.7-33.9)	65	21.5	(13.3-33.0)	151	23.2	(17.2-30.5)
Trimetoprim-sulphamethoxazole	111	76.6	(67.9-83.5)	179	80.4	(74.0-85.6)	240	71.7	(65.7-77.0)	63	73.0	(61.0-82.4)	65	69.2	(57.2-79.1)	152	73.0	(65.5-79.4)
Cefotaxime	112	14.3	(9.0-22.0)	173	25.4	(19.5-32.4)	235	19.1	(14.6-24.7)	62	11.3	(5.6-21.5)	64	32.8	(22.6-45.0)	151	33.8	(26.7-41.6)
Ceftazidime	112	2.7	(0.9-7.6)	173	3.5	(1.6-7.4)	234	3.4	(1.7-6.6)	61	3.3	(0.9-11.2)	64	6.2	(2.5-15.0)	151	7.9	(4.6-13.4)
Meropenem	93	0.0	(0.0-4.0)	145	0.0	(0.0-2.6)	204	0.0	(0.0-1.8)	55	0.0	(0.0-6.5)	51	0.0	(0.0-7.0)	140	0.0	(0.0-2.7)
Azithromycin	78	12.8	(7.1-22.0)	107	15	(9.4-22.9)	168	7.1	(4.1-12.1)	52	17.3	(9.4-29.7)	NA	NA	NA	NA	NA	NA
Piperacillin-tazobactam	74	0.0	(0.0-4.9)	102	0.0	(0.0-3.6)	152	0.0	(0.0-2.5)	40	2.5	(0.4-12.9)	44	0.0	(0.0-8.0)	123	1.6	(0.4-5.7)

Shigella spp., from faecal samples

In 2022, 167 isolates of Shigella in feacal samples were reported in Svebar and AST results were available for 152 isolates. The majority of isolates with AST were *S. sonnei* and *S. flexneri*, with 51% and 23% of the isolates respectively. The remaining isolates were reported as *Shigella* species and a few isolates were *S. boydii*. None of the isolates were carbapenem resistant (Table 3.13).

Comments

The number of isolates with an AST available for analysis are low. Hence, results should be interpreted with caution. The increase in cefotaxime resistance indicates a higher presence of ESBL among the tested isolates.

Mycobacterium tuberculosis, mandatory reporting

During 2022 a total of 386 cases of tuberculosis (TB) were reported compared to 365 cases during 2021 which is a marginal increase of 6 %. Out of the 386 cases seven were already on TB treatment when arriving in Sweden. The number and proportion of culture confirmed cases were 318 (82 %) compared to 286 (79 %) in 2021.

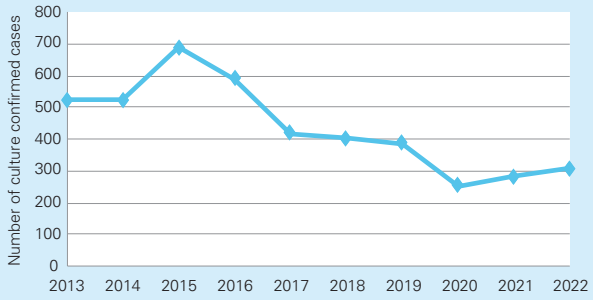
Mycobacterium bovis was identified in six cases, *Mycobacterium africanum* in four cases, *Mycobacterium canetti* in one case and *Mycobacterium tuberculosis* in 307 cases (Figure 3.33). The proportions of *Mycobacterium tuberculosis* cases diagnosed with MDR-TB was 4.9 % (15/307) compared to 2.1% (6/282) in 2021. Two of the MDR-cases were classified as pre-XDR-TB (additional resistance to fluoroquinolons) and XDR-TB (also resistant to bedaquilin).

Isolates of *M. tuberculosis* resistant to at least one of the four first line drugs (isoniazid, rifampicin, ethambutol or pyrazinamid) were identified in 39 patients corresponding to 12.7% of the 307 with culture confirmed *M. tuberculosis*, (Figure 3.34). As always the most common resistance found was against isoniazid.

Of 59 cases with *M. tuberculosis* born in Sweden one of 50 with culture confirmed diagnosis had resistant TB which was a case of MDR-TB. Of all the TB cases reported in Sweden 2022, 84 % were born in another country. In total, 257 in this group had a culture confirmed infection with *M. tuberculosis* and 38 (15 %) had some kind of resistance out of which 14 had MDR-TB.

Genetic typing of TB isolates has been performed in Sweden since the late 1990's. This is done to identify clusters of cases as clustering indicates possible recent transmission and helps to identify missed opportunities of infection control. Of all the cases 20 % (79/386) were reported as infected in Sweden and of 302 (including *M. bovis*) cases analysed with whole genome sequencing 78 % were unique isolates not belonging to any cluster.

Figure 3.33. The number of culture confirmed *M. tuberculosis* in Sweden cases in Sweden 2013-2022.

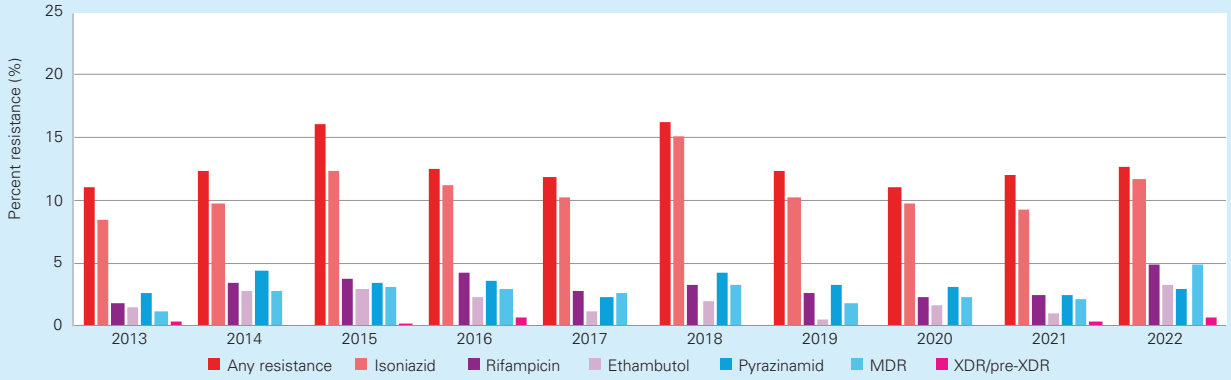


Source: The Public Health Agency of Sweden

The number of reported cases of TB has increased slightly during 2021 and 2022 after the sharp decrease during 2020 attributed to the covid-19 pandemic. As the majority of cases in Sweden is diagnosed in migrants from high burden countries, the reduced migration during the pandemic affects the number.

In 2022 there has been an increase in the number of MDR-TB cases which at least partly can be attributed to the war in Ukraine and the arrival of migrants from a country with a high percentage of their TB being MDR-TB.

Figure 3.34. Drug resistance and number of culture confirmed *M. tuberculosis* in Sweden 2013-2022.



Source: The Public Health Agency of Sweden

Neisseria gonorrhoeae, mandatory reporting

Gonorrhoea is a notifiable infection and in 2022, 3356 cases (32 cases per 100 000 inhabitants) of gonococcal infections were reported to the Public Health Agency of Sweden. This represents an increase with 23% compared to 2021 (2700 cases, 26 cases per 100 000 inhabitants). As in earlier years, most of the gonorrhoea cases in 2022 were identified in the three largest counties of Sweden, which comprise the cities Stockholm, Göteborg, and Malmö, respectively. Clinical isolates are in the present report described from the National Reference Laboratory for Sexually Transmitted Infections (an external body of the Public Health Agency of Sweden), Department of Laboratory Medicine, Clinical Microbiology, Örebro University Hospital, Örebro. In 2022, 894 clinical *N. gonorrhoeae* isolates were characterised in regard to antimicrobial susceptibility.

Antimicrobial susceptibility testing was performed according to standardized and quality assured methodology using Etest for MIC determination of ceftriaxone, cefixime, azithro-

Table 3.14. Proportion (%) of antibiotic resistant clinical *Neisseria gonorrhoeae* isolates 2012-2022.

Antibiotic	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Number of AST isolates	**967**	**384**	**462**	**601**	**528**	**580**	**1 035**	**1 713**	**1 583**	**984**
Cefixime	4.0	2.0	2.0	1.0	<1 (0.6)	1 (1.2)	<1 (0.8)	2.0	<1 (0.5)[b]	1.0
Ceftriaxone	<1 (0.3)	<1 (0.3)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	<1 (0.1)
Azithromycin	13	9	10	3.0	5.0	5[a]	12[a]	19[a]	25[a]	30[a]
Ciprofloxacin	53	60	53	53	47	57	60	58	69	64
Spectinomycin	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0[b]	0.0

[a]Using EUCAST ECOFF of 1 mg/L to distinguish isolates with azithromycin resistance mechanisms. [b]1 343 isolates examined.

mycin, spectinomycin, and ciprofloxacin. The clinical resistance breakpoints from the European Committee on Antimicrobial Susceptibility Testing (EUCAST) were used. Since January 2019, EUCAST does not state any clinical resistance breakpoint for azithromycin and in this report the Epidemiological Cutoff (ECOFF), distinguishing strains with azithromycin resistance mechanisms, is instead used for azithromycin.

In Table 3.14, the antimicrobial resistance in clinical gonococcal isolates cultured in 2022 are compared with those from 2012 to 2021. Briefly, the level of resistance to ciprofloxacin remains very high (64% in 2022). The proportion of isolates above the azithromycin ECOFF (MIC>1 mg/L) was 30%, which represents an increase since 2021 (25%). Notably, 95% of the isolates with an azithromycin MIC above the azithromycin ECOFF had an MIC of 2-4 mg/L, i.e. only 1-2 MIC doubling dilution above the ECOFF. It remains unknown if these isolates would fail clinical treatment with azithromycin 2 g, and a clinical resistance breakpoint for azithromycin would be valuable. The resistance to cefixime slightly increased from 0.5% in 2021 to 1.2% in 2022. For the first time since 2014 in Sweden, one (0.1%) ceftriaxone-resistant isolate was identified. Ceftriaxone is the last remaining option for empirical antimicrobial monotherapy of gonorrhoea and it is a major concern if ceftriaxone-resistant strains will start to spread, which have been recently observed in especially some Asian countries such as China, Japan, Vietnam, and Cambodia. No gonococcal isolates resistant to spectinomycin have yet been detected in Sweden. However, the availability of spectinomycin can be limited (in Sweden as in most countries globally), and it is not suitable as monotherapy for pharyngeal gonorrhoea.

Neisseria meningitidis, mandatory reporting

Invasive meningococcal disease is a notifiable disease and in 2022, 23 cases (0.2 cases per 100 000 inhabitants) of the disease were reported. This represents an increase from the all-time low incidence with 10 cases in 2021 but still a decrease compared to 28 cases in 2020 and 66 cases in 2019. Typing of 19 of the 23 clinical invasive isolates from blood and/or cerebrospinal fluid, and joint fluid (one isolate per patient) in 2022 was performed at the National Reference Laboratory for Neisseria meningitidis (an external body of the Public Health Agency of Sweden), Department of Laboratory Medicine, Clinical Microbiology, Örebro University Hospital and cultures were performed on 12 isolates. The pronounced decrease in incidence of invasive meningococcal disease since 2020 is most likely associated with the COVID-19 pandemic restrictions, e.g. social and physical distancing, and travel restrictions. The coming years will elucidate what this sudden interruption with the COVID-19 pandemic will lead to in terms of disease burden, group and age distribution.

Antimicrobial susceptibility testing was performed according to standardized and quality assured methodology using Etest for determination of MIC values for penicillin G, cefotaxime, meropenem, chloramphenicol, ciprofloxacin and rifampicin. The used clinical resistance breakpoints have been determined by The European Committee on Antimicrobial Susceptibility Testing (EUCAST). Production of β-lactamase was examined by nitrocefin solution.

Three isolate had an intermediate susceptibility to penicillin G (MIC=0.125 mg/L (n=2) and MIC=0.25 mg/L (n=1)). All isolates (100%) were susceptible to cefotaxime (MIC values of 0.002-0.016 mg/L), meropenem (MICs: 0.008-0.032 mg/L), chloramphenicol (MICs: 0.25-1 mg/L), ciprofloxacin (0.002-0.008 mg/L), and rifampicin (MICs: <0.002-0.064 mg/L). None of the isolates obtained in 2022 produced β-lactamase, and in fact no β-lactamase-producing meningococcal isolate has ever been identified in Sweden.

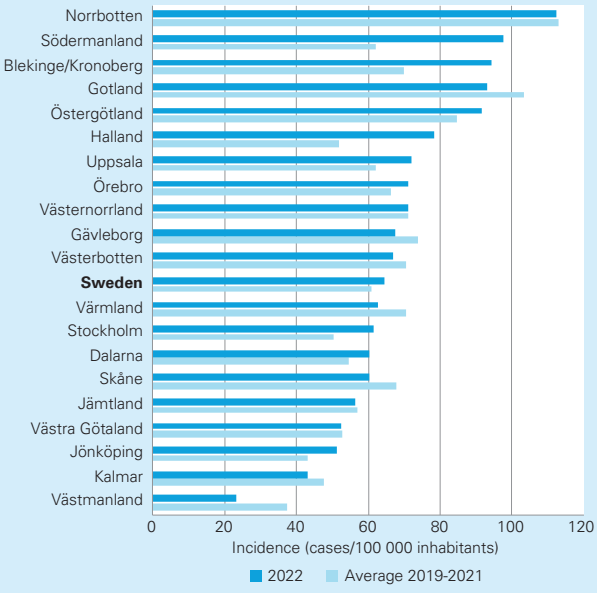
Clostridioides difficile

Incidence of CDI

In 2022, 6 798 new CDI cases were reported corresponding to an incidence of 65 cases per 100 000 inhabitants (data corrected for reccurent CDI for two laboratories reporting all cases). This is an increase compared with the average for the last three years (incidence 61). As in previous years, there are major differences between regions (spread 23-112 cases per 100 000 inhabitants; Figure 3.35).

Since the resistance situation has been stable in recent years, no testing of isolates for antibiotic susceptibility was done in 2022.

Figure 3.35. The incidence of new cases with *C. difficile* (cases/100 000 inhabitants) by region in 2022 and average for the years 2019-2021. The regions are ranked from highest to lowest incidence in 2022. A case is considered new if at least eight weeks have elapsed since the previous positive test, otherwise it is counted as an ongoing illness episode or recurrence.



Source: The Public Health Agency of Sweden

Zoonotic pathogens: *Campylobacter*

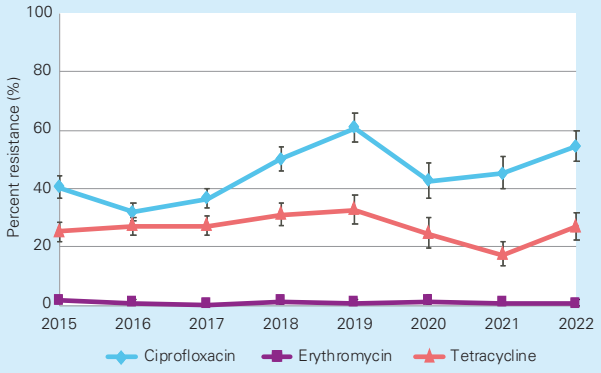
Mandatory reporting of *Campylobacter*

Results from 2022

- Total number of reported cases: 5 165 (previous year: 4 059)

The majority of notified cases, 57%, were reported as acquired in Sweden, and the proportion of domestically infected were unchanged compared to previous year. The proportion of cases infected abroad more than doubled compared with previous year, reaching levels seen pre-pandemic.

Figure 3.36. Antibiotic resistance in *Campylobacter jejuni* from faecal samples 2015-2022. The numbers of AST isolates for all years and antibiotics ranges from 254 to 816. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Campylobacter jejuni, from faecal samples

A total of 2 222 *Campylobacter* species were found in faecal sampling. Three-quarters of the isolates were reported as *C. jejuni*, nine percent as *C. jejuni/C. coli* and the rest were other species. The presence of AST data, and in a sufficient number of isolates, were highest for *C. jejuni* (71% of all *reported* isolates). For *C. jejuni* the resistance to ciprofloxacin was 55% and 27% for tetracycline in 2022. Resistance to erythromycin were 0.5% (Figure 3.36). The proportion of isolates fully susceptible to erythromycin, ciprofloxacin and tetracycline were 43% and fully resistant were 0.3% (Table 3.15). It should be noted that the number of isolates with combined AST are low and only one fully resistant isolate was reported.

Comments

During 2018-2019, the majority of notifiable Campylobacter infections were acquired abroad. During the pandemic years, 2020-2021, the total number of notified cases have decreased and the proportion of cases infected in Sweden have increased. The resistance to ciprofloxacin and tetracycline is slightly lower in 2020 and 2021, compared to 2019. In 2016 and 2017, there was a large outbreak of campylobacter in humans, linked to domestic poultry production. During these two years, the proportion of isolates with Swedish origin were higher. It can be noted that the resistance to ciprofloxacin were lower 2016-2017 (Figure 3.36) and a higher percentage of isolates were fully susceptible as well (Table 3.15).

Table 3.15. Combined susceptibility and resistance to erythromycin, ciprofloxacin and tetracycline in *Campylobacter jejuni* from faecal samples 2015-2022.

Sample: Faeces	2015	2016	2017	2018	2019	2020	2021	2022
Number of AST isolates	**659**	**793**	**697**	**544**	**352**	**253**	**304**	**360**
Proportion (S %) fully suseptitible to erythromycin, ciprofloxacin and tetracycline.	54	61	60	47	38	56	53	43
Proportion (R %) fully resistant to erythromycin, ciprofloxacin and tetracycline.	1.4	0.8	0.4	0.9	0.6	1.2	0.3	0.3

Salmonella

Mandatory reporting of *Salmonella*

Infection with *Salmonella* species are divided into three notifiable diseases in Sweden, infection with *Salmonella enterica* (*S.* Typhi and *S.* Paratyphi excluded), typhoid fever and paratyphoid fever. In addition, cases with *Salmonella* carrying ESBL or $ESBL_{CARBA}$ are also notified in the mandatory reporting of ESBL-producing Enterobacterales.

- Total number of reported cases with *Salmonella enterica*: 1 137 (previous year: 946)
- Total number of reported cases with typhoid fever: 14 (previous year: 11)
- Total number of reported cases with paratyphoid fever: 8 (previous year: 8)
- Total number of *Salmonella* carrying ESBL: 21 (previous year: 8)
- Total number of *Salmonella* carrying $ESBL_{CARBA}$: 0 (previous year: 0)

The majority of the *Salmonella* cases, 58%, were acquired in Sweden and 39% of the cases were reported as acquired abroad, almost a doubling in the proportion of imported cases compared with 2021. Information about country of acquisition was lacking for three percent. The number of *Salmonella* cases increased compared with previous year, but the number of reported cases are considerbly lower compared with 2019 and the years before. During these previous years, the number of cases with infection acquired abroad have been higher. No cases were reported with *Salmonella* species carrying $ESBL_{CARBA}$.

Table 3.16. Poportion (%) of antibiotic resistance in *Salmonella enterica* (*S.* Typhi and *S.* Paratyphi excluded) isolated from blood or from faeces and urine samples in 2022. NA: not applicable.

Antibiotic	Blood isolates, % R (n = 95)	Faeces and urine, % R (n= 456)
Azithromycin	NA	3.4
Cefotaxime	5.3	6.1
Ceftazidime	4.3	6.1
Fluoroquinolone	32.6	23.7
Meropenem	0.0	0.0
Piperacillin-tazobactam	1.1	2.6
Trimethoprim-sulphamethoxazole	7.4	8.8

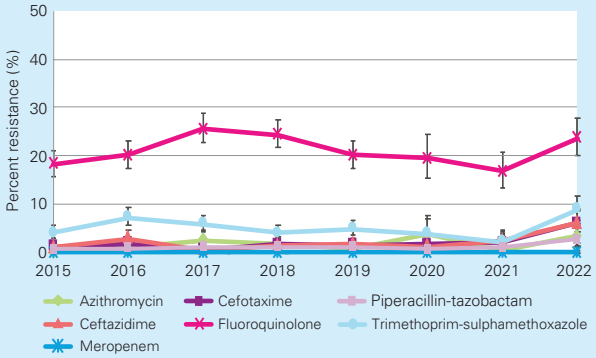
Salmonella spp., from blood or faecal and urine samples

A total of 1 296 *Salmonella enterica* isolates were reported in Svebar, three-quarters from faecal samples, 14% from blood and 9% from urine. In 2022, there were 182 isolates of *Salmonella* reported in blood and 964 isolates from feaces, for both sampling materials approximately half had an AST reported. A comparison for 2022 is presented in Table 3.16.

Comments

Previous years the number of isolates found in blood, with an AST, have ranged between 47-125 per year and antibiotic (Table 3.17). The data may contain duplicates and there is a risk of overestimation of the resistance. Hence, results should be interpreted with caution. The general increase in resistance among faecal and urine isolates seen in 2022 (Figure 3.37) is probably linked to the increase of *Salmonella* isolates carrying ESBL. The resistance to cefotaxim increased to six percent in 2022, compared to 2015-2021 were the resistance have been between zero point five to two percent. Almost three-quarters of the *Salmonella* from faecal and urine samples are fully susceptible to azithromycin, cefotaxime and ciprofloxacin (Table 3.18). During 2015-2022, no carbapenem-resistent *Salmonella* have been reported.

Figure 3.37. Antibiotic resistance in *Salmonella enterica* from faecal and urine samples 2015-2022. Results from *S.* Typhi and *S.* Paratyphi have been excluded. The numbers of AST isolates for all years and antibiotics ranges from 187 to 875. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Table 3.17. Antibiotic resistance in *Salmonella enterica* from blood samples 2015-2022. Results for *S. Typhi and S. Paratyphi* are excluded. The numbers of AST isolates for all years and antibiotics ranges from 32 to 125.

	2015			2016			2017			2018			2019			2020			2021			2022		
Sample: Blood	**n**	**% R**	**95% CI**	**n**	**% R**	**95% CI**	**n**	**% R**	**95% CI**	**n**	**% R**	**95% CI**	**n**	**% R**	**95% CI**	**n**	**% R**	**95% CI**	**n**	**% R**	**95% CI**	**n**	**% R**	**95% CI**
Number of AST isolates	**78**			**73**			**107**			**93**			**125**			**59**			**76**			**95**		
Azithromycin	53	1.9	(0.3-9.9)	47	0	(0.0-7.6)	75	4	(1.4-11.1)	64	4.7	(1.6-12.9)	70	0	(0.0-5.2)	32	3.1	(0.6-15.7)	NA	NA	NA	NA	NA	NA
Cefotaxime	78	0	(0.0-4.7)	73	2.7	(0.8-9.5)	107	0.9	(0.2-5.1)	92	0	(0.0-4.0)	125	1.6	(0.4-5.6)	59	10.2	(4.7-20.5)	76	7.9	(3.7-16.2)	95	5.3	(2.3-11.7)
Ceftazidime	77	0	(0.0-4.8)	73	2.7	(0.8-9.5)	103	1	(0.2-5.3)	87	0	(0.0-4.2)	124	1.6	(0.4-5.7)	57	10.5	(4.9-21.1)	76	7.9	(3.7-16.2)	94	4.3	(1.7-10.4)
Fluoroquinolone	76	36.8	(26.9-48.1)	65	12.3	(6.4-22.5)	100	25	(17.5-34.3)	90	27.8	(19.6-37.8)	117	27.4	(20.1-36.1)	59	32.2	(21.7-44.9)	74	25.7	(17.1-36.7)	95	32.6	(24.0-42.6)
Meropenem	78	0	(0.0-4.7)	73	0	(0.0-5.0)	107	0	(0.0-3.5)	93	0	(0.0-4.0)	125	0	(0.0-3.0)	59	0	(0.0-6.1)	76	0.0	(0.0-4.8)	95	0	(0.0-3.9)
Piperacillin-tazobactam	75	0,0	(0.0-4.9)	71	0	(0.0-5.1)	100	2,0	(0.6-7.0)	89	0	(0.0-4.1)	123	0,0	(0.0-3.0)	56	3.6	(1.0-12.1)	73	0.0	(0.0-5.0)	90	1.1	(0.2-6.0)
Trimethoprim-sulphamethoxazole	72	20.8	(13.1-31.6)	70	8.6	(4.0-17.5)	105	9.5	(5.3-16.6)	93	3.2	(1.1-9.1)	125	6.4	(3.3-12.1)	59	15.3	(8.2-26.5)	76	1.3	(0.2-7.1)	95	7.4	(3.6-14.4)

Table 3.18. Combined susceptibility and resistance to azithromycin, cefotaxime and ciprofloxacin in *Salmonella enterica* from faecal and urine samples 2015-2022. Results from *S.* Typhi and *S.* Paratyphi have been excluded.

Sample: Faeces and urine	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**
Number of AST isolates	**424**	**328**	**426**	**454**	**404**	**183**	**238**	**290**
Proportion (S %) fully susceptible to azithromycin, cefotaxime and ciprofloxacin.	80	75	74	76	79	77	75	74
Proportion (R %) fully resistant to azithromycin, cefotaxime and ciprofloxacin.	0.0	0.6	0.0	0.2	0.3	0.0	0.0	1.7

Antibiotic resistance in animals

Notifiable diseases

In Sweden, findings of $ESBL_{CARBA}$-producing Enterobacterales and methicillin-resistant coagulase-positive staphylococci in animals are notifiable (SJVFS 2021:10 and previously SJVFS 2012:24 with amendments). In the monitoring, the attention regarding methicillin-resistant coagulase-positive staphylococci is mainly directed towards methicillin-resistant *Staphylococcus aureus* (MRSA) and *Staphylococcus pseudintermedius* (MRSP). Furthermore, as Enterobacterales producing $ESBL_A$ or $ESBL_M$ as well as vancomycin resistant enterococci (VRE) are notifiable when detected in humans, specific attention is also paid to these bacteria in animals.

ESBL-producing Enterobacterales

Healthy farm animals

Escherichia coli

In Sweden, carbapenemase-producing Enterobacterales ($ESBL_{CARBA}$) in animals are notifiable but not classical ESBLs ($ESBL_A$) or plasmid-mediated AmpC ($ESBL_M$). During 2022, various samples from healthy farm animals were screened for *Escherichia coli* resistant to ESCs and carbapenems using selective media. Isolates with reduced susceptibility were further investigated by genome sequencing for presence of transferable genes coding for ESC resistance (for details see Material and methods, resistance in bacteria from animals).

Active screening for *E. coli* resistant to ESCs in healthy farm animals using faecal samples collected at slaughter has been performed since 2008. The proportions of samples positive for *E. coli* with $ESBL_A$ or $ESBL_M$ in screenings of healthy animals are available as supplementary material on the SVA web page (www.sva.se/svarm).

Broilers

Samples from broilers were randomly selected among caeca collected at slaughter within the Swedish Campylobacter programme, in which whole caeca are collected from each batch of broilers slaughtered. Each sample was from a unique flock but not always from a unique production site. Samples cultured were collected at seven abattoirs that in 2022 accounted for approximately 98% of the total volume of broilers slaughtered. The number of samples from each abattoir was roughly proportional to the annual slaughter volume of the abattoir and the sampling was distributed over the year. In 2022, the methodology was slightly changed due to alterations of the legislation regulating the harmonised resistance monitoring in EU, i.e., a new sampling procedure specified in the implementing decision 2020/1729. In short, instead of sampling only one caecum per slaughter batch, a pooled sample consisting of caecal material from ten birds per slaughter batch was cultured.

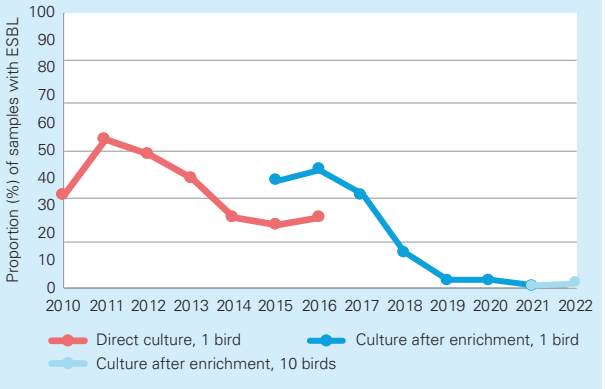
Carbapenem resistant *Escherichia coli* were not isolated from any of 305 investigated samples.

Escherichia coli with ESC-resistance was isolated from 9 (3%) of 305 investigated samples and a transferable gene coding for ESC resistance was detected in 5 isolates, i.e., 2% of the samples (Table 4.1). All the isolates with a transferable gene had an $ESBL_A$ phenotype and carried $bla_{CTX\text{-}M\text{-}1}$. The remaining isolates with ESC-resistance all had an AmpC phenotype and genome sequencing revealed a mutation causing hyperproduction of AmpC beta-lactamases, i.e., a shift from C to T at position 42 of the ampC promoter.

Three of the isolates with transferable ESC-resistance were also resistant to sulphonamides and tetracycline. This was the only resistance apart from resistance to beta-lactams, including ESCs, detected among the ESC-resistant isolates.

Due to differences in methodology over the years, changes in the proportion of positive samples over the whole time period cannot be directly assessed. However, some comparison with earlier years is possible as the samples from 2015 and the first half of 2016 as well as the samples from 2021 were cultured in duplicate with both methods that were relevant for the respective years (for details on methodology see Material and methods, resistance in bacteria from animals in relevant Swedres-Svarm reports). The difference in the proportion of broiler caecal samples positive for *E. coli* with $ESBL_A$ or $ESBL_M$ since 2016 is statistically significant ($p<0.01$, X^2; Figure 4.1). This decrease is most likely explained by decreased occurrence of such bacteria in the breeding pyramid as described by Nilsson et al. (2020).

Figure 4.1. Proportion (%) of samples from broilers positive for *Escherichia coli* with $ESBL_A$ or $ESBL_M$ from 2010 to 2022. The number of samples each year varies (n=100-305, 2022 n=305).



Turkeys

Samples from turkey consists of caecal content of healthy turkeys sampled at slaughter. Each sample is from a unique flock but not always from a unique production site. Sampling was performed from January to December at one abattoir that in 2022 accounted for approximately 90% of the total volume of turkeys slaughtered in Sweden.

Carbapenem resistant *Escherichia coli* or *E. coli* with ESC-resistance were not isolated from any of 34 investigated samples (Table 4.1).

Laying hens

Samples from laying hens consist of caecal content of healthy hens sampled at slaughter. Each sample is from a unique flock but not always from a unique production site. Sampling was performed from February 2021 to December 2022 at the only abattoir slaughtering laying hens in Sweden. However, a large proportion of laying hens in Sweden are either sent for slaughter in other countries or euthanised instead of being sent for slaughter. Hence, the sampling is perhaps not representative of the whole laying hens population in Sweden.

Carbapenem resistant *E. coli* were not isolated from any of 128 investigated samples.

Escherichia coli with ESC-resistance was isolated from 3 (2%) of 128 investigated samples and a transferable gene coding for ESC resistance was detected in all 3 of these, i.e., 2% of the samples (Table 4.1). All of these were $ESBL_M$ and carried bla_{CMY-2}.

None of the isolates showed resistance to any other substances than beta-lactams, including ESCs.

Meat samples

Escherichia coli

In Sweden, neither carbapenemase-producing Enterobacterales ($ESBL_{CARBA}$), nor classical ESBLs ($ESBL_A$) or plasmid-mediated AmpC ($ESBL_M$) are notifiable in food. Active screening for *Escherichia coli* resistant to ESCs in meat samples collected at retail has been performed since 2008. During 2022, various poultry meat samples were screened for *E. coli* resistant to ESCs and carbapenems using selective media. Isolates with reduced susceptibility were further investigated by genome sequencing for presence of transferable genes coding for ESC resistance (for details see Material and methods, resistance in bacteria from animals).

Samples from broiler and turkey meat were collected at retail by municipal environmental departments in eleven different municipalities in Sweden. The samples were distributed throughout the year and among the municipalities in order to get a representative sampling.

In 2022, there were no consignments of poultry meat from countries outside EU imported via border control posts in Sweden. Hence, no sampling of poultry meat was performed.

The proportions of samples positive for *E. coli* with $ESBL_A$ or $ESBL_M$ in screenings of meat of Swedish origin are available as supplementary material on the SVA web page (www.sva.se/svarm).

Broiler meat

A total of 296 samples of fresh broiler meat were collected at retail. The samples comprised of meat originating both from Sweden (n=280) and other EU countries (n=16).

Carbapenem resistant *E. coli* were not isolated from any samples of broiler meat.

Escherichia coli with ESC-resistance was isolated from five of the samples, one of Swedish origin and four originating from other EU countries. A transferable gene coding for ESC resistance was detected in four of the isolates, i.e., 1% of the samples.

All four isolates with a transferable gene were isolated from meat samples originating from other EU countries (Table 4.1). Two were $ESBL_A$ and carried $bla_{CTX-M-32}$ and $bla_{CTX-M-55}$ respectively whereas two were $ESBL_M$ and both carried bla_{CMY-2}. The remaining isolate with ESC-resistance, i.e. the one of Swedish origin, had an AmpC phenotype and genome sequencing revealed a mutation causing hyper-production of AmpC beta-lactamases, i.e., a shift from C to T at position 42 of the ampC promoter.

Turkey meat

A total of 81 samples of fresh turkey meat were collected at retail. All samples comprised of meat originating from Sweden.

Carbapenem resistant *Escherichia coli* or *E. coli* with ESC-resistance were not isolated from any of the samples (Table 4.1).

Table 4.1. Proportion (%) of samples positive for *Escherichia coli* with $ESBL_A$ or $ESBL_M$ in different matrixes, 2022.

Origin	Healthy broilers	Healthy turkey	Healthy laying hens	Broiler meat	Turkey meat
Swedish	2	0	2	0	0
Other EU countries	–	–	–	25	–

Clinical isolates from companion animals and horses

In Svarm, there are no recurring active screenings for ESBL-producing Enterobacterales in healthy companion animals or horses. However, results of the screenings for ESC resistant *E. coli* that have been performed are available as supplementary material on the SVA web page (www.sva.se/svarm).

For a number of years, funding from the Swedish Board of Agriculture has enabled SVA to perform confirmation of suspected ESC-resistance in clinical isolates of Enterobacterales free of charge for referring laboratories. Isolates were submitted to the Dept. of Animal Health and Antimicrobial Strategies, SVA as bacterial isolates.

During 2022, 41 submitted isolates of Enterobacterales with phenotypic resistance to ESCs from companion animals and horses were confirmed to produce $ESBL_A$ and/or $ESBL_M$ by genome sequencing (Table 4.2). The isolates were from cats (n=3), dogs (n=15) and horses (n=23). The majority of the isolates from cats and dogs were *E. coli* and the most common gene was $bla_{CTX-M-15}$. For horses, the majority of the isolates were *Enterobacter cloacae* group and the most common gene was bla_{SHV-12}. Data regarding clinical isolates from cats, dogs and horses confirmed to produce $ESBL_A$ and/or $ESBL_M$ is available as supplementary material on the SVA web page (www.sva.se/svarm).

Assessment of resistance to substances besides beta-lactams including ESCs is hampered as ECOFF:s for many combinations of bacteria and substances are not defined. However, about three quarters of the investigated isolates were also resistant to at least two other antibiotics, i.e. multiresistant. The most common resistances were against trimethoprim-sulphonamides (73%) and gentamicin (56%). Resistance to quinolones and tetracycline were also common traits. The occurrence of resistance to quinolones was slightly higher among isolates from companion animals than among isolates from horses. On the contrary, the occurrence of resistance to gentamicin and trimethoprim-sulphonamides was higher among isolates from horses than among isolates from companion animals. Of note is that resistance to gentamicin was only detected among isolates from horses.

Table 4.2. Clinical isolates of different bacterial species of Enterobacterales, producing $ESBL_A$ or $ESBL_M$, from companion animals and horses, 2022.

Animal species	Beta-lactamase		Bacterial species	No. of isolates
	group	gene		
Cats	**All**	**All**	**Enterobacteriaceae**	**3**
	CTX-M-1	CTX-M-15	*Escherichia coli*	1
	CTX-M-9	CTX-M-27	*Escherichia coli*	1
	SHV	SHV-12	*Escherichia coli*	1
Dogs	**All**	**All**	**Enterobacteriaceae**	**15**
	CIT	CMY-2	*Escherichia coli*	3
	CTX-M-1	CTX-M-1	*Escherichia coli*	2
		CTX-M-15	*Escherichia coli*	6
			Klebsiella pneumoniae	1
	CTX-M-9	CTX-M-13	*Proteus mirabilis*	1
	DHA	DHA-1	*Escherichia coli*	2
Horses	**All**	**All**	**Enterobacteriaceae**	**23**
	CTX-M-1	CTX-M-1	*Escherichia coli*	1
	SHV	SHV-12	*Escherichia coli*	1
			Klebsiella oxytoca	2
			Enterobacter cloacae group	9
			Citrobacter species	1
	SHV+ACT	SHV-12 + ACT-17	*Enterobacter cloacae* group	8
	SHV+DHA	SHV-12 + DHA-1	*Enterobacter cloacae* group	1

Methicillin-resistant *Staphylococcus aureus* (MRSA)

In Sweden, methicillin-resistant *Staphylococcus aureus* (MRSA) in animals was first verified in 2006 and made notifiable in 2008. Since then, most cases in domesticated animals have been detected in passive monitoring of clinical sampling from infected animals. Isolates of *S. aureus* with resistance to oxacillin or cefoxitin have been further analysed with confirmatory tests. Screening studies for active monitoring have been performed in pigs, cattle, horses, dogs, and hedgehogs during different years (see below). Cases from 2022 are presented in Table 4.3 and aggregated data, including index cases of clinical isolates and isolates from screenings, are available as supplementary material on the SVA webb (www.sva.se/svarm).

Farm animals

Screening studies in pigs have been performed five times since 2006, with only two positive samples from pigs at slaughter in 2010; one MRSA with *mecA*, spa-type t011, and one MRSA with *mecC*, spa-type t373. The most recent screening was performed in all 39 nucleus and multiplying herds in 2014 and all samples were negative. Other herd types have not been investigated since 2010. Therefore, information about the occurrence of MRSA in Swedish pig herds is currently not complete.

In dairy cattle, active monitoring of selected isolates of beta-lactamase producing *S. aureus* from milk samples has been ongoing since 2010, and about 1400 isolates have been tested up to and including 2022. The monitoring is performed on isolates with anonymised origin. Since 2010 PVL-negative MRSA with *mecC* (spa-types t524, t843 and t9111), PVL-negative MRSA with *mecA* (spa-types t008 and t127) and PVL-positive MRSA with *mecA* (spa-type t002) have been detected. Also, between 2012 and 2014, PVL-positive MRSA with *mecA* and spa-type t002 was isolated from cows and the farmer in a dairy herd (Unnerstad et al., 2018). In 2022 no MRSA was detected of the 50 isolates screened for occurrence of *mecA* and *mecC*.

In 2016 and early 2017 there was an outbreak of MRSA with *mecC* among goats and sheep connected to a zoo. In addition, MRSA with *mecC* was found in 8 out of 21 sam-

Table 4.3. Isolates of methicillin-resistant *Staphylococcus aureus* (MRSA) in Swedish animals 2022. All isolates were positive for the *nuc* gene and *mecA* or *mecC* genes. Shaded areas indicate MIC above EUCAST ECOFF.

		Antibiotic, MIC (mg/L)										
Animal species	**Beta-lactams**	**Cli**	**Ery**	**Tet**	**Fus**	**Gen**	**Cip**	**Tmp**	**Chl**	**Lin**	***spa*-type**	***mec*-gene**
Cat	R	0.25	0.5	≤0.5	0.5	≤0.5	0.5	≤1	8	4	t20721	*C*
Cat	R	0.25	>8	≤0.5	≤0.25	≤0.5	>8	≤1	8	2	t304	*A*
Cat	R	0.25	≤0.25	≤0.5	≤0.25	≤0.5	0.5	≤1	8	≤1	t843	*C*
Cat	R	0.25	≤0.25	≤0.5	≤0.25	≤0.5	≤0.25	≤1	8	2	t843	*C*
Cat	R	0.25	≤0.25	≤0.5	≤0.25	≤0.5	≤0.25	≤1	8	2	t843	*C*
Cat	R	≤0.12	0.5	≤0.5	0.5	≤0.5	0.5	≤1	8	2	t148	*A*
Cat	R	≤0.12	0.5	≤0.5	≤0.25	≤0.5	0.5	2	8	2	t067	*A*
Cat	R	≤0.12	0.5	≤0.5	≤0.25	≤0.5	≤0.25	≤1	8	2	t304	*A*
Cat	R	≤0.12	≤0.25	≤0.5	≤0.25	1	≤0.25	≤1	8	2	t223	*A*
Cat	R	≤0.12	≤0.25	≤0.5	≤0.25	≤0.5	0.5	≤1	8	≤1	t359	*A*
Cat	R	≤0.12	≤0.25	≤0.5	0.5	≤0.5	0.5	≤1	8	2	t2345	*C*
Dog	R	>4	>8	>16	≤0.25	>16	>8	>16	8	≤1	t034	*A*
Dog	R	>4	≤0.25	>16	≤0.25	1	≤0.25	>16	8	2	t034	*A*
Dog	R	≤0.12	>8	>16	≤0.25	≤0.5	≤0.25	≤1	8	2	t127	*A*
Dog	R	≤0.12	0.5	≤0.5	≤0.25	≤0.5	≤0.25	≤1	8	2	t304	*A*
Parrot	R	≤0.12	≤0.25	≤0.5	≤0.25	≤0.5	≤0.25	>16	≤4	≤1	t4793	*A*
Horse	R	4	≤0.25	>16	≤0.25	≤0.5	0.5	>16	≤4	≤1	t034	*A*
Horse	R	0.25	0.5	>16	>4	>16	0.5	≤1	8	2	t084	*A*
Horse	R	≤0.12	0.5	>16	≤0.25	>16	>8	>16	8	2	t011	*A*
Horse	R	≤0.12	0.5	>16	≤0.25	>16	>8	>16	8	2	t1971	*A*
Horse	R	≤0.12	>8	>16	≤0.25	>16	0.5	>16	≤4	2	t011	*A*
Horse	R	≤0.12	≤0.25	>16	≤0.25	16	8	>16	8	2	t011	*A*
Horse	R	≤0.12	≤0.25	>16	≤0.25	16	0.5	>16	8	2	t011	*A*
Horse	R	≤0.12	≤0.25	>16	≤0.25	16	0.5	>16	8	2	t011	*A*
Horse	R	≤0.12	≤0.25	>16	≤0.25	16	0.5	>16	8	2	t011	*A*
Horse	R	≤0.12	≤0.25	>16	≤0.25	16	≤0.25	>16	8	2	t011	*A*
Horse	R	≤0.12	≤0.25	>16	≤0.25	>16	>8	>16	8	≤1	t1971	*A*
Horse	R	≤0.12	≤0.25	≤0.5	≤0.25	>16	≤0.25	≤1	8	≤1	t252	*A*
Horse	R	≤0.12	≤0.25	≤0.5	≤0.25	≤0.5	0.5	≤1	≤4	≤1	t230	*A*

pled goats in a herd in 2017 and in one goat sold from the same herd. In 2019 an additional goat herd with MRSA was identified. The farm had an epidemiological link to the herd detected in 2017 and shared the same *spa*-type, t373. Six goats were sampled, and samples were pooled two and two for cultivation with all pools being positive for *mecC*-MRSA. In 2019, twenty-two dairy goat herds were screened for occurrence of MRSA, using bulk-milk samples and pooled swabs, with no positive samples found (Persson et al., 2021).

Companion animals and horses

Up to and including 2022, a total of 226 cases of MRSA in companion animals and horses have been confirmed. These include 66 dogs, 46 cats, 2 rabbits, one parrot and 111 horses. In these animal species, there is currently no regular active monitoring of MRSA, but screenings in dogs were performed in 2006 and 2012 without detection of MRSA. Furthermore, a study on 325 clinically healthy dogs in 2017-2018 detected no MRSA or other methicillin-resistant coagulase positive staphylococci (Börjesson et al., 2020). Screening studies in horses have been performed twice, in 2007 and 2010, with one positive sample in 2007.

In 2022, MRSA was detected in clinical samples from four dogs (wound infections, urine and abscesses), eleven cats (wound infections, nose, ear and abscess) and from one parrot (nostril) (Table 4.3). During the years the identified *spa*-types have varied, and most have previously been detected in humans (supplementary material on the SVA web page, www.sva.se/svarm). In addition, MRSA was isolated from 13 horses in 2022. This is less compared to 2020-2021, but still more cases compared to 2007-2019, when one to nine cases were notified per year (supplementary material on the SVA web page, www.sva.se/svarm). In 2020 and 2021 the increase was partly explained by outbreaks of MRSA in equine hos-

pitals (*spa*-type t1971, t034 and t011). Historically, MRSA *spa*-type t011, CC398, has been dominating among horses in Sweden and in 2022 the *spa*-type was detected in seven of the thirteen cases. The remaining six MRSA belonged to four different *spa*-types (Table 4.3). All the mentioned *spa*-types have also been detected more or less frequently in samples from humans.

Wild animals

As in other countries, high occurrence of *mecC*-MRSA (64%) has been described in hedgehogs in Sweden (Bengtsson et al., 2017). Recent studies suggest that *mecC*-MRSA likely originate from hedgehogs, as the result of selective pressure of beta-lactams produced by dermatophytes, and that this occurred long before introduction of clinically used antibiotics (Larsen et al., 2022).

Methicillin-resistant *Staphylococcus pseudintermedius* (MRSP)

In 2022, there were 54 confirmed cases with methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) (52 dogs, 1 cat, and 1 orangutan) reported to the Swedish Board of Agriculture. This number is around the same level as in previous years (Figure 4.2).

All isolates were available for further susceptibility testing and genome sequencing. Information on the sampling site was available for 49 cases; skin 12 cases, external ear canal 4 cases, wounds 18 cases and the remaining 15 were isolated from abscesses, furuncles, urine, eye, and various other sites. For resistance phenotypes, see Table 4.4.

Genome sequencing of 52 isolates, resulted in 31 different multi-locus sequence types, of which ST551 was the most common type with 17 isolates. The ST551 was first detected in 2016 and was also the most common ST in 2019 and 2020, with 13/42 and 18/49 genome sequenced isolates respectively. In earlier years, ST71, a sequence type spread in Europe and described by Perreten et al. (2010), was dominating among Swedish isolates. In 2022 there was one isolate of this type. The other sequence types occurring in 2022 were: ST1095 (4 isolates), ST937 (2 isolates), ST2636 (2 isolates) and single isolates of ST1, ST25, ST181, ST258, ST265, ST294, ST301, ST315, ST649, ST826, ST1149, ST1331, ST2270, ST2273, ST2353, ST2635, ST2637-ST2646.

Figure 4.2. Number of cases of methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) in Sweden 2006-2022. In 2006-2007 the numbers represent the isolates that were sent to SVA and confirmed as *mecA*-positive and from 2008 the number of cases notified to the Swedish Board of Agriculture.

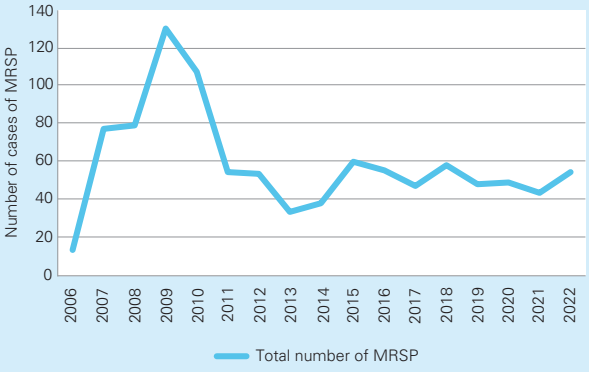


Table 4.4. Resistance phenotypes (beta-lactams excluded) of isolates of methicillin resistant *Staphylococcus pseudintermedius* (MRSP) in 2022. All isolates were positive for the *mecA* gene. Shaded areas indicate resistance.

	Antibiotic MIC (mg/L)								
Beta-lactams	Tet	Tsu	Ery	Cli	Gen	Enr	Fus	Nit	Number of isolates
R	>4	>4	>2	>2	>4	>1	>2	≤16	1
R	>4	4->4	>2	>2	4->4	1->1	≤0.5	≤16	32
R	>4	4->4	>2	>2	>4	≤0.25-0.5	≤0.5	≤16	5
R	>4	>4	>2	>2	≤1	>1	≤0.5	≤16	1
R	>4	>4	>2	1->2	≤1	≤0.25	≤0.5	≤16	2
R	>4	>4	≤0.5	≤0.5	≤1	≤0.25	≤0.5	≤16	1
R	>4	0.5	>2	>2	4	>1	≤0.5	≤16	1
R	>4	0.5	>2	>2	4	0.5	≤0.5	≤16	1
R	>4	0.5	≤0.5	≤0.5	>4	>1	≤0.5	≤16	2
R	>4	≤0.25	>2	>2	≤1	≤0.25	>2	≤16	1
R	≤0.25	>4	>2	>2	>4	>1	≤0.5	≤16	1
R	≤0.25	>4	>2	>2	4	≤0.25	≤0.5	≤16	1
R	≤0.25	>4	>2	>2	≤1	≤0.25	≤0.5	≤16	1
R	≤0.25	>4	≤0.5	≤0.5	>4	>1	≤0.5	≤16	1
R	≤0.25	4	≤0.5	≤0.5	≤1	≤0.25	≤0.5	≤16	1
R	≤0.25	≤0.25	>2	>2	≤1	≤0.25	>2	≤16	1
R	≤0.25	≤0.25	>2	>2	≤1	≤0.25	≤0.5	≤16	1

Zoonotic pathogens

Zoonoses are diseases that can be naturally transmitted between animals and humans. Antibiotic resistance in zoonotic bacteria such as *Salmonella* and *Campylobacter* from animals is therefore of direct public health concern.

Salmonella

Findings of *Salmonella* in animals are notifiable in Sweden. In Svarm, antibiotic susceptibility is determined in one isolate from each notified incident in farm animals or horses each year. Isolates from incidents previously notified but still under restrictions are also included. In incidents involving more than one serovar, one isolate of each serovar is tested. In the case of poultry, one isolate from each infected flock is included. More than one flock can be affected on the same farm, in such cases one isolate from each of the infected flocks is included. The majority of *Salmonella* from wild birds are usually from cases of salmonellosis among passerines during the winter season, while most *Salmonella* from cats are cases when cats have eaten these birds lying dead or diseased on the ground. Such isolates are often *S.* Typhimurium and susceptible to all tested antibiotics. Therefore, only the first 5 and 25 index cases of *Salmonella* from wild birds and cats, respectively, and thereafter every eighth case is serotyped. For details on methodology, see Materials and methods, resistance in bacteria from animals.

A total of 150 *Salmonella* isolates were tested in 2022, all belonging to the species *S. enterica* and with two subspecies represented, subsp. *enterica* (101 isolates) and subsp. *diarizonae* (49 isolates). Of all tested isolates 115 were from domestic animals (Table 4.5). Among the subsp. *enterica* isolates, *S.* Typhimurium was the most dominant serovar with 47 isolates, including a monophasic variant. Of these 37 were from domestic animals (Table 4.6)

The highest number of isolates was from cattle (n=30) belonging to 13 different serovars dominated by *S.* Typhimurium and *S.* Dublin. In pigs and poultry *S.* Typhimurium was the dominating serovar.

Distributions of MICs and resistance for all isolates from domestic animals are presented in Table 4.5 and for the subset *S.* Typhimurium in Table 4.6. The majority of the isolates (147 of 150; 98%) were susceptible to all antibiotics tested and all isolates from wildlife were fully susceptible. No interpretation was done for colistin due to uncertainties on ECOFFs and differences in MIC distributions between serovars. EUCAST does no longer suggest a colistin ECOFF for *Salmonella*. Eleven isolates had an MIC of 4 mg/L for colistin (Table 4.5). These isolates were tested by PCR for presence of *mcr*-1 – *mcr*-9 genes, which may confer resistance to colistin, but all isolates were negative for these genes. These eleven isolates all belonged to serovar Dublin that often display slightly higher MIC to colistin than most other serovars.

Table 4.5. Distribution of MICs and resistance (%) in *Salmonella enterica* from domestic animals, 2022.

Antibiotic	Resistance %	Distribution (%) of MICs (mg/L)																
	n=115	≤0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	>512
Amikacin	<1									99.1	0.9							
Ampicillin	0							89.6	9.6	0.9								
Azithromycin	0								18.3	75.7	6.1							
Cefotaxime	0					100												
Ceftazidime	0					91.3	8.7											
Chloramphenicol	0										100							
Ciprofloxacin	0	97.4	2.6															
Colistin[a]	NA							83.5	7.0	9.6								
Gentamicin	0						88.7	11.3										
Meropenem	0		97.4	2.6														
Nalidixic acid	0									97.4	2.6							
Sulphamethoxazole	0										7.8	83.5	8.7					
Tetracycline	2								98.3					1.7				
Tigecycline	0					99.1	0.9											
Trimethoprim	0					89.6	10.4											

[a]The isolates with colistin MIC >2 were tested with PCR for the *mcr-1* to *mcr-9* genes and found negative. NA: Not Applicable.

Table 4.6. Distribution of MICs and resistance (%) in *Salmonella* Typhimurium, including a monophasic variant from domestic animals, 2022.

Antibiotic	Resistance % n=37	Distribution (%) of MICs (mg/L) ≤0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	>512
Amikacin	3									97.3	2.7							
Ampicillin	0							78.4	21.6									
Azithromycin	0								24.3	75.7								
Cefotaxime	0					100												
Ceftazidime	0					86.5	13.5											
Chloramphenicol	0										100							
Ciprofloxacin	0	94.6	5.4															
Colistin	NA							83.8	16.2									
Gentamicin	0						70.3	29.7										
Meropenem	0		94.6	5.4														
Nalidixic acid	0									97.3	2.7							
Sulphamethoxazole	0										5.4	73.0	21.6					
Tetracycline	3								97.3					2.7				
Tigecycline	0					100												
Trimethoprim	0					91.9	8.1											

NA: Not applicable

Campylobacter

The isolates of *Campylobacter jejuni* and *Campylobacter coli* tested are from caecal content of broilers collected at abattoirs and were isolated within the framework of the Swedish Campylobacter control programme 2022. In 2022 approximately 4% of 4 104 flocks were culture positive for *C. jejuni* or *C. coli*. For details on methodology see Materials and methods, resistance in bacteria from animals.

In total 163 isolates of *C. jejuni* and 16 of *C. coli* were tested. Of the 163 *C. jejuni* isolates, 130 (80%) were susceptible to all six antibiotics tested and 33 were resistant to fluoroquinolones (20%) (Table 4.7). Of the 16 *C. coli* isolates, 4 were resistant to fluoroquinolones (data not shown).

In 2016 resistance to tetracycline was more common than usual (16%) but in 2022 no isolates were resistant to tetracycline (Figure 4.3). The percentage of culture positive flocks was high in 2016 because of an outbreak. The probable explanation for the tetracycline resistance peak and for the fluoroquinolone resistance is spread of certain resistant (or susceptible) clones. Selection through use of antibiotics is unlikely since these substances almost never are used in broiler production in Sweden.

Figure 4.3. Ciprofloxacin, nalidixic acid and tetracycline resistance (%) in *Campylobacter jejuni* from broilers, 2001-2022. In years 2001-2002 enrofloxacin was tested instead of ciprofloxacin. The number of isolates per year varies (n=38-180, 2022 n=163).

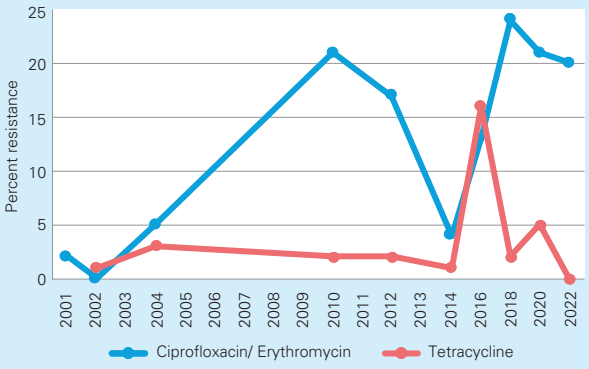


Table 4.7. Distribution of MICs and resistance (%) for *Campylobacter jejuni* from healthy broilers, 2022. Isolates from caecal content.

Antibiotic	Resistance (%) n=163	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	>512
Chloramphenicol	0					98.8	1.2								
Ciprofloxacin	20	70.6	9.2					17.2	3.1						
Ertapenem	0	98.2	1.8												
Erythromycin	0				97.5	2.5									
Gentamicin	0		19.6	77.3	3.1										
Tetracycline	0			100											

Clinical isolates from animals

Isolates tested are from clinical submissions of samples to SVA, if not otherwise stated. For many samples, information on the indication for sampling was not available but the vast majority of submissions were likely from animals with infections. Therefore, data may be biased towards samples from treated animals or from herds where antibiotic treatment is common. Any assessments of trends are based on the assumption that this bias is inherent throughout the observation period. Furthermore, in some cases there are more than one animal sampled from the same herd. Likewise, regarding horses, dogs and cats, duplicates based on animal identity have not been excluded.

In Svarm, isolates are, when possible, classified as susceptible or resistant by ECOFFs issued by EUCAST (see Guidance for readers for details). This classifies isolates with acquired reduced susceptibility as resistant, which is relevant for monitoring purposes, but it should be understood that this does not always imply clinical resistance.

Pigs

Escherichia coli

Isolates of *E. coli* are from clinical submissions of faecal samples or samples taken post-mortem from the gastro-intestinal tract. The isolates are tested by PCR for genes coding for the virulence factors enterotoxin (LT), heat-stable enterotoxin a and b (STa and STb), verocytotoxin (VT2e) and adhesion factors F4, F5, F6, F18 and F41. Only isolates with virulence factors are included in Table 4.8.

As in previous years, resistance to ampicillin, tetracycline and trimethoprim-sulphamethoxazole were the most common resistance traits. Resistance to ampicillin and to trimethoprim-sulphamethoxazole has increased considerably from 1995 with a peak in 2015-2016 but from 2019 there is a downward trend (Figure 4.4). Resistance to neomycin was comparatively low throughout this period (1995-2022).

Co-resistance between trimethoprim-sulphonamides and other antibiotics is common. Projects with randomised (i.e. non-biased) sampling was carried out both in 2016-2017

Figure 4.4. Resistance (%) in *Escherichia coli* from pigs 1995-2022 with a three-year moving average. Clinical isolates from faecal samples or from samples taken post-mortem from the gastro-intestinal tract. The number of isolates each year varies (n=52-482, 2022 n=61). From 2020 and onwards only results from isolates with virulence factors are shown.

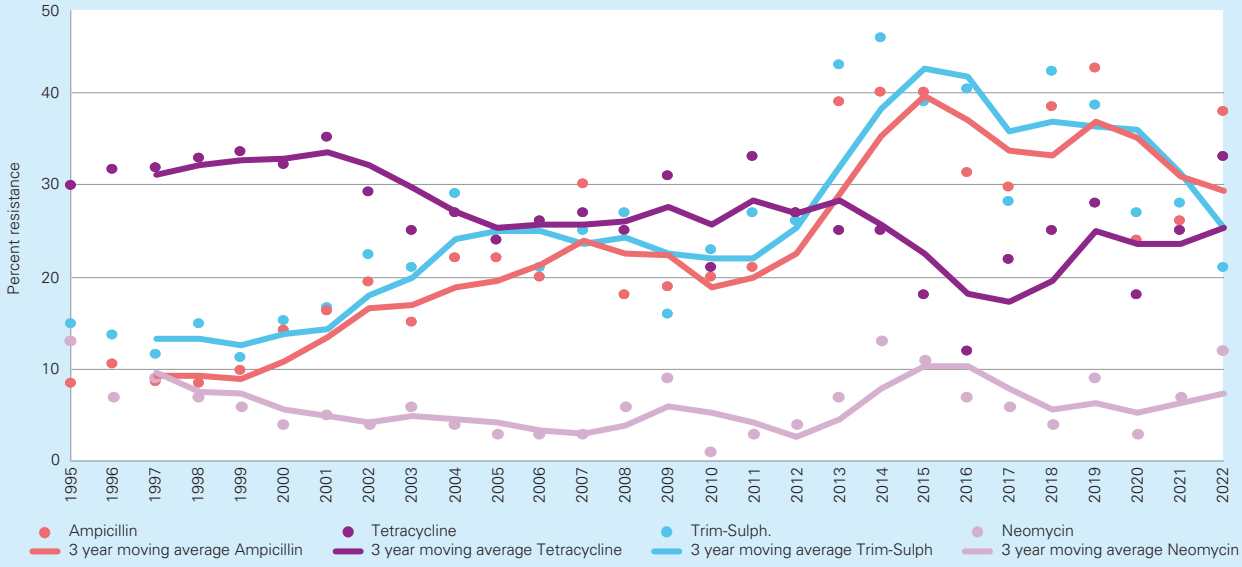


Table 4.8. Distribution of MICs and resistance (%) in enterotoxigenic *Escherichia coli* from pigs 2022.

Antibiotic	Resistance (%) 2022 n=61	Distribution (%) of MICs (mg/L) ≤0.06	0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	38						39.3	23.0			37.7	
Cefotaxime	0			100								
Colistin	3[b]					96.7		3.3				
Enrofloxacin	2		98.4		1.6							
Gentamicin	2						98.4	1.6				
Meropenem	0	98.4	1.6									
Neomycin	11							88.5		1.6	4.9	4.9
Tetracycline	33						67.2			1.6	31.1	
Trim-sulph.[a]	21				78.7				21.3			

[a]Concentration of trimethoprim is given, tested in concentration ratio 1/20 (trimethoprim/sulphamethoxazole). [b]Two isolates resistant to colistin were tested with PCR for the *mcr-1* to *mcr-9* genes and found negative.

and 2020. The results showed no major difference in resistance compared to the material from clinical submissions (see Swedres-Svarm 2017 and 2020). This indicates that a biased sampling is not the cause of high occurrence of resistance to ampicillin and trimethoprim-sulphamethoxazole in the isolates from material from clinical submissions received by SVA.

Multiresistance occurred in 20% (12/61) of the isolates in 2022 and has varied over the years (16% in 2021, 11% in 2020, 33% in 2019, 31% in 2018, 20% in 2017). Forty-nine percent of the isolates were susceptible to all tested antibiotics.

Brachyspira hyodysenteriae

Isolates of *Brachyspira hyodysenteriae* are from clinical submissions of faecal samples. Only one isolate from each herd and year is included in the analysis. The number of isolates each year varies (n=5-29, 2022 n=6). In routine diagnostics at SVA clinical breakpoints at >2 mg/L for tiamulin and >16 mg/L for tylosin are used. These breakpoints were also used in Svarm until 2011. Analysis of antibiotic susceptibility data from isolates of *B. hyodysenteriae* from Sweden 1990-2010 has resulted in a proposal for wild type cut-off values (Pringle et al., 2012). In Table 4.9 these cut-off values are used on all data. With the suggested wild type cut-off value >0.25 mg/L for tiamulin, resistance is detected throughout the period. However, during 2016, isolates with MICs above the clinical breakpoint (>2 mg/L) were detected for the first time from Swedish pigs. Therapeutic failure was also observed. Three isolates from 2016 and two from 2017 were classified as clinically resistant. The proposed cut-off value for tylosin (>16 mg/L), which is the same as the clinical breakpoint, has not been changed compared to previous years. Tylosin resistance has decreased over the years but increased slightly in 2018-2022.

Brachyspira pilosicoli

Isolates of *Brachyspira pilosicoli* are from clinical submissions of faecal samples. ECOFFs for *B. pilosicoli* are not defined for the antibiotics tested. The assessed percentage of resistance using the same wild type cut-off value as for *B. hyodysenteriae* is shown in Table 4.10. If clinical breakpoints for *Brachyspira hyodysenteriae* are used as guide for the choice of antibiotic for treatment of spirochaetal diarrhoea, 9% are resistant to tiamulin.

Resistance to tylosin has decreased from around 2010 but has started to increase the past years, whereas resistance to tiamulin has remained at a steady level (figure 4.5). However, the number of isolates analysed per year is low.

Figure 4.5. Resistance (%) to tylosin and tiamulin in *Brachyspira pilosicoli* from pigs 2005-2022 with a three-year moving average. The number of isolates per year has varied (n=7-67).

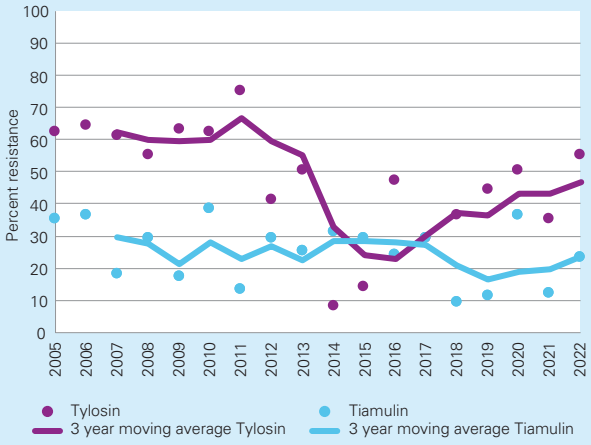


Table 4.9. Resistance (%) in *Brachyspira hyodysenteriae* from pigs 2005-2022 and distribution of MICs for isolates from 2018-2022. Clinical isolates from faecal samples.

Antibiotic	Resistance (%)					Distribution (%) of MICs (mg/L)												
	2005-06 n=54	2007-08 n=38	2009-11 n=40	2012-17 n=55	2018-22 n=38	≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	>128
Doxycycline	9	3	5	0	0			18.4	63.2	18.4									
Tiamulin	7	18	8	16[a]	11[b]		39.5	10.5	39.5	7.9	2.6								
Tylosin	81	76	60	42	68							7.9	7.9	15.8		2.6			65.8
Tylvalosin		93	55	51	68				2.6	10.5	18.4	2.6	7.9	26.3	23.7		7.9		
Valnemulin	0	18	3	24	8	47.4	39.5	5.3		5.3		2.6							

[a]Five isolates with MICs >2 mg/L are from a defined outbreak in 2016-2017, [b]One isolate with MIC >0,5 and two isolates with MICs >0,25 were from 2018 and 2019, respectively.

Table 4.10. Resistance (%) in *Brachyspira pilosicoli* from pigs 2012-2022, and distribution of MICs for 2012-2022. Clinical isolates from faecal samples.

Antibiotic	Resistance (%)	Distribution (%) of MICs (mg/L)													
	2012-2022 n=175	≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	>128
Doxycycline	4			42.3	49.7	4.6	2.3	0.6	0.6						
Tiamulin	22		60	8.6	9.1	9.7	1.7	1.7	1.7	2.3	5.1				
Tylosin	38							12.6	20.0	25.1	4.6	5.7	3.4	8	20.6
Tylvalosin	48				5.7	16	30.3	21.1	6.9	4	4	5.1	6.9		
Valnemulin	25	62.3	6.9	6.3	10.9	9.1	2.3	1.1		1.1					

Actinobacillus pleuropneumoniae

Isolates of *Actinobacillus pleuropneumoniae* are mostly from post-mortem investigations of lungs, but also from cases of arthritis. Data from 2021-2022 and back to 2005 show that the resistance situation is favourable and almost no resistance has been detected to tested antibiotics including penicillin during this period (Table 4.11). Since pneumonia caused by *A. pleuropneumoniae* is an important disease in pig production, sampling and susceptibility testing is desirable if emerging resistance is to be detected early. For treatment of *Actinobacillus pleuropneumoniae* with MICs within the wild type distribution of penicillin (MIC 0.12 – 0.5 mg/L), increased exposure to penicillin is required (Medical Products Agency, 2022). Exposure includes e.g., administration route, dose, and dose interval.

Pasteurella multocida

Clinical isolates of *Pasteurella multocida* are from post-mortem investigations of lungs. The last ten years the number of isolates has decreased to 3-10 isolates per year which is too few for a representative sample to present in a MIC distribution table. Almost all tested isolates are susceptible to all tested antibiotics including penicillin.

Streptococcus suis

Isolates of *Streptococcus suis* are from post-mortem examination of different organs in diseased pigs from 2013-2018 (n=37) and 2019-2022 (n=64). Resistance to penicillin was rarely found before 2020 (Table 4.12).

Table 4.11. Resistance (%) in *Actinobacillus pleuropneumoniae* and distribution of MICs from pigs 2021-2022, most samples are from lungs.

Antibiotic	Resistance (%)	Distribution (%) of MICs (mg/L)											
	2021-2022 n=36	≤ 0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32
Ampicillin	0			8.3	66.7	25.0							
Doxycycline	0					2.8	91.7	5.6					
Enrofloxacin	0		83.3	16.7									
Florfenicol	0							100					
Gamithromycin	0							2.8	19.4	77.8			
Penicillin	0			2.8	13.9	50.0	33.3						
Tetracycline	0					13.9	72.2	13.9					
Trim-Sulph.[a]	0		2.8	22.2	47.2	27.8							

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphamethoxazole).

Table 4.12. Resistance (%) in *Streptococcus suis* from pigs 2013-2018 and 2019-2022 and distribution of MICs for 2019-2022. Samples are from various organs.

Antibiotic	Resistance (%)		Distribution (%) of MICs (mg/L)								
	2013-2018 n=37	2019-2022 n=64	≤ 0.03	0.06	0.12	0.25	0.5	1	2	4	>4
Clindamycin	11	24					76.6		4.7	18.8	
Enrofloxacin	NR[b]	NR[b]				37.5	59.4	3.1			
Erytromycin	8	6					93.8	1.6	1.6	3.1	
Gentamicin	NR[b]	NR[b]						3.1	35.9	45.3	15.6
Penicillin	3	14	79.7	6.3		3.1	6.3	3.1	1.6		
Tetracycline	65	64				31.3	4.7	3.1	35.9	10.9	14.1
Trim-Sulph.[a]	11	17				82.8	3.1	9.4	1.6	1.6	1.6

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphamethoxazole); [b]Not relevant as the genus has inherently low susceptibility to the antibiotic.

Staphylococcus hyicus

Most isolates of *Staphylococcus hyicus* are from post-mortem investigations of joints in piglets with arthritis. The majority (72%) was collected in a project within SvarmPat in 2021 (for further information see In Focus: SvarmPat). A few isolates (n=5) were from skin or wounds. Resistance to penicillin was the most common trait followed by resistance to trimethoprim-sulphonamides (Table 4.13).

Streptococcus dysgalactiae subsp. *equisimilis*

Most isolates of *Streptococcus dysgalactiae* subsp. *equisimilis* are from post-mortem investigations of joints in piglets with arthritis, the majority (85%) of which was collected in a project within SvarmPat in 2021 (In Focus: SvarmPat). One isolate was from brain and another from a wound. All isolates were sensitive to penicillin (Table 4.14).

Table 4.13. Resistance (%) and distribution of MICs for *Staphylococcus hyicus* from pigs 2018-2022. Samples are from joints, skin, or wounds.

Antibiotic	Resistance (%)	Distribution (%) of MICs (mg/L)								
	2018-2022 n=88	≤ 0.03	0.06	0.12	0.25	0.5	1	2	4	>4
Clindamycin	2					97.7			2.3	
Enrofloxacin	3				96.6	3.4				
Erytromycin	3					95.5	1.1	1.1	2.3	
Fusidic acid	3					96.6	2.3		1.1	
Oxacillin	0				89.7	8.0	2.3			
Penicillin	72[b]	26.1	1.1	1.1		2.3	1.1	68.2		
Tetracycline	6				77.3	17.0				5.7
Trim-Sulph.[b]	27				72.7	4.5	12.5	8.0	1.1	1.1

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphamethoxazole); [b]Denotes beta-lactamase production.

Table 4.14. Distribution of MICs and resistance (%) for *Streptococcus dysgalactiae* subsp. *equisimilis* from pigs 2018-2022. Samples mostly from joints.

Antibiotic	Resistance (%)	Distribution (%) of MICs (mg/L)								
	2018-2022 n=52	≤ 0.03	0.06	0.12	0.25	0.5	1	2	4	>4
Clindamycin	12					88.5			11.5	
Enrofloxacin	NR[b]					78.8	21.2			
Erythromycin	13					86.5	1.9		11.5	
Gentamicin	NR[b]							5.8	42.3	51.9
Penicillin	0	100								
Tetracycline	NR[b]								40.4	59.6
Trim-sulph.[a]	0				94.2	5.8				

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphamethoxazole); [b]Not relevant as the genus has inherently low susceptibility to the antibiotic.

Cattle

Escherichia coli from faecal samples

Isolates of *E. coli* are from the gastro-intestinal tract of calves. Most of the isolates are from calves no more than a few weeks old, i.e. during a period when resistance in enteric bacteria often is high in cattle (Duse et al., 2015). Resistance was high to ampicillin, neomycin, and tetracycline (Table 4.15 and Figure 4.6). Multiresistance has varied through the years and occurred in 26% (12/46) of the isolates from 2021-2022. Seven percent (3/46) of the isolates were susceptible to all tested antibiotic substances.

Escherichia coli from milk samples

Isolates of *E. coli* are from clinical submissions of milk samples from dairy cows. It is likely that most sampled cows had clinical mastitis.

Most of the isolates (85%, 39/46) were susceptible to all antibiotics tested. Resistance to ampicillin (11%) and tetracycline (11%), were the most common traits, followed by enrofloxacin (7%) (Table 4.16). Two isolates (4%) were multiresistant, i.e. resistant to three or more antibiotics.

Figure 4.6. Resistance (%) in *Escherichia coli* from calves 2007-2022. Clinical isolates from faecal samples or from samples taken post-mortem from the gastro-intestinal tract. The number of isolates each year varies (n=12-58, 2021-2022=46).

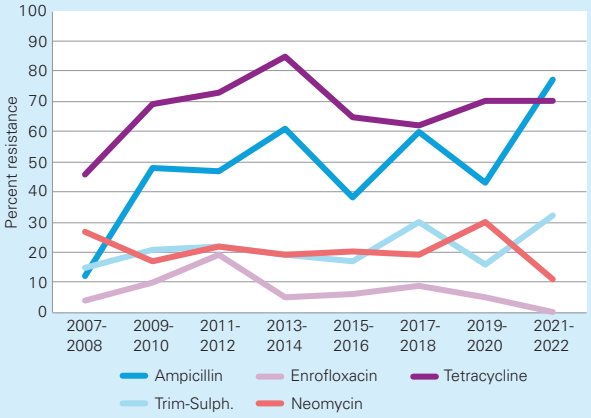


Table 4.15. Distributions of MICs and resistance (%) in *Escherichia coli* from calves 2021-2022. Clinical isolates from faecal samples or from samples taken post-mortem from the gastro-intestinal tract.

Antibiotic	Resistance (%) 2021-2022 n=46	Distribution (%) of MICs (mg/L) ≤ 0.06	0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	76						19.6	4.3			76.1	
Cefotaxime	9[b]			91.3	8.7							
Colistin	2[c]					95.7	2.2			2.2		
Enrofloxacin	0		100									
Gentamicin	0						100					
Meropenem	0	100										
Neomycin	11							89.1			2.2	8.7
Tetracycline	72						28.3				71.7	
Trim-sulph.[a]	30				69.6				30.4			

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphamethoxazole); [b]Four isolates with MICs 0.5 mg/L were further tested, and ESBL-A was detected; [c]One isolate with MIC >8 mg/L was tested with PCR for *mcr-1* to *mcr-9* genes and found negative.

Table 4.16. Resistance (%) in *Escherichia coli* from dairy cows 2018-2022. Distribution of MICs from 2022 in clinical isolates from milk.

Antibiotic	Resistance (%) 2018 n=100	2019 n=74	2020 n=60	2021 n=55	2022 n=46	Distribution (%) of MICs (mg/L) ≤ 0.06	0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	24	24	15	18	11						39.1	43.5	6.5		10.9	
Cefotaxime	0	0	0	0	0			100								
Colistin	0	0	0	0	0					95.7	4.3					
Enrofloxacin	1	3	2	0	7		93.5	2.2					4.3			
Gentamicin	1	3	2	0	0						100					
Meropenem			0	0	0	100										
Neomycin	5	1	2	4	4							93.5	2.2	4.3		
Tetracycline	8	18	7	9	11						89.1				10.9	
Trim-sulph.[a]	14	11	5	20	7				93.5				6.5			

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphamethoxazole).

Klebsiella pneumoniae from milk samples

Isolates of *Klebsiella pneumoniae* are from clinical submissions of milk samples from dairy cows (Table 4.17). Acquired low susceptibility was only detected to tetracycline. There is an inherent low susceptibility to ampicillin.

Staphylococcus aureus from milk samples

Isolates of *Staphylococcus aureus* are from clinical submissions of milk samples from dairy cows with clinical mastitis. In 2022, 774 isolates of *Staphylococcus aureus* were analysed for penicillinase production of which 3.1% (n=24) were positive. Corresponding numbers for 2021 were 1.2% (7/605), 2020 1.8% (10/551) and 2019 2.8% (15/551).

Pasteurella multocida

Most isolates of *Pasteurella multocida* are from nasal swabs from calves with respiratory disease or from post-mortem investigations of lungs. Because of change of panel design, comparison with data from earlier years was not possible. For older data see earlier Swedres-Svarm reports.

Antibiotic resistance was generally rare among isolates of *Pasteurella multocida* (Table 4.18), but beta-lactamase producing *P. multocida* have been isolated every year since 2016. In 2022, 13 isolates from the same farm were included. Of these, three were penicillin resistant. All penicillin resistant isolates (n=5) were also ampicillin resistant and produced beta-lactamase. Penicillin is considered the first-choice antibiotic for pneumonia in cattle in Sweden. Sampling and susceptibility testing are of importance for early detection of resistance, especially if therapeutic failure is seen.

Table 4.17. Resistance (%) in *Klebsiella pneumoniae* from dairy cows 2018-2022. Distributions of MICs from 2022. Clinical isolates from milk.

Antibiotic	Resistance (%)					Distribution (%) of MICs (mg/L)									
	2018 n=52	2019 n=34	2020 n=45	2021 n=39	2022 n=35	≤ 0.06	0.12	0.25	0.5	1	2	4	8	16	>16
Ampicillin	NR[b]	NR	NR	NR	NR								2.9	17.1	80.0
Cefotaxime	0	0	0	0	0			100							
Colistin	0	0	4[c]	0	0					100					
Enrofloxacin	8	6	4	0	0		100								
Gentamicin	0	0	2	0	0						100				
Meropenem			0	0	0	97.1	2.9								
Neomycin	5	1	0	0	0							100			
Tetracycline	8	18	11	0	9						91.4				8.6
Trim-sulph.[a]	14	11	13	0	0				100						

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphamethoxazole); [b]Not relevant as the genus has inherently low susceptibility to the antibiotic; [c]Two isolates with MIC 16 mg/L were negative for *mcr-1, mcr-2, mcr-3, mcr-4* and *mcr-5* genes with PCR. One isolate with MIC 4 mg/L was not available for PCR detection of *mcr* genes.

Table 4.18. Distribution of MICs and resistance (%) in *Pasteurella multocida* from calves 2022. Clinical isolates from the respiratory tract, isolated from nasal swabs or from post-mortem investigations of lungs.

Antibiotic	Resistance (%) n=35	Distribution (%) of MICs (mg/L)												
		≤ 0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	14				42.9	42.9			14.3					
Ceftiofur	0				100									
Enrofloxacin	0	85.7	11.4	2.9										
Florfenicol	0							100						
Gamithromycin	3						14.3	42.9	37.1	2.9		2.9		
Penicillin	14			17.1	62.9	5.7			14.3					
Tetracycline	0				2.9	57.1	40							
Trim-Sulph.[a]	0		28.6	62.9	8.6									

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphamethoxazole).

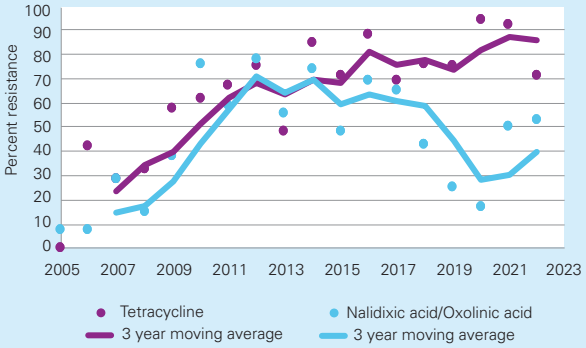
Farmed fish

Flavobacterium psychrophilum

Isolates of *Flavobacterium psychrophilum* are from clinical submissions of farmed fish, most of them from outbreaks of disease. More than one isolate can be analysed from the same outbreak. More than one phenotype is detected in more than half of the cases (data not shown). Data from 2017-2022 are compiled and presented as distributions of MICs in Table 4.19. Most isolates are from rainbow trout. Epidemiological cut-offs issued by CLSI are being used (CLSI, 2020b). Resistance to oxolinic acid and oxytetracycline was high in this material whereas no resistance to florfenicol was detected.

In Figure 4.7 resistance to tetracycline and quinolones (nalidixic acid or oxolinic acid) in *F. psychrophilum* 2005-2022 is shown. A three-year moving average is used. There is a marked increase in resistance to these antibiotics over the years despite a limited use up until recently (Svarm 2011, Svarm 2019). For nalidixic acid/oxolinic acid a downward trend is seen after a peak in 2012, however this downward trend seems to have turned in the latest years. Genome sequencing was used for analysis of a temporally and geographically representative set of *F. psychrophilum* isolates from outbreaks among Swedish farmed salmonid fish. The results indicate repeated nationwide introductions of new clones, presumably by trade of fish and eggs. It is probable that such introductions have contributed to the observed increase in resistance (Söderlund et al., 2018).

Figure 4.7. Resistance (%) in *Flavobacterium psycrophilum* to tetracycline and nalidixic acid/oxolinic acid from farmed fish 2005-2022 with a three-year moving average. No resistance to florfenicol was detected in this period. The number of isolates each year varies (n=8-31, 2022 n=17).



Laying hens

Escherichia coli

Isolates of *E. coli* are from laying hens from commercial farms and isolated at post-mortem. Usually more than one hen from the same farm is submitted for examination in disease outbreaks. Compared to 2017-2018 resistance was lower in 2022 for ampicillin and enrofloxacin but not for tetracycline (Table 4.20).

Table 4.19. Distributions of MICs and resistance (%) in *Flavobacterium psychrophilum* from farmed fish 2017-2022. The number of isolates each year varies (n=8-31).

Antibiotic	Resistance (%) 2017-2022 n=76	Distribution (%) of MICs (mg/L) ≤0.008	0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	>8
Florfenicol	0					9.2	28.9	42.1	18.4	1.3			
Oxolinic acid	38	1.3			1.3	28.9	30.3	2.6	5.3	30.3			
Oxytetracycline	82			1.3	14.5	2.6	1.3	3.9	3.9	21.1	40.8	10.5	

Table 4.20. Distributions of MICs 2022 and resistance (%) in *Escherichia coli* from laying hens 2017-2018 and 2022.

Antibiotic	Resistance (%) 2017-2018 n=100	2022 n=52	Distribution (%) of MICs (mg/L) ≤ 0.06	0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	11	0						48.1	50	1.9			
Cefotaxime	1[b]	0			100								
Colistin	1[c]	0					96.2	3.8					
Enrofloxacin	39	8		92.3	5.8	1.9							
Gentamicin	1	2						98.1	1.9				
Meropenem		0	100										
Neomycin	0	0							100				
Tetracycline	13	17						80.8	1.9			17.3	
Trim-sulph.[a]	3	0				100							

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphamethoxazole); [b]One isolate with MIC >2 mg/L carried a bla_{CMY-2} gene; [c]one isolate with MIC >8 mg/L was negative for *mcr-1* to *mcr-5* genes with PCR.

SvarmPat – monitoring of resistance in pathogens from farm animals

The SvarmPat programme (Swedish Veterinary Antibiotic Resistance Monitoring – farm animal pathogens) is a project in co-operation between Farm & Animal Health and SVA that started in 2005. It is financed by the Swedish Board of Agriculture.

The purpose of SvarmPat is to reduce emergence and spread of antibiotic resistance in pathogenic bacteria from farm animals, including farmed fish. This is achieved by monitoring and documenting antibiotic resistance in farm animal pathogens, by activities that increase knowledge of antibiotic resistance and prudent use of antibiotics, and by communication of knowledge to practitioners and farmers. Respiratory pathogens from farm animals are generally susceptible to benzylpenicillin, but penicillin resistance is common in *Staphylococcus hyicus* from pigs. Resistance in *E. coli* is most prominent in enteric isolates from young calves and pigs. Susceptibility testing for guidance in antibiotic therapy is warranted, especially for staphylococci, *E. coli*, and *Brachyspira* spp.

Selected studies within SvarmPat

Some of the results regarding resistance in various pathogens are available in Clinical isolates from animals.

Milk samples from dairy cows

Continuous monitoring of resistance in bacteria from clinical mastitis in dairy cows started in 2013. Randomly collected milk samples from dairy cows with clinical mastitis are cultured, isolated bacteria are susceptibility tested, and information about the cow and the herd is registered.

Between 2013 and 2018 samples from cows with clinical mastitis were cultured and 664 isolates susceptibility tested (Duse et al, 2021). The five most common pathogens isolated were *Staphylococcus aureus* (28%), *Streptococcus dysgalactiae* (16%), *Escherichia coli* (15%), *Streptococcus uberis* (11%) and *Trueperella pyogenes* (8%). Most pathogens were susceptible to antibiotics used in Sweden. Resistance to penicillin in *S. aureus* was low (3%), compared to a previous study (7%) from 2002-2003 (Bengtsson et al, 2009). The study also showed that the bacterial panorama was influenced by housing, season, and previous cases of mastitis in the individual cow.

Screening for MRSA in milk samples from dairy cows has been going on since 2010 within the SvarmPat program. Isolates of beta-lactamase producing *Staphylococcus aureus* from routine submissions to SVA are investigated for methicillin resistance. Between 2010 and 2022 about 1400 isolates of anonymous origin have been tested. Within the screening program, MRSA has been confirmed in ten isolates, most recently in 2017.

Respiratory tract samples from calves

One of the most common infections in calves is pneumonia caused by *Pasteurella multocida*, for which penicillin is considered the first-choice antibiotic in Sweden. However, since beta-lactamase producing *P. multocida* isolates have been isolated every year since 2016, sampling and susceptibility testing is important, especially if therapeutic failure is seen in a herd. PCR diagnostics are increasingly used to detect respiratory pathogens. Within SvarmPat, respiratory samples from calves that are PCR-positive for *P. multocida*, *Mannheimia haemolytica* or *Histophilus somni*, are being cultured, to obtain isolates for susceptibility testing.

Mycoplasma bovis - few treatment options

In SvarmPat samples from calves PCR-positive for *Mycoplasma bovis* have been cultured and susceptibility tested. MICs were high for most antibiotics available for treatments, except for enrofloxacin (Backhans et al, 2022). Standardized methods and clinical breakpoints are lacking, however, using sequencing, preliminary data show that the clone that is dominant in Swedish herds has mutations in ribosomal RNA that cause resistance to macrolides and tetracyclines. Overall, the results indicate that the treatment options for infections with *M. bovis* are few.

Respiratory tract samples from pigs

The important respiratory pathogens *Actinobacillus pleuropneumoniae* and *Pasteurella multocida* isolated from pigs are continuously susceptibility tested within SvarmPat. Resistance to penicillin in these bacteria is uncommon, supporting the recommendation to primarily use penicillin for treatment of pneumonia in pigs.

Streptococcus suis

Streptococcus suis is one of the most important pathogens in pigs. Penicillin is the primary choice of treatment but in recent years an increasing occurrence of penicillin resistance has been seen. In the years 2018-2021, 17% of *S. suis* were resistant using the clinical breakpoint >0,12 mg/L (Backhans & Pringle, 2022). Diagnostics and susceptibility testing should be performed when infection with *S. suis* is suspected. In case of longer treatment in a pig herd, sampling and testing should be repeated.

Enteric samples from pigs

Escherichia coli

Resistance to ampicillin and trimethoprim-sulphamethoxazole in *Escherichia coli* isolated from piglets with diarrhoea has been increasing over the years but stabilized around 2015. This emphasizes the importance of susceptibility testing in herds with neonatal and post-weaning diarrhoea.

Brachyspira hyodysenteriae

Swine dysentery is a severe disease in pigs, with a few cases each year in Sweden. The resistance situation in the causative agent *B. hyodysenteriae* is favourable compared to many other countries, but clinical resistance to tiamulin in *B. hyodysenteriae* was detected for the first time 2016 in an outbreak in several herds. Within SvarmPat whole genome sequencing was used, and it confirmed that the outbreak was caused by the same clone. Since 2018 no tiamulin resistant isolates have been detected.

Brachyspira pilosicoli

Spirochaetal diarrhoea is a less severe but more common disease than swine dysentery. Cases with treatment failure have been reported, but breakpoints for antibiotic resistance specific for *B. pilosicoli* are lacking.

Bacteria in arthritis in pigs

During 2021, 130 suckling piglets with lameness were euthanized and submitted for necropsy and bacteriological examinations. Macroscopic changes indicating a chronic process were observed in 38% of the 130 pigs (Berglund, 2022), indicating that lameness in piglets is difficult to detect in the early stages. Results from bacteriology showed that *Streptococcus dysgalactiae* subsp. *equisimilis* and *Staphylococcus hyicus* were the most common pathogens (Sandström, 2022). All isolates of *S. dysgalactiae* subsp. *equisimilis* were sensitive to penicillin while almost 70% of the *S. hyicus* isolates were penicillin resistant. Thus, penicillin may be ineffective for a large part of cases of septic arthritis in suckling pigs in Sweden.

Bacteria from farmed fish

In case of outbreaks of disease caused by pathogenic bacteria among farmed fish, up to five isolates from each outbreak are being susceptibility tested within SvarmPat. Bacterial species vary depending on the fish species. In 2022 isolates of *Flavobacterium psychrophilum*, *Flavobacterium columnare*, atypical *Aeromonas salmonicida*, *Aeromonas* spp., *Aeromonas salmonicida* ssp. *salmonicida*, *Aeromonas hydrophila*, *Yersinia ruckeri*, *Vibrio anguillarum*, *Pseudomonas* spp., *Pseudomonas fluorescens* and *Lactobacillus* species were susceptibility tested. In the most commonly isolated bacteria *F. psychrophilum*, resistance to oxolinic acid and tetracycline was high but no resistance to florfenicol was detected. In the other bacteria from farmed fish, resistance was uncommon.

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Horses

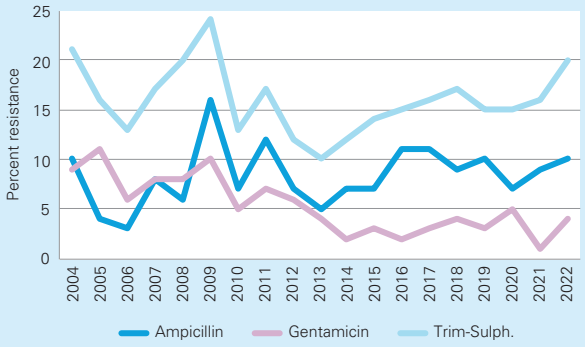
Escherichia coli

Isolates of *Escherichia coli* are from clinical submissions of samples from the genital tract of mares. As in previous years, resistance to trimethoprim-sulphamethoxazole was the most common trait in 2022 and the resistance has gradually increased from 10% in 2013 to 20% in 2022 (Table 4.21 and Figure 4.8). The resistance to gentamicin is continuously low, from 2013 and onwards ≤5% (Figure 4.8). However, this resistance has differed somewhat over the years and trends are difficult to estimate.

Seventy-six percent (215/282) of the isolates were susceptible to all the tested antibiotics. The proportion of multiresistance for the tested isolates was the same as in 2020-2021, i.e., 5% (15/282). The proportion has somewhat declined since 2019 (9%) (see previous Swedres-Svarm reports). Six of the fifteen multiresistant isolates were resistant to three antibiotics and nine to four antibiotics. The most common phenotype was resistance to ampicillin, tetracycline and trimethoprim-sulphamethoxazole, occurring in thirteen of the fifteen multiresistant isolates. This phenotype was also the most common in *E. coli* isolated from dogs (74%). Eight of the nine isolates resistant to four antibiotics had the common phenotype and all eight were in addition resistant to gentamicin. For comparison of resistance in *E. coli* of different origin see "Comparative analysis".

None of the isolates were resistant to cefotaxime, colistin or meropenem.

Figure 4.8. Resistance (%) in clinical isolates of *Escherichia coli* from horses 2004-2022. Isolates are from clinical sampling of the genital tract of mares. The number of isolates each year varies (n=124-324, 2022 n=282).



Streptococcus equi ssp. *zooepidemicus*

Isolates of *Streptococcus equi* ssp. *zooepidemicus* are from clinical submissions, and mainly from the respiratory tract (82%) of horses. Over the years, most of the isolates have been susceptible to all relevant tested antibiotics, apart from clindamycin and trimethoprim-sulphamethoxazole. The proportion of resistance has varied, for clindamycin between 4% and 11% in 2015-2022. For trimethoprim-sulphamethoxazole there was an increase in resistance between 2015-2018, from 7 to 18%, and from 2018 and onwards a decline to 1% in 2022 (Table 4.22 and previous Swedres-Svarm reports). The number of isolates is few and varies each year (n=43-85, and in 2022 n=102) which could somewhat cause minor variations between years.

Table 4.21. Distribution of MICs and resistance (%) in *Escherichia coli* from horses, 2022. Clinical isolates from the genital tract of mares.

Antibiotic	Resistance (%) 2022 n=282	≤0.06	0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	10						30.5	55.3	4.3	0.7	9.2	
Cefotaxime	0			100								
Colistin	0					98.2	1.8					
Enrofloxacin	<1		99.6	0.4								
Gentamicin	4						96.1	0.7		1.8	1.4	
Meropenem	0	99.6	0.4									
Neomycin	<1							98.9	0.4	0.7		
Tetracycline	9						90.8			0.4	8.9	
Trim-Sulph.[a]	20				79.8	0.7		0.4	19.1			

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphamethoxazole).

Table 4.22. Distribution of MICs and resistance (%) in *Streptococcus equi* ssp. *zooepidemicus* isolated from horses, 2022. Clinical isolates mainly from the respiratory tract.

Antibiotic	Resistance (%) 2022 n=102	Distribution (%) of MICs (mg/L) ≤0.03	0.06	0.12	0.25	0.5	1	2	4	>4
Cephalotin	0						100			
Clindamycin	9					91.2	8.8			
Erythromycin	1					99.0	1.0			
Gentamicin	NR[b]						1.0	1.0	3.9	94.1
Penicillin	1	98.0	1.0	1.0						
Tetracycline	NR[b]				2.0	1.0	2.9	24.5	59.8	9.8
Trim-Sulph.[a]	1				90.2	8.8	1.0			

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphamethoxazole); [b]NR= Not relevant as the inherent susceptibility is above concentrations that can be obtained during therapy.

The one isolate with penicillin MIC 0.12 mg/L, above the epidemiological cut-off (Table 6.9), was not available for further analysis. Though, as the clinical breakpoint for *S. equi* ssp. *zooepidemicus* and penicillin is MIC >0.25 mg/L, the isolate was still interpreted as clinically susceptible to penicillin. Any reduced susceptibility to penicillin in beta-haemolytic streptococci should be controlled, i.e., if tested on pure culture and ensured that antimicrobial susceptibility test results and organism identification are accurate and reproducible.

Streptococcus equi ssp. *zooepidemicus* has a low inherent susceptibility to aminoglycosides (as gentamicin) and tetracyclines.

Staphylococcus aureus

Isolates of *Staphylococcus aureus* are from clinical submissions of samples from skin lesions, excluding wounds and abscesses, from horses.

Resistance to penicillin due to penicillinase production is still the most common trait, but the proportion has overall declined from 36% in 2008 to 17% in 2022 (Figure 4.9 and Table 4.23). The proportions of resistance to gentamicin, tetracycline and trimethoprim-sulphamethoxazole have differed slightly over the years and trends are difficult to estimate (Figure 4.9). In addition, the EUCAST ECOFF for trimethoprim-sulphamethoxazole and *S. aureus* was changed from MIC >0.5 mg/L to > 0.25 mg/L in 2022. In Figure 4.9 the proportion of resistance for trimethoprim-sulphamethoxazole has been adjusted back to 2015, as before 2015 the tested range of concentrations of trimethoprim-sulphamethoxazole did not match the new cut-off. Resistance to fusidic acid among the tested isolates has varied since 2017, from 5 to 17% and was in 2022 11% (Table 4.23 and previous Swedres-Svarm reports).

Fifty-eight percent (74/128) of the isolates were susceptible to all the tested antibiotics. Six isolates (5%) were resistant to three of the tested antibiotics (i.e., multiresistant), and comparable to the figures in 2015-2021 (0-5%) (see previous Swedres-Svarm reports). No specific phenotype was noticed.

One isolate was resistant to cefoxitin (MIC >4 mg/L), but negative when tested with PCR for detection of the *mecA* and *mecC* genes. For more information about MRSA isolated from horses in Sweden, see "Notifiable diseases, Methicillin-resistant *Staphylococcus aureus* (MRSA)".

Figure 4.9. Resistance (%) in clinical isolates of *Staphylococcus aureus* 2008-2022 from skin of horses. Figures for trimethoprim-sulphamethoxazole 2015-2022.The number of isolates each year varies (n=75-145, 2022 n=128).

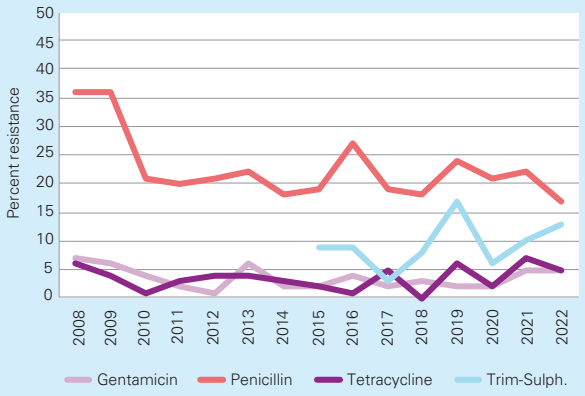


Table 4.23. Distribution of MICs and resistance (%) in *Staphylococcus aureus* isolated from horses, 2022. Clinical isolates from the skin.

Antibiotic	Resistance (%) 2022 n=128	Distribution (%) of MICs (mg/L)									
		≤0.25	0.5	1	2	4	8	16	32	64	>64
Cefoxitin	<1[c]				10.2	89.1	0.8				
Cephalotin	5			95.3	3.1	1.6					
Clindamycin	4		96.1	3.1	0.8						
Enrofloxacin	2	89.1	8.6	2.3							
Erythromycin	2		92.2	5.5	2.3						
Fusidic acid	11		89.1	3.9	1.6	5.5					
Gentamicin	5			86.7	8.6	2.3	2.3				
Nitrofurantoin	4							89.8	6.3	2.3	1.6
Penicillin[a]	17										
Tetracycline	5	75.6	18.0	1.6	3.9	0.8					
Trim-Sulph.[b]	13	87.5	6.3	3.9	0.8	1.6					

[a]Denotes beta-lactamase production; [b]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphamethoxazole); [c]The isolate (n=1) resistant to cefoxitin (MIC >4 mg/L) was tested with PCR for the *mecA* and *mecC* genes and found negative.

Actinobacillus

Isolates of *Actinobacillus* spp. are from clinical submissions of samples from various locations, of which the most common were wounds (36%) and respiratory tract (23%). Fifteen percent of the samples are from various internal organ.

For *Actinobacillus* spp. isolated from horses, ECOFFs for *A. pleuropneumoniae* have been used regarding penicillin, tetracycline and trimethoprim-sulphamethoxazole. For other antibiotics clinical breakpoints have been applied (Table 4.24). Isolates with MIC >0.25 mg/L for penicillin (37%, 36/97) have been tested for penicillinase production. All isolates with MIC 0.5 and 1 mg/L were negative, while seven of the nine isolates with MIC >1 mg/L were positive for penicillinase production. These results agree with those from a previous study where 149 isolates of *Actinobacillus* spp. from horses in Sweden were tested (Sternberg et al., 1999).

For treatment the *Actinobacillus* spp. wild type distribution of penicillin (MIC 0.03 - 1 mg/L) requires increased exposure to penicillin (Medical Products Agency, 2015). Exposure includes e.g. administration route, dose, and dose interval.

Table 4.24. Distribution of MICs and resistance (%) in *Actinobacillus* spp. from horses, 2022. Clinical isolates from various locations.

Antibiotic	Resistance (%) 2022 n=97	Distribution (%) of MICs (mg/L) ≤0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	>4
Enrofloxacin	4	66.0	17.5	11.3	1.0	2.1		2.1			
Gentamicin	NR[b]							11.3	46.4	30.9	11.3
Penicillin	9		3.1	5.2	19.6	35.1	19.6	8.2	9.3		
Tetracycline	0				2.1	30.9	57.7	8.2	1.0		
Trim-Sulph.[a]	8		46.4	28.9	13.4	3.1	2.1	4.1	2.1		

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphamethoxazole); [b]NR = Not relevant as the inherent susceptibility is above concentrations that can be obtained during therapy.

Dogs

Escherichia coli

Isolates of *Escherichia coli* are from clinical submissions of urine from dogs, submitted either as urine or cultures from dipslides or other agar plates. As in previous years, resistance to ampicillin was the most common trait in 2022, 13% (Table 4.25 and Figure 4.10). Although the proportion of resistance in the tested isolates has varied somewhat between 2005 and 2022 there is a slight decline for the four antibiotics ampicillin, enrofloxacin, nitrofurantoin and trimethoprim-sulphamethoxazole (Figure 4.10).

Eighty percent (768/956) of the isolates were susceptible to all the tested antibiotics. The proportion of multiresistance was 3% (31/956), and comparable to 2020-2021 (3 and 2%), but slightly lower compared to 2015-2019 (between 6 and 9%) (see previous Swedres-Svarm reports). Fifty-five percent (17/31) of the multiresistant isolates were resistant to three antibiotics, 29% (9/31) to four, and 16% (5/31) to five antibiotics. For comparison of resistance in *E. coli* of different origin see "Comparative analysis".

The most common phenotype, resistance to ampicillin, tetracycline and trimethoprim-sulphamethoxazole, was detected in 74% (23/31) of the multiresistant isolates. Of the fourteen isolates resistant to four or five antibiotics all isolates, except one, were of the common phenotype, and commonly also resistant to enrofloxacin (9/14, 64%). Of the five isolates resistant to 5 antibiotics, four were resistant to both enrofloxacin and gentamicin.

Fifteen (2%) of the *E. coli* isolates were resistant to cefotaxime (MIC >0.25mg/L), and all were available for further testing. Genes conferring transferable ESC resistance were detected in four of the isolates. Three of the isolates carried the gene $bla_{CTX\text{-}M\text{-}15}$ and one carried $bla_{CTX\text{-}M\text{-}1}$. For more information about ESBL-producing Enterobacterales isolated from dogs in Sweden, see Notifiable diseases, ESBL-producing Enterobacterales. None of the isolates were resistant to meropenem (MIC >0.12mg/L).

Five of the isolates were resistant to colistin (MIC >2mg/L). All five isolates were available for PCR detection of the *mcr-1* to *mcr-9* genes, and all were negative.

Figure 4.10. Resistance (%) in clinical isolates of *Escherichia coli* from dog urine 2005-2022. The number of isolates each year varies (n=304-1162, 2022 n=956).

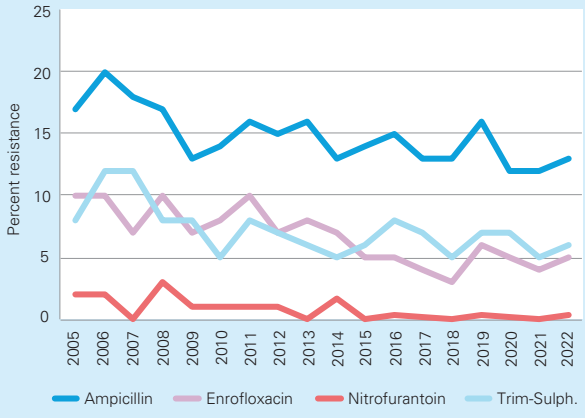


Table 4.25. Distribution of MICs and resistance (%) in *Escherichia coli* from dogs, 2022. Clinical isolates from urine.

Antibiotic	Resistance (%) 2022 n=956	Distribution (%) of MICs (mg/L) ≤0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	13						45.3	39.1	2.5	0.3	12.8		
Cefalexin	1							8.4	80.1	10.1	0.1	1.3	
Cefotaxime	2[b]			98.4	0.4	0.4	0.2	0.5					
Colistin	<1[c]					98.6	0.8	0.2		0.3			
Enrofloxacin	5		94.9	1.8	1.5	0.8	0.2		0.8				
Gentamicin	1						98.8	0.3	0.2		0.6		
Meropenem	0	99.7	0.3										
Neomycin	<1							99.3		0.3	0.2	0.2	
Nitrofurantoin	<1										98.4	1.2	0.4
Tetracycline	5						93.4	1.0	0.1		5.4		
Trim-Sulph.[a]	6				92.8	1.0	0.4	0.1	5.6				

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphamethoxazole); [b]All isolates (n=15) with MIC >0.25 mg/L were available for verification. Genes conferring transferable ESC resistance were detected in four of them; [c]All isolates (n=5) with MIC >2mg/L were available for PCR detection of the *mcr-1* to *mcr-9* genes, and all were negative.

Staphylococcus pseudintermedius

Isolates of *Staphylococcus pseudintermedius* are from clinical submissions of samples from dogs. Until 2017, only resistance of *S. pseudintermedius* isolated from clinical submissions of sample from skin lesions were reported (see previous Swedres-Svarm reports). From 2017 and onwards three different sample collections have been compared, namely skin lesions (S1), wounds (S2) and external ear (S3) (see Table 4.26 and previous Swedres-Svarm reports). In Swedres-Svarm 2022 some data from the sample collection ear (S3) will be presented under "In Focus Interpretation of antibiotic susceptibility for topical treatment".

Resistance to penicillin due to penicillinase production is high for all three sample collections (S1: 70%, S2 and S3: 74% Table 4.26), compared to 4% in *S. schleiferi* (Table 4.27) isolated from dogs, 14% in *S. felis* (Table 4.31) from cats and 17% in *S. aureus* (Table 4.23) from horses. Although still high, the proportion of resistance to penicillin for isolates from skin lesions has declined from 90% in 2009 to 70% in 2022 (see previous Swedres-Svarm reports). Any decline of resistance in the two sample collections S2 and S3 is less obvious as figures could be compared only back to 2017. Compared to penicillin, resistance to clindamycin and tetracycline remains at lower levels, but has also declined since

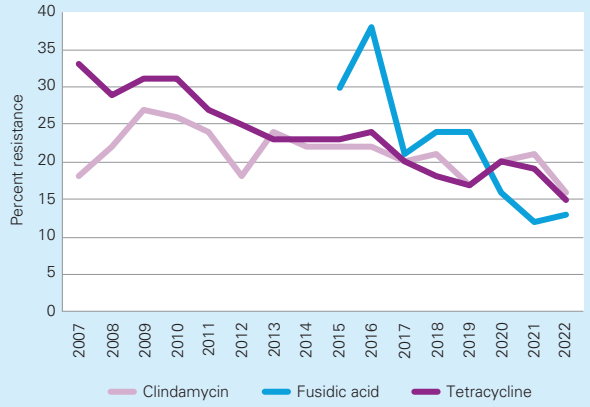
Table 4.26. Distribution of MICs and resistance (%) in *Staphylococcus pseudintermedius* from dogs 2022. Clinical isolates from skin (S1), wounds (S2) and external ear (S3).

Antibiotic	Resistance (%) 2022 n=478 S3	2022 n=852 S2	2022 n=505 S1	Distribution (%) of MICs (mg/L), isolates from skin (S1) ≤0.25	0.5	1	2	4	8	16	32	64	>64
Cephalothin	<1	<1	2			98.4	1.2	0.4					
Cefoxitin[a]				57.6	38.6	2.6	0.8	0.4					
Clindamycin	14	13	16		84.4	1.6	0.4	13.7					
Enrofloxacin	<1	1	<1	94.3	5.1	0.6							
Erythromycin	16	15	17		83.0	1.4	0.8	14.9					
Fusidic acid	11	10	13		86.7	1.8	0.8	10.7					
Gentamicin	6	4	4			96.0	1.8	0.8	1.4				
Nitrofurantoin	<1	<1	1							97.2	1.6	1.2	
Oxacillin	<1[d]	<1[d]	<1[d]	99.8	0.2								
Penicillin[b]	74	74	70										
Tetracycline	19	18	15	83.0	2.4	1.2	0.4		13.1				
Trim-Sulph.[c]	10	7	7	62.6	30.3	4.2	0.6	0.2	2.2				

[a]No cut-off available for *S. pseudintermedius;* [b]Denotes beta-lactamase production; [c]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphamethoxazole); [d]The six isolates with MIC>0.25 for oxacillin were tested with PCR for detection of the *mecA* and *mecC* genes, and all were negative.

2007. The proportion of resistance to fusidic acid is not comparable before 2015, due to change in cut off and in the tested range of concentrations but has, since 2015, declined (Table 4.26 and Figure 4.11).

Figure 4.11. Resistance (%) in *Staphylococcus pseudintermedius* from dogs, 2007-2022. Figures for fusidic acid 2015-2022. Clinical isolates from skin (S1). The number of isolates each year varies (n=220-567, 2022 n=505).



Compared to other staphylococci isolated from animals, the proportion of resistance is high in the tested isolates. Twenty-three percent (118/505) in sample collection skin (S1), 21% (178/852) in collection wounds (S2) and 19% (88/473) in collection ear (S3) were susceptible to all the tested antibiotics. The proportion of multiresistance for the S1 isolates was 18% (93/505), S2 17% (148/852) and S3 20% (94/473). This could be compared to 4% multiresistance in *S. schleiferi* isolated from dogs and 5% in *S. aureus* from horses and *S. felis* from cats. Forty-four percent (41/93) of the multiresistant S1 isolates were resistant to three antibiotics; 41% (38/93 to four; 11% (10/93) to five; 3% (3/93) to six and 1% (1/93) to seven antibiotics. The proportion of isolates resistant to five or more antibiotics has declined over the recent years. In 2016 almost one-third of the multiresistant isolates were resistant to five or more antibiotics, compared to 15-22% in 2017-2021, and 15% (14/93) in 2022.

Of the multiresistant isolates, resistance to penicillin, clindamycin and erythromycin was the most common phenotype for all three sample collections, S1: 74% (69/93), S2: 66% (97/148) and S3: 62% (58/94). Eighty-seven percent (45/52) of the isolates resistant to four or more antibiotics of sample collection S1 had the common phenotype and combined with resistance to fusidic acid (46%, 24/52) and/or tetracycline (44% 23/52) and/or trimethoprim/sulphamethoxazole (17%, 9/52).

One of the S1 isolates, three S2 and two S3 isolates were resistant to oxacillin (MIC >0.25 mg/L). All six isolates were tested with PCR for detection of the *mecA* and *mecC* genes and all six were negative. For more information on MRSP isolated from dogs in Sweden, see Notifiable diseases, Methicillin-resistant *Staphylococcus pseudintermedius* (MRSP).

Staphylococcus schleiferi

Isolates of *Staphylococcus schleiferi* are from clinical submissions of samples of various locations from dogs, but mainly from the external ear canal (55%) or skin (28%). In Swedres-Svarm 2022 some data from the sample collection of *S. schleiferi* will be presented under "In Focus Interpretation of antibiotic susceptibility for topical treatment".

The proportion of resistance in isolates of *S. schleiferi* (Table 4.27) was low for most antibiotics compared to isolates of the more common staphylococci, *S. pseudintermedius* (Table 4.26), isolated from dogs. The proportion of penicillinase producing isolates among the tested *S. schleiferi* isolates was 4%, which is low compared to other *Staphylococcus* spp. from animals, and comparable to figures in 2014-2021 (<1-4%) (see previous Swedres-Svarm reports). Resistance to enrofloxacin seems high compared to other staphylococci presented in Swedres-Svarm, although the figure has declined,

Table 4.27. Distribution of MICs and resistance (%) in *Staphylococcus schleiferi* from dogs, 2022. Clinical isolates from various locations.

Antibiotic	Resistance (%) 2022 n=170	Distribution (%) of MICs (mg/L)									
		≤0.25	0.5	1	2	4	8	16	32	64	>64
Cephalothin	0			100							
Cefoxitin[a]		29.4	68.8	1.2	0.6						
Clindamycin	7		93.5	2.9	0.6	2.9					
Enrofloxacin	8	82.4	10.0	6.5	1.2						
Erythromycin	7		93.5	1.8	0.6	4.1					
Fusidic acid	24		75.9	10.6	10.0	3.5					
Gentamicin	4			95.9	2.9	1.2					
Nitrofurantoin	1							95.3	3.5	1.2	
Oxacillin	0	99.4	0.6								
Penicillin[b]	4										
Tetracycline	6	88.2	5.9	2.9	2.9						
Trim-Sulph.[c]	0	96.5	3.5								

[a]No cut-off available for *S. schleiferi*; [b]Denotes beta-lactamase production; [c]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphamethoxazole).

from 20% in 2016 to 8% in 2022. For the other tested antibiotics there is no major difference between years (see Table 4.27 and previous Swedres-Svarm reports).

Sixty-one percent (103/170) of the *S. schleiferi* isolates were susceptible to all the tested antibiotics. This is a negative trend, as 81% of the isolates were susceptible to all tested antibiotics in 2018 and since the figures have gradually declined to 61% in 2022. Multiresistance was detected in 4% (7/170) of the isolates and is comparable to figures in 2018-2021 (1-7%). Of the seven multiresistant isolates, three were resistant to three of the tested antibiotics, two isolates to four, and one to five and six antibiotics respectively. Five of the seven multiresistant isolates were resistant to erythromycin, clindamycin, and tetracycline. No other specific phenotype was noticed.

Pseudomonas aeruginosa

Isolates of *Pseudomonas aeruginosa* are from clinical submissions of samples from the external ear canal in dogs.

In Swedres-Svarm 2022 some of the sample collection of *P. aeruginosa* will be presented under "In Focus Interpretation of antibiotic susceptibility for topical treatment".

Pseudomonas aeruginosa is inherently resistant to trimethoprim-sulphonamides, tetracyclines and aminopenicillins (including combinations with clavulanic acid). The isolates of *P. aeruginosa* were prior to 2014 tested for polymyxin B susceptibility and all tested isolates have been sensitive throughout the years (see previous Swedres-Svarm reports). In 2014 polymyxin B was replaced by the equivalent colistin and since, 0-1% of the tested isolates have been resistant to colistin. The proportion of resistance to enrofloxacin has gradually declined from 25% in 2009 to 7% in 2022. The figures for gentamicin have stabilized at ≤1-2% over the recent years (see Table 4.28 and previous Swedres-Svarm reports). Of the resistant isolates, none were resistant to more than one of the tested antibiotics.

Pasteurella canis/oralis

Isolates of *Pasteurella* spp. are from clinical submissions of samples from various locations from dogs, mainly wounds (59%), abscesses (13%) and skin and external ear canal (12%).

Pasteurella canis/oralis was the most common *Pasteurella* sp. isolated in samples from dogs, 70% (246/349). The isolates were species identified with MALDI-TOF MS and *P. canis* and *P. oralis* cannot be separated by the method.

The cut-off for *Pasteurella multocida* has been applied for all *Pasteurella* spp. isolates tested. *Pasteurella* spp. have a low inherent susceptibility to aminoglycosides, e.g., gentamicin. If not including gentamicin, 99% (243/246) of the isolates were susceptible to all antibiotics tested. No tested substance had a resistance level above 1% (Table 4.29). The proportion of resistance has been constantly low in previous years.

The proportion of resistance to enrofloxacin is generally low, with variations between <1% (2014) and 4% (2020) during the last years. Resistance to trimpethoprim-sulphamethoxazole has been detected in one isolate each year 2020- 2021 and, in 2022, two isolates (Table 4.29 and previous Swedres-Svarm reports). Before 2020, all tested isolates were susceptible to trimethoprim-sulphamethoxazole (see previous Swedres-Svarm reports).

Out of the three resistant isolates, one was resistant to both enrofloxacin and trimethoprim-sulphamethoxazole, the other two were resistant to enrofloxacin.

Table 4.28. Distribution of MICs and resistance (%) in *Pseudomonas aeruginosa* from dogs, 2022. Clinical isolates from the external ear canal.

Antibiotic	Resistance (%) 2022 n=202	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	>16
Enrofloxacin	7	3.5	7.4	39.1	32.2	10.9	5.0	2.0		
Colistin[a]	0				72.3	22.8	5.0			
Gentamicin	1					86.1	10.0	2.5	1.0	0.5

[a]Colistin is equivalent to polymyxin B.

Table 4.29. Distribution of MICs and resistance (%) in *Pasteurella canis/oralis* from dogs, 2022. Clinical isolates from various locations.

Antibiotic	Resistance (%) 2022 n=246	Distribution (%) of MICs (mg/L) ≤0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	>4
Ampicillin	0			86.2	12.6	1.2					
Enrofloxacin	1	92.3	4.5	2.0				1.2			
Gentamicin	NR[b]							95.1	4.1	0.8	
Penicillin	0		40.2	54.5	4.9	0.4					
Tetracycline	0				15.9	73.6	9.3	1.2			
Trim-Sulph.[a]	<1		93.1	5.3	0.8	0.4			0.4		

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphamethoxazole); [b]*Pasteurella* spp. have a low inherent susceptibility to aminoglycosides, as gentamicin.

Cats

Escherichia coli

Isolates are from clinical sampling of urine, submitted either as urine or cultures from dip-slides or other agar plates. As in previous years, and in *Escherichia coli* isolated from urine in dogs (Table 4.25), resistance to ampicillin was the most common trait in 2022 (Table 4.30 and Figure 4.12). In comparison, in *E. coli* isolated from the genital tract of horses (mares) resistance to trimethoprim-sulphamethoxazole was most common (Table 4.21 and Figure 4.8). The proportions of resistance in the *E. coli* isolated from cat urine have differed somewhat throughout the years and trends are difficult to estimate (Figure 4.12).

Seventy-seven percent (338/439) of the *E. coli* isolates were susceptible to all the tested antibiotics. The proportion of multiresistance was 2% (8/439), and comparable to figures from 2010-2021 (1-5%) (see previous Swedres-Svarm reports). Seven of the eight multiresistant isolates were resistant to three antibiotics and one to four antibiotics. No specific phenotype was noticed. For comparison of resistance in *E. coli* of different origin see "Comparative analysis".

Eleven of the *E. coli* isolates were resistant to cefotaxime (MIC >0.25 mg/L). Genes conferring transferable ESC resistance were detected in one of the isolates (bla_{SHV-12}). For more information of ESBL isolated from cats in Sweden, see Notifiable diseases, ESBL-producing Enterobacterales.

One isolate was resistant to colistin (MIC >2mg/L) but found negative in PCR detection of the *mcr-1* to *mcr-9* genes.

Figure 4.12. Resistance (%) in clinical isolates of *Escherichia coli* from urine of cats, 2007-2022. The number of isolates each year varies (n=131-545, 2022 n=439).

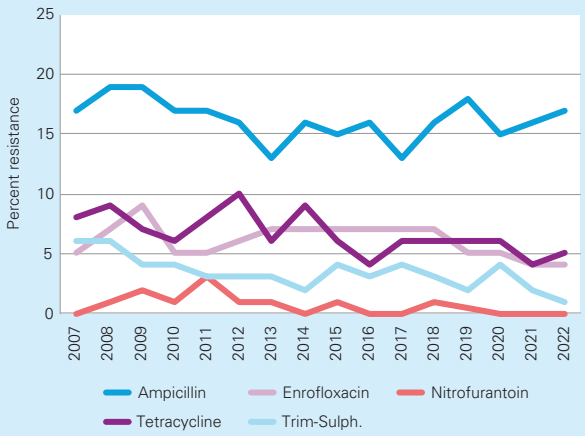


Table 4.30. Distribution of MICs and resistance (%) in *Escherichia coli* isolated from cats, 2022. Clinical isolates from urine.

Antibiotic	Resistance (%) 2022 n=439	Distribution (%) of MICs (mg/L) ≤0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	17						53.8	28.0	0.9	0.2	17.1		
Cefalexin	3							13.4	77.4	6.4	0.2	2.5	
Cefotaxime	3[b]			97.5	1.4	0.7	0.2	0.2					
Colistin	<1[c]					99.3	0.5	0.2					
Enrofloxacin	4		95.9	3.2	0.5				0.5				
Gentamicin	<1						99.1	0.2	0.2	0.5			
Meropenem	0	100											
Neomycin	<1							99.1				0.9	
Nitrofurantoin	0										98.6	1.4	
Tetracycline	5						95.0	0.2	0.2		4.6		
Trim-Sulph.[a]	1				98.4	0.2			1.4				

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphamethoxazole); [b]Eleven isolates with MIC >0.25mg/L were available for verification. Genes conferring transferable ESC resistance were detected in one of the isolates; [c]The one isolate with MIC >2mg/L was available for PCR detection of the *mcr-1* to *mcr-9* genes and the isolate was negative.

Staphylococcus felis

Isolates of *Staphylococcus felis* are from clinical submissions of samples from various locations, mainly abscesses and wounds (35%), the external ear canal (25%), and urine (23%).

The proportion of resistance to the tested antibiotics in isolates of *S. felis* (Table 4.31) were, as in previous years, lower than for *S. pseudintermedius* in dogs (Table 4.26 and previous Swedres-Svarm reports). Resistance to penicillin due to penicillinase production was 14% in *S. felis*, compared to 70-74% (three different sample collections) in *S. pseudintermedius*.

Seventy-two percent (265/368) of the *S. felis* isolates were susceptible to all the tested antibiotics. The proportion of multiresistance has varied between <1-7% during 2015-2021 (see previous Swedres-Svarm reports). In 2022, multiresistance was detected in 5% (19/368) of the isolates. The most common phenotype was resistance to penicillin, clindamycin, and erythromycin (14/19).

Pasteurella multocida

Isolates of *Pasteurella* spp. are from clinical submissions of samples from various locations, but mainly from wounds or skin lesions, abscesses, and the external ear canal (82%) in cats.

Pasteurella multocida was the most common *Pasteurella* sp. isolated in samples from cats, 90%. The proportion of resistance was low in the tested isolates (Table 4.32). *Pasteurella* spp. have a low inherent susceptibility to aminoglycosides (gentamicin).

The proportion of resistance in *P. multocida* isolated from cats has been low throughout the years. In comparison the

occurrence of resistance in 2022 have not increased from previous years (2014-2019). For enrofloxacin the figures have varied between 0 and 2% and for trimethoprim-sulphamethoxazole between <1 and 4%.

Beta-haemolytic streptococci

Isolates of beta-haemolytic streptococci are from clinical submissions of samples from various locations, but mainly from wounds or skin lesions, pus, abscesses, and the external ear canal (76%) in cats. The same cut-off as for *Streptococcus equi* subsp. *zooepidemicus* has been applied for the tested beta-haemolytic streptococci isolates.

Data of resistance for beta-haemolytic streptococci isolated from cats were included also in Swedres-Svarm 2011 (n=184). As then, all the tested isolates were susceptible to penicillin (Table 4.33). Any reduced susceptibility to penicillin in beta-haemolytic streptococci should be controlled, i.e., if tested on pure culture and ensured that antimicrobial susceptibility test results and organism identification are accurate and reproducible. The proportion of resistance in 2011 (4% resistant to trimethoprim-sulphamethoxazole, 14% to clindamycin and 19% to erythromycin) was comparable to the figures in 2022 (Table 4.33), except for erythromycin. In 2022, all the isolates except one, resistant to clindamycin was also resistant to erythromycin.

Beta-haemolytic streptococci have a low inherent susceptibility to fluoroquinolones (as enrofloxacin) aminoglycosides (as gentamicin) and tetracyclines.

Table 4.31. Distribution of MICs and resistance (%) in *Staphylococcus felis* from cats, 2022. Clinical isolates from various locations.

Antibiotic	Resistance (%) 2022 n=368	Distribution (%) of MICs (mg/L) ≤0.25	0.5	1	2	4	8	16	32	64	>64
Cephalothin	2			98.1	1.4	0.3	0.3				
Cefoxitin[a]		92.5	5.5	0.8	1.0	0.7					
Clindamycin	6		93.8	1.1	0.3	4.9					
Enrofloxacin	1	96.5	2.4	0.8	0.3						
Erythromycin	11		89.4	4.1	0.5	6.0					
Fusidic acid	6		93.8	2.4	1.9	1.9					
Gentamicin	4			96.2	2.7	1.1					
Nitrofurantoin	<1							96.7	3.0	0.3	
Oxacillin	0	99.5	0.5								
Penicillin[b]	14										
Tetracycline	2	94.0	4.3	0.8	0.3		0.5				
Trim-Sulph.[c]	<1	97.3	2.2	0.3	0.3						

[a]No cut-off available for *S. felis*; [b]Denotes beta-lactamase production; [c]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphamethoxazole).

Table 4.32. Distribution of MICs and resistance (%) in *Pasteurella multocida* from cats, 2022. Clinical isolates from various locations.

Antibiotic	Resistance (%) 2022 n=408	Distribution (%) of MICs (mg/L) ≤0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	>4
Ampicillin	<1			2.0	30.9	64.5	2.5	0.2			
Enrofloxacin	2	78.7	17.9	1.2	0.2	0.2	1.0	0.7			
Gentamicin	NR[b]							2.7	52.7	41.7	2.9
Penicillin	0		0.7	20.8	74.0	4.2	0.2				
Tetracycline	0				3.2	44.1	51.2	1.0	0.5		
Trim-Sulph.[a]	4		47.3	40.2	8.6	1.5	1.2	0.2	1.0		

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphamethoxazole); [b]*Pasteurella* have a low inherent susceptibility to aminoglycosides, as gentamicin.

Table 4.33. Distribution of MICs and resistance (%) in beta-haemolytic streptococci isolated from cats, 2022. Clinical isolates from various locations.

Antibiotic	Resistance (%) 2022 n=128	≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Cephalotin	0						100							
Clindamycin	9					90.6	0.8		8.6					
Enrofloxacin	NR[b]					7.0	63.3	28.9	0.8					
Erythromycin	9					91.4		8.6						
Gentamicin	NR[b]						2.3	6.3	58.6	32.8				
Nitrofurantoin	0										97.7	2.3		
Penicillin	0	100												
Tetracycline	NR[b]				6.3		2.3	31.3	35.2	25.0				
Trim-Sulph.[a]	0				96.9	3.1								

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphamethoxazole); [b]NR= Not relevant as the inherent susceptibility is above concentrations that can be obtained during therapy.

Interpretation of antibiotic susceptibility for topical treatment

At SVA it is possible to choose antibiotic susceptibility testing of bacteria that is tailored for topical treatment since the fall of 2021. Both the antibiotics included in the test and the interpretation of the results differ from traditional testing for systemic treatment. The design of the panel for topical use covers substances included in veterinary medicinal products authorized for topical use and sold on veterinary prescription in Sweden, mainly for treatment of external eye and ear infections. In addition, some substances are included for the sole purpose of screening for methicillin resistance in coagulase positive staphylococci and ESBL in Enterobacterales.

It has been suggested by EUCAST that ECOFFs could be used to exclude acquired resistance to topical agents. They acknowledge that such an approach might underestimate the activity of the agents in some cases. However, it will at least demonstrate the presence of phenotypically detectable resistance mechanisms, which may result in a higher probability of clinical failure. Therefore, when bacteria are tested against substances for topical treatment at SVA, the breakpoints for interpretation are either EUCAST ECOFFs, or when no ECOFF is available based on MIC distributions in Swedres-Svarm or other publications. As pharmacokinetic data have not been taken into consideration the interpretation cannot be applied for systemic treatment.

Some combinations of antibiotic substance and bacterial species are not reported to the clinician for systemic treatment. For example, gentamicin for *Pasteurella* spp. or streptococci, and fusidic acid for streptococci. This is because it is not possible to reach therapeutic concentrations systemically against these bacteria while with topical treatment the concentration at the site of the infection is much higher. Furthermore, some substances are not tested for systemic treatment because they are only used for topical treatment such as chloramphenicol and tobramycin.

In this In Focus, the distribution of MICs for some bacteria tested against substances for topical treatment at SVA in 2022 are summarised (Table 1-6).

Occurrence of resistance varies among bacterial species and substances. However, in most cases there are products available on the Swedish market that would be effective if topical antibiotic treatment is considered necessary.

Table 1. Distribution of MICs and resistance (%) for beta-haemolytic streptococci from dogs, 2022. Clinical isolates from various locations.

Antibiotic	Resistance (%)	Distribution (%) of MICs (mg/L)										
	n=185	≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Chloramphenicol	0					17.8	80.0	2.2				
Enrofloxacin	<1	1.6	1.6	47.0	49.2		0.5					
Florfenicol	0				23.8	75.7	0.5					
Fusidic acid	1								98.4	0.5	0.5	0.5
Gentamicin	2				1.6	2.7	38.4	54.6	0.5	1.1	1.1	
Tetracycline	17				5.4	22.2	47.6	8.1	16.8			

Table 2. Distribution of MICs and resistance (%) for *Pseudomonas aeruginosa* from dogs, 2022. Clinical isolates from the external ear canal.

Antibiotic	Resistance (%)	Distribution (%) of MICs (mg/L)									
	n=168	≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Enrofloxacin	5	3.0	6.5	35.7	36.9	10.1	2.4	5.4			
Gentamicin	1				50.0	30.4	13.1	5.4	0.6	0.6	
Polymyxin B	2				88.1	9.5	0.6	1.8			
Tobramycin	3				91.7	5.4	1.8	1.2			

Table 3. Distribution of MICs and resistance (%) for *Staphylococcus pseudintermedius* from dogs, 2022. Clinical isolates from the external ear canal.

Antibiotic	Resistance (%)	Distribution (%) of MICs (mg/L)									
	n=354	≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Chloramphenicol	12					2.5	76.0	9.0	0.3	12.1	
Enrofloxacin	<1	92.7	2.8	3.7	0.6			0.3			
Florfenicol	<1				4.5	86.7	7.6	0.8		0.3	
Fusidic acid	13		85.6	1.7	2.5	10.2					
Gentamicin	6				92.9	1.4	1.7	2.5	0.8	0.3	0.3
Neomycin[a]	15					85.0	8.2	5.9	0.8		
Oxacillin	<1		99.7			0.3					
Tetracycline	24				76.0	1.4	0.6	0.6	21.5		
Tobramycin	5				94.4	0.8	2.5	2.3			

[a]The interpretation of neomycin MICs is also valid for framycetin.

Table 4. Distribution of MICs and resistance (%) for *Staphylococcus schleiferi* from dogs, 2022. Clinical isolates mainly from the external ear canal.

Antibiotic	Resistance (%)	Distribution (%) of MICs (mg/L)									
	n=65	≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Chloramphenicol	0					7.7	89.2	3.1			
Enrofloxacin	11	76.9	7.7	4.6	10.8						
Florfenicol	0				20.0	76.9	1.5	1.5			
Fusidic acid	26		72.3	1.5	15.4	10.8					
Gentamicin	0				95.4	4.6					
Neomycin[a]	3					96.9	3.1				
Oxacillin	0		98.5	1.5							
Tetracycline	4				95.4		1.5	1.5	1.5		
Tobramycin	2				96.9	1.5	1.5				

[a]The interpretation of neomycin MICs is also valid for framycetin.

Table 5. Distribution of MICs and resistance (%) for *Pasteurella multocida* from cats, 2022. Clinical isolates from various locations.

Antibiotic	Resistance (%)	Distribution (%) of MICs (mg/L)									
	n=48	≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Chloramphenicol	2					97.9	2.1				
Enrofloxacin	0	100									
Florfenicol	4				95.8	2.1	2.1				
Gentamicin	2				2.1	20.8	68.8	6.3	2.1		
Polymyxin B	17				64.6	18.8	12.5	4.2			
Tetracycline	2				95.8	2.1		2.1			

Table 6. Distribution of MICs and resistance (%) for *Staphylococcus felis* from cats, 2022. Clinical isolates mainly from the external ear canal.

Antibiotic	Resistance (%)	Distribution (%) of MICs (mg/L)									
	n=63	≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Chloramphenicol	0						90.5	9.5			
Enrofloxacin	0	96.8	1.6	1.6							
Florfenicol	0				6.3	82.5	9.5	1.6			
Fusidic acid	2		96.8	1.6		1.6					
Gentamicin	2				98.4		1.6				
Neomycin[a]	3					96.8	3.2				
Oxacillin	0		100								
Tetracycline	2				98.4		1.6				
Tobramycin	0				100						

[a]The interpretation of neomycin MICs is also valid for framycetin.

Indicator bacteria from animals

In programmes monitoring antibiotic resistance in the veterinary field, *Escherichia coli*, *Enterococcus faecalis* and *Enterococcus faecium* from the enteric flora of healthy animals, or the bacteria contaminating food, serve as indicators for the presence of acquired resistance. The level of resistance in these so-called indicator bacteria reflects the magnitude of the selective pressure from antibiotic use in an animal population. Moreover, although these bacteria are unlikely to cause disease, they can be reservoirs for resistance genes that can spread to bacteria pathogenic to animals or humans. Resistance in indicator bacteria contaminating meat indicates the potential exposure of humans through the food chain.

During 2022, indicator *E. coli* from healthy broilers, turkeys and laying hens were studied.

Samples from broilers were collected at slaughter within the Swedish Campylobacter programme in which whole caeca are collected from each batch of broilers slaughtered. Each sample was from a unique flock but not always from a unique production site. Samples cultured were collected at seven abattoirs that in 2022 accounted for approximately 98% of the total volume of broilers slaughtered. The number of samples from each abattoir was roughly proportional to the annual slaughter volume of the abattoir and the sampling was distributed over the year.

Samples from turkey consists of caecal content of healthy turkeys sampled at slaughter. Each sample is from a unique flock but not always from a unique production site. Sampling was performed from January to December at one abattoir that in 2022 accounted for approximately 90% of the total volume of turkeys slaughtered in Sweden.

Samples from laying hens consists of caecal content of healthy hens sampled at slaughter. Each sample is from a unique flock but not always from a unique production site. Sampling was performed from February 2021 to December 2022 at the only abattoir slaughtering laying hens in Sweden. However, a large proportion of laying hens in Sweden are either sent for slaughter in other countries or euthanised instead of being sent for slaughter. Hence, the sampling is perhaps not representative of the whole laying hens population in Sweden.

All samples were also screened for *E. coli* resistant to ESCs by selective culture on media supplemented with cefotaxime. For details on methodology see Material and methods, resistance in bacteria from animals.

In 2022, there were no consignments of poultry meat from countries outside EU imported via border control posts in Sweden. Hence, no sampling of poultry meat was performed.

Escherichia coli

Broilers

Escherichia coli was isolated from 179 (97%) of 184 cultured caecal samples from broilers. The majority of the isolates (69%) was susceptible to all antibiotics tested (Table 4.34 and Figure 4.13). Resistance to ampicillin (19%), sulphonamides (11%), trimethoprim (9%) and tetracycline (7%) were the most common traits (Table 4.34 and 4.35). Fourteen isolates (8%) were multiresistant, i.e. resistant to three or more antibiotics (Table 4.34 and Figure 4.13). All of these had resistance to ampicillin, sulphonamides, and trimethoprim in their phenotype.

Levels of resistance in *E. coli* from broilers are low in an international perspective. The proportion of isolates susceptible to all antibiotics tested has been stable in the latest years (75% in 2014, 71% in 2016, 69% in 2018, 72% in 2020, and 69% in 2022). Yet, for some substances the situation has become less favourable in the latest years (Figure 4.14). More precisely, occurrence of resistance to ampicillin, sulphonamides and trimethoprim in *E. coli* from broilers has increased considerably since 2007. Likewise, occurrence of resistance to tetracycline has increased during these years even if the occurrence in 2022 dropped considerably compared to 2018. Notably, it was only for ampicillin that the occurrence of resistance increased from 2020 to 2022. Phenoximethylpenicillin is basically the only substance that is used when broilers in Sweden are treated with antibiotics. However, as only 0.03 to 1.6 percent of broiler flocks were treated in 2018 to 2022, selection of resistance due to use of

Figure 4.13. Proportion (%) of indicator *Escherichia coli* from broilers, turkey, laying hens, pigs and cattle under one year with resistance to none, one-two, or three or more tested substances.

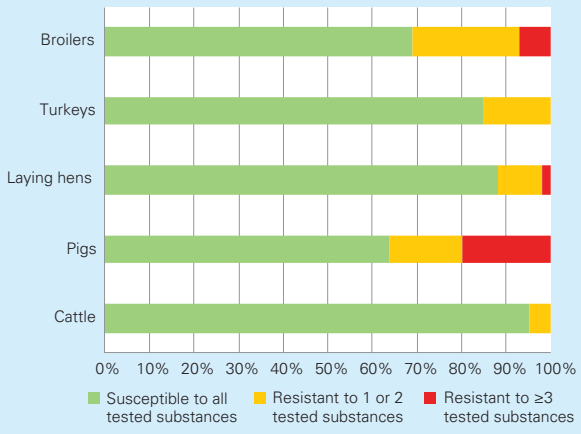
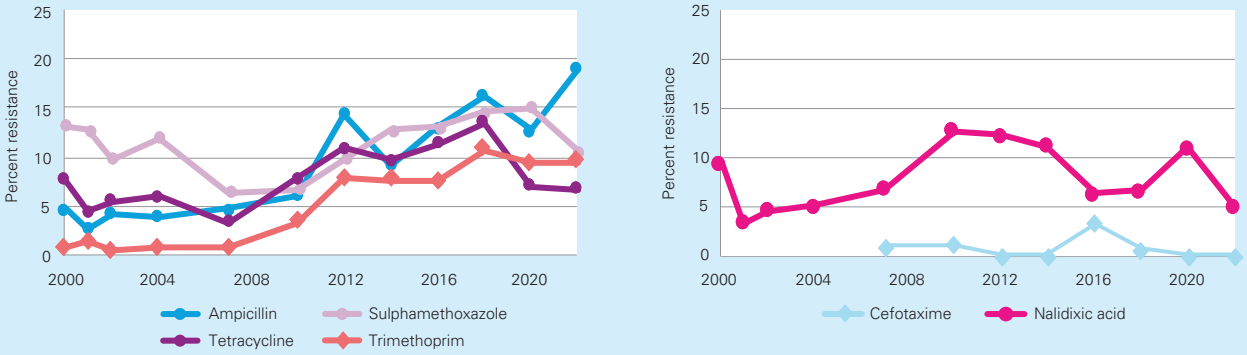


Figure 4.14. Resistance (%) in *Escherichia coli* from broilers 2000-2022. The number of isolates each year varies (n=172-307, 2022 n=179).



Resistance to colistin is not included in the figure showing substances in category B of the AMEG categorisation (EMA, 2019[a]) as it has not been detected during the years it has been investigated (2010-2022).

antibiotics for treatment of broilers in Sweden is unlikely to be the explanation of these increases in occurrence of resistance. For more details and comments, see section Sales of antibiotics for animals, Comments on trends by animal species.

Regarding substances in the category B (restrict) of the AMEG classification (EMA, 2019), resistance to polymyxins (colistin) has been tested for since 2010 but has not been detected, and resistance to cefotaxime (tested since 2007) has been stable at a low occurrence (Figure 4.14). However, the occurrence of resistance to quinolones has varied over the years. Quinolones have not been used in Swedish broiler production for at least ten years and the reason(s) for these variations in resistance is not known.

None of the isolates were resistant to cefotaxime or ceftazidime. However, using selective culture, ESC resistant *E. coli* was isolated from 9 (3%) of 305 samples. In five isolates (2%), transferable genes for resistance to ESC were found and all of these had the $bla_{CTX\text{-}M\text{-}1}$ gene. The remaining four isolates had an AmpC phenotype and genome sequencing of these isolates revealed mutations causing hyperproduction of AmpC beta-lactamases, i.e., a shift from C to T at position 42 of the ampC promoter. For more details and comments on occurrence of resistance to ESC, see section Antibiotic resistance in animals, Notifiable diseases.

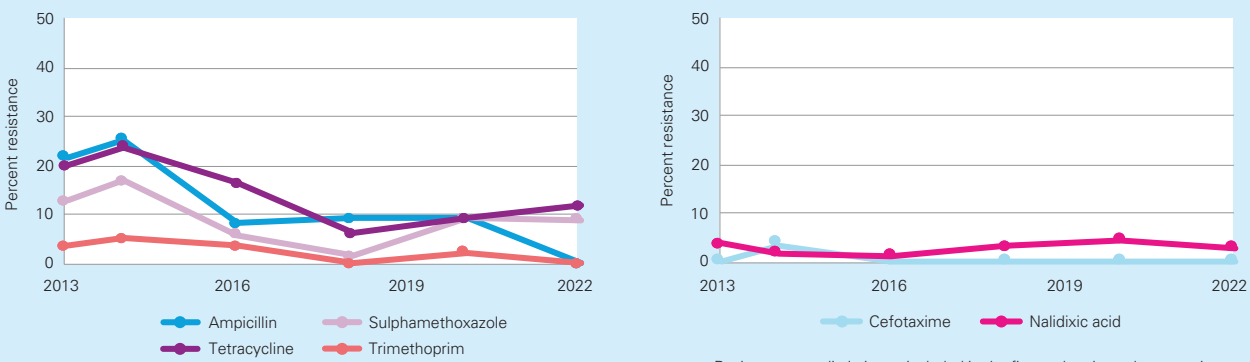
Turkeys

Escherichia coli was isolated from 34 (100%) of 34 cultured caecal samples from turkeys. The majority of the isolates (85%) was susceptible to all antibiotics tested (Table 4.34 and Figure 4.13). Resistance to tetracycline (12%) and sulphonamides (9%) were the most common traits (Table 4.34 and 4.35). None of the isolates were multiresistant, i.e. resistant to three or more antibiotics (Table 4.34 and Figure 4.13).

Levels of resistance in *E. coli* from turkeys are low in an international perspective. The proportion of isolates susceptible to all antibiotics tested has increased considerably since 2014 and increased even further the latest years (44% in 2014, 71% in 2016, 80% in 2018, 80% in 2020, and 85% in 2022). This change is driven by decreased occurrence of resistance to some substances, namely ampicillin, sulphonamides and tetracycline (Figure 4.15). The differences over time are statistically significant ($p<0.05$, X_2). The reason(s) for these changes is not known.

None of the isolates were resistant to cefotaxime or ceftazidime. Moreover, also when using selective culture, no ESC resistant *E. coli* was isolated from the 34 samples. For more details and comments on occurrence of resistance to ESC, see section Antibiotic resistance in animals, Notifiable diseases.

Figure 4.15. Resistance (%) in *Escherichia coli* from turkeys 2013-2022. The number of isolates each year varies (n=34-85, 2022 n=34).



Resistance to colistin is not included in the figure showing substances in category B of the AMEG categorisation (EMA, 2019[a]) as it has not been detected during the years it has been investigated (2010-2022).

Laying hens

Escherichia coli was isolated from 110 (100%) of 110 cultured caecal samples from laying hens. The majority of the isolates (88%) was susceptible to all antibiotics tested (Table 4.34 and Figure 4.13). Concordantly, resistance to specific substances was generally low and resistance to tetracycline (5%) was the most common traits (Table 4.34 and 4.35). Two isolates (2%) were multiresistant, i.e. resistant to three or more antibiotics (Table 4.34 and Figure 4.13).

None of the isolates were resistant to cefotaxime or ceftazidime. However, using selective culture, ESC resistant *E. coli* was isolated from 3 (2%) of 110 samples. In all of these, a transferable gene for resistance to ESC was found and all were $ESBL_M$ and carried bla_{CMY-2}. For more details and comments on occurrence of resistance to ESC, see section Antibiotic resistance in animals, Notifiable diseases.

Table 4.34. Resistance (%) and multiresistance (%) in indicator *Escherichia coli* from broilers and turkey, 2022, and laying hens, 2021-2022. Most recent data on indicator *E. coli* from other sample categories are given for comparison.

Antibiotic	ECOFF (mg/L)	Resistance (%)								
		Broilers	Broiler meat	Cattle[b]	Laying hens	Pigs	Sheep	Turkeys	Dogs	Horses
		2022 n=179	2012 n=92	2020-21 n=101	2021-22 n=110	2021 n=175	2006-09 n=115	2022 n=34	2012 n=74	2010-11 n=274
Amikacin	>8	0	-	0	0	0	-	0	-	-
Ampicillin	>8	19	18	2	3	25	2	0	9	2
Azithromycin	>16	0	-	0	0	<1	-	0	-	-
Cefotaxime	>0.25	0	0	0	0	<1	0	0	1	0
Ceftazidime	>1	0	-	0	0	<1	-	0	-	-
Chloramphenicol	>16	0	0	0	1	8	0	0	0	<1
Ciprofloxacin	>0.06	5	4	0	2	2	<1	3	3	<1
Colistin	>2	0	1	0	0	0	-	0	0	<1
Gentamicin	>2	0	3	0	0	0	3	0	0	<1
Meropenem	>0.12	0	-	0	0	0	-	0	-	-
Nalidixic acid	>8	5	4	0	2	2	0	3	0	<1
Sulphamethoxazole	>64	11	16	2	3	23	7	9	4	15
Tetracycline	>8	7	14	2	5	17	<1	12	8	2
Tigecycline	>0.5	0	-	0	0	0	-	0	-	-
Trimethoprim	>2	9	7	2	4	20	2	0	1	16
Resistance (%) to 0->3 antibiotics[a]										
Susceptible to all above		69	66	95	88	64	89	85	84	83
Resistant to 1		23	18	4	8	10	8	6	8	2
Resistant to 2		1	7	2	2	6	3	9	7	12
Resistant to 3		4	3		2	12	<1			2
Resistant to >3		3	5			8			<1	1

[a]Ciprofloxacin and nalidixic acid as well as cefotaxime and ceftazidime were considered as one antibiotic class. [b]Cattle older than 6 months.

Table 4.35. Distribution of MICs and resistance (%) in *Escherichia coli* from intestinal content from broilers (n=179) and turkeys (n=34), 2022, and laying hens (n=110), 2021-2022.

Antibiotic	Source	Resistance %	Distribution (%) of MICs (mg/L)																
			≤0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	>512
Amikacin	Broilers	0									97.2	2.8							
	Turkeys	0									97.1	2.9							
	Laying hens	0									97.3	2.7							
Ampicillin	Broilers	19							4.5	26.8	46.9	2.8			19.0				
	Turkeys	0								35.3	55.9	8.8							
	Laying hens	3							5.5	36.4	53.6	1.8			2.7				
Azithromycin	Broilers	0								6.1	76.0	17.9							
	Turkeys	0								8.8	67.6	23.5							
	Laying hens	0								2.7	62.7	33.6	0.9						
Cefotaxime	Broilers	0					100												
	Turkeys	0					100												
	Laying hens	0					100												
Ceftazidime	Broilers	0					98.9	1.1											
	Turkeys	0					100												
	Laying hens	0					96.4	3.6											
Chloramphenicol	Broilers	0										100							
	Turkeys	0										100							
	Laying hens	1										97.3	1.8	0.9					
Ciprofloxacin	Broilers	5	94.4	0.6		2.8	2.2												
	Turkeys	3	97.1				2.9												
	Laying hens	2	98.2				0.9						0.9						
Colistin	Broilers	0							98.9	1.1									
	Turkeys	0							100										
	Laying hens	0							100										
Gentamicin	Broilers	0						91.6	8.4										
	Turkeys	0						82.4	17.6										
	Laying hens	0						88.2	9.1	2.7									
Meropenem	Broilers	0		100															
	Turkeys	0		100															
	Laying hens	0		100															
Nalidixic acid	Broilers	5									94.4	0.6			1.7	3.4			
	Turkeys	3									94.1	2.9	2.9						
	Laying hens	2									96.4	1.8				1.8			
Sulphamethoxazole	Broilers	11										43.0	44.7	1.1	0.6				10.6
	Turkeys	9										47.1	44.1						8.8
	Laying hens	3										70.9	26.4						2.7
Tetracycline	Broilers	7								92.7	0.6				6.7				
	Turkeys	12								88.2					11.8				
	Laying hens	5								94.5				0.9	4.5				
Tigecycline	Broilers	0					99.4	0.6											
	Turkeys	0					100												
	Laying hens	0					100												
Trimethoprim	Broilers	9					34.6	50.3	5.6					9.5					
	Turkeys	0					26.5	70.6	2.9										
	Laying hens	4					49.1	45.5	1.8					3.6					
			≤0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	>512

Comparative analysis

Comparison of antibiotic sales in human and veterinary medicine

Data included and calculations

The numbers on the total amount of antibiotics consumed for systemic use to humans (ATC group J01 excluding methenamine, and A07AA oral glycopeptides; sales to hospitals and on prescriptions to individuals; ATC/DDD index version 2021) were retrieved as defined daily doses and calculated to kg active substance.

Figures on sales of antibiotics for use in animals (QJ01 and QA07AA) are those presented in Sales of antibiotics for animals except products for intramammary and intrauterine use (QG01 and QJ51). Sales for aquaculture were not included, nor were sales of drugs authorised for human use but sold for animals. The contribution of such sales to the total volumes is minor. As reported under 'Sales of antibiotics for animals', there was an unexpected decrease in total antibiotic sales in 2022 as compared to 2021. Despite efforts to ensure the accuracy of these figures, there is currently no definitive explanation for this decrease and these figures are considered somewhat uncertain. However, the general conclusions described below are in line with observations from previous years and can therefore be considered reliable.

To estimate the biomass of the human population, data on population numbers by age were multiplied with the corresponding average body weights from studies made by Statistics Sweden in 2016. For animal body mass, the data on population correction unit for 2021 was used as a proxy for 2022 (EMA, 2022). This unit roughly corresponds to the total biomass of major animal populations, excluding dogs and cats.

Comparison of sales in tonnes active substance

A total of 59.3 and 8.8 tonnes of antibiotics were consumed in human and veterinary medicine, respectively, in 2022 from the included ATC classes, as shown in Table 5.1. Beta-lactam antibiotics remain the most commonly prescribed antibiotics in both human and veterinary medicine and also represent the largest volumes consumed, measured in kilograms. Narrow-spectrum penicillins (J01CE, J01CF, QJ01CE and QJ01RA) make up the majority of antibiotics sold in kg active substance for both humans and animals; 55 and 58%, respectively. Other antibiotic products were consumed in smaller quantities than beta-lactams but considering their chemical and pharmacological properties, they could have a greater impact on the environment and the emergence of antibiotic resistance.

Table 5.1. Sales of antibiotics for human and veterinary medicine, expressed in kg active substance and as mg active substance per estimated kg biomass 2022.

ATC human	ATC veterinary	Antibiotic class(es)	Humans, kg	Animals, kg	Total, kg	Human, mg/kg biomass	Animals, mg/kg biomass
J01AA	QJ01AA	Tetracyclines	2 969	573	3 542	4.2	0.7
J01CA, J01CR	QJ01CA, QJ01CR	Penicillins with extended spectrum, with and without beta-lactamase inhibitors	12 734	612	13 346	18.2	0.8
J01CE, J01CF	QJ01CE, QJ01RA	Beta-lactamase sensitive and beta-lactamase resistant penicillins	32 883	5 070	37 953	46.9	6.5
J01D	QJ01D	Cephalosporins and carbapenems[a]	2 818	150	2 968	4.0	0.2
J01E, J01XE	QJ01E, QA07AB	Sulphonamides, trimethoprim and nitrofuran derivatives	3 205	1 417	4 622	4.6	1.8
J01F	QJ01F	Macrolides and lincosamides	1 925	400	2 326	2.7	0.5
J01MA	QJ01MA	Fluoroquinolones	2 452	16	2 468	3.5	<0.1
[b]	[c]	Others	360	548	909	0.5	0.7
		Total	**59 346**	**8 787**	**68 134**	**84.6**	**11.3**

[a]There were no sales of products with carbapenems for animals. [b]A07AA09 and other antibiotics included in J01 excl methenamine (J01XX05). [c]QA07AA, QJ01BA, QJ01GB, QJ01RA, QJ01XQ.

Comparison of sales expressed as mg per kg estimated biomass

In total, 84.6 and 11.3 mg active antibiotic substance per kg estimated biomass were sold in 2022 in human and veterinary medicine, respectively, as shown in Table 5.1. Total sales data do not take the heterogeneity of likelihood of exposure within the population into account. This is especially true for data on sales for use in animals, as certain substances may only or mainly be sold for use in one particular animal species. Consequently, the selective pressure in a particular subset of the population (i.e. a particular animal species) could be far larger than in the total population. Nevertheless, the largest difference is noted for fluoroquinolones, where sales for humans are almost 170 times higher than for animals.

Both in tonnes active substance and in mg per kg estimated biomass, antibiotic sales are higher for humans than for animals in Sweden. The sales for humans dominate for all separately analysed classes of antibiotics.

Comparison of antibiotic resistance in human and veterinary medicine

ESBL-producing Enterobacterales

Enterobacterales with $ESBL_A$ or $ESBL_M$, and their corresponding genes, can transfer between animals and humans (EFSA, 2011, de Been, 2014). The main route would be via food, but the possibility for direct transfer when handling animals should also be kept in mind.

The available data show that ESBL-producing bacteria are generally rare in animals and on food in Sweden. Previously the occurrence in intestinal samples from broilers was high but it has decreased considerably in recent years. Moreover, previous investigations when the occurrence was higher has shown that $ESBL_A$- or $ESBL_M$-producing *E. coli* only constitute a small part of all the *E. coli* in the intestinal flora in a majority of the broiler samples. Finally, it has been previously shown that most isolates from humans in Sweden are not of the same types of $ESBL_A$ or $ESBL_M$ as in broilers. Hence, nothing indicates a need to revise the conclusion that food on the Swedish market is a limited source for ESBLs for humans (Börjesson et al., 2016). Nevertheless, continued vigilance against development of reservoirs of ESBL-producing Enterobacterales in animals is warranted.

MRSA

Zoonotic transmission of MRSA occurs by direct or indirect contacts. MRSA is reported globally in farm animals, companion animals, horses, and wildlife. However, MRSA is still rare among animals in Sweden and the situation among humans is also favourable.

Livestock-associated MRSA

During more than ten years, the zoonotic aspects on MRSA in farm animals has widened in many countries, due to spread of livestock-associated MRSA, and mostly clonal complex (CC) 398. Mostly this concerns pigs but also veal calves, broilers and dairy cows are affected.

Based on our active and passive surveillance of MRSA in livestock, with occasional findings in samples from cow, pig, goat and sheep, the situation is considered favourable in Sweden. However, MRSA CC398 occurs among horses and *spa*-type t011 (n=7) and t034 (n=1) were detected in 2022. All eight isolates were PVL negative.

MRSA CC398 acquired in Sweden is uncommon in humans. Among all MRSA cases with available typing results in 2022, there were sixteen cases with *spa*-types t034 (n=12), t011 (n=2), t2383 (n=1) and t3625 (n=1). Twelve of the isolates were PVL-negative while no information on PVL status was available for the remaining four isolates. The possibility of animal contacts as a source is often not pursued, consequently epidemiological information regarding this is scarce. Nevertheless, the low number of MRSA CC398 in humans in Sweden may indicate that MRSA is not widespread among animals in Sweden, as a high occurrence would lead to transmission to humans in contact with animals.

MRSA with *mecC*

Isolates of MRSA with *mecC* were first reported internationally from dairy cows and humans in 2011 (García-Álvarez et al., 2011, Shore et al., 2011, Ito et al., 2012). Throughout the years, MRSA with *mecC* has been isolated from several animal species (cat, cow, dog, hedgehog, goat, pig, and sheep). The total number of cases are low even if there are a number of isolates from hedgehogs in research projects and from goats in an outbreak at a zoo.

In humans, cases of MRSA acquired in Sweden with *mecC* are also uncommon. In 2022, there were eight reported cases with *spa*-types t843 (n=4), t9111 (n=3) and t5711 (n=1). The epidemiological information concerning possible animal contacts is scarce but some of the *spa*-types in cases from humans have also been found in cases from animals. However, even if there would be zoonotic transfer it is currently not considered a public health problem as the number of cases of MRSA with *mecC* in humans in Sweden is low.

MRSA-types typically associated with humans

MRSA isolated from dogs and cats often belong to *spa*-types seen in MRSA from humans. This supports the view that humans often are the source of MRSA in companion animals (EFSA 2009, CVMP, 2009). Spread can subsequently occur from animals to humans. However, the impact of companion animals as vectors for spread between humans is not known.

Conclusions

The MRSA situation in Sweden is still favourable both in humans and in animals. If this situation is preserved in animals, a reservoir of MRSA in animals with risk of spread to humans can be prevented. Biosecurity, with caution in trade of live animals and measures to prevent introduction by indirect routes, is important for preventing introduction and spread of MRSA in animal populations. Furthermore, antibiotic stewardship as well as infection prevention and control measures are important to prevent health care related spread between people, between animals or between people and animals.

For more information on MRSA in Sweden, see Antibiotic resistance in humans and Antibiotic resistance in animals.

MRSP

Staphylococcus pseudintermedius may act as an opportunistic pathogen in humans and there are several reports in the literature of infections in humans with a varying degree of severity. However, MRSP is not generally considered to be a zoonotic pathogen.

VRE

Using selective media, VRE has historically been isolated from a large proportion of broilers in Sweden. This occurrence has however decreased considerably in recent years. The occurrence in humans varies between years, mainly due to outbreaks of nosocomial spread causing high occurrence in some years. However, based on genotypical investigations of isolates there are no indications that the presence of VRE in broilers in Sweden has affected the situation in Swedish healthcare.

Salmonella

Occurrence of *Salmonella* among farm animals, as well as among other animals, is low in Sweden and few incidents involve multiresistant strains. In 2022 the majority of the isolates (147 of 150; 98%) were susceptible to all antibiotics tested. None of the isolates were resistant against fluoroquinolones. Resistance to fluoroquinolones (e.g. ciprofloxacin) is rare and in 2019 a strain with ESBL was for the first time detected, this in an environmental sample from a farm. Thus, the overall situation in the veterinary sector is favourable which is largely due to the strategies in the Swedish salmonella control programme initiated in the 1950-ies.

The origin of the isolates is not known for the majority of the salmonella infections in humans. Considering the low occurrence of *Salmonella* in food-producing animals in Sweden, the majority of food-related infections presumably has a foreign source. The high occurrence of resistance to fluoroquinolones in isolates from humans (24%) in comparison to the very rare occurrence of such resistance in isolates from Swedish food-producing animals also suggests that most of these isolates from human infections do not have a domestic origin.

Campylobacter

Resistance to fluoroquinolones, tetracycline and erythromycin among faecal isolates of *Campylobacter jejuni* from humans was 55%, 27% and 0,5 % respectively. From animals, 163 isolates of *C. jejuni* and 16 of *C. coli* from healthy broilers were tested. The only resistance found was against fluoroquinolones (20% in *C. jejuni*).

Resistance to erythromycin, the drug of choice for treatment of human campylobacteriosis, is rare among isolates from humans as well as animals in Sweden. In animals it has only been found in two isolates from Swedish broiler meat (Svarm 2013) and in 2017 in one isolate from a pig.

Clinical resistance in *Escherichia coli* from humans and animals

Comparison of resistance in bacteria from humans and different animal categories may indicate the magnitude of possible transfer of resistance between sectors and give insight into the drivers for resistance in the specific populations. However, in Swedres-Svarm direct comparison of resistance is hampered because different interpretative criteria are used for bacteria from humans and animals. Data for bacteria from humans are interpreted with clinical breakpoints and presented as the proportion of isolates with clinical resistance. In contrast, data for bacteria from animals are mainly interpreted with epidemiological cut-off values (ECOFF) and presented as the proportion of isolates of non-wild type. For further information on interpretive criteria see sections Guidance for readers and Materials and methods.

For the purpose of the comparison in this section, some data sets for *E. coli* from animals presented in Swedres-Svarm have been interpretated using clinical breakpoints for humans (Table 5.2).

Resistance was generally more common in *E. coli* from humans than in isolates from animals (Table 5.2). Notably, clinical resistance to fluoroquinolones or 3rd generation cephalosporins is considerably more common in *E. coli* from humans than in isolates from animals with the highest occurrence in blood stream isolates from humans (Table 5.2). This agrees with a very low use of these antibiotic classes in animals (see section on sales of antibiotics above). However, although few isolates of *E. coli* from animals show clinical resistance to fluoro-quinolones, reduced susceptibility (i.e. non wild-type) is more common in some categories of diseased and healthy animals (see Antibiotic resistance in animals in this and previous reports). Possibly, the selection pressure from use of fluoroquinolones in animal populations is not sufficient to select for further mutations to clinical resistance in isolates with reduced susceptibility.

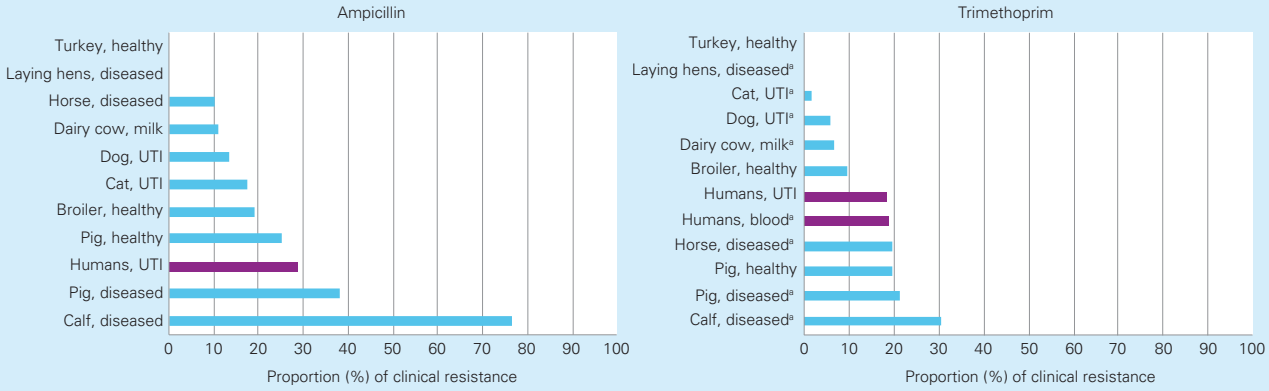
For the antibiotics commonly used in both animals and humans, e.g. ampicillin and trimethoprim, resistance is more frequent. In particular, the occurrence of resistance is high among clinical isolates from calves, pigs and humans (Table 5.2, Figure 5.1). When comparing resistance to trimethoprim, it should be kept in mind that for some categories (i.e. clinical isolates from animals and blood isolates from humans)

trimethoprim-sulphonamide was tested. This could possibly result in a lower occurrence of resistance than if susceptibility to only trimethoprim had been tested. The comparatively high level of trimethoprim resistance in *E. coli* from the genital tract of mares most likely reflects the relatively common use of trimethoprim-sulphonamide combinations in horses.

Occurrence of resistance to ampicillin or trimethoprim could also be due to co-selection by use of other antibiotics or to other factors selecting for resistance. For example, although exact data are missing, use of ampicillin or amoxicillin in cattle is believed to be low in Sweden. Nevertheless, resistance to ampicillin is common in both isolates from diseased calves and dairy cows. However, it is well known that multiresistant *E. coli* is common in pre-weaned dairy calves but that resistant strains are cleared as calves mature.

Moreover, the high occurrence of resistance to ampicillin or trimethoprim, may, in some categories be influenced by a possible sampling bias where humans and animals are sampled due to therapeutic failures, inferring a selection of problematic cases.

Figure 5.1 A and B. Proportion of resistance (%) to ampicillin and trimethoprim in *Escherichia coli* from humans and animals interpreted with clinical breakpoints. For details see Table 5.2.



[a]Trimethoprim-sulphamethoxazole tested, BP >4 mg/L, NordicAST v. 12.0.

Table 5.2. Resistance (%) in *Escherichia coli* from various sample types from humans and different animal categories interpreted with clinical breakpoints (in brackets, mg/L) according to NordicAST v. 12.0 if not indicated by footnotes that other interpretive criteria were used.

Category	Sample type	Year	Number of isolates	Amp (>8)	Cip (>0.5)	Ctx (>2)	Gen (>2)	Mer (>8)	Nit (>64)	Tmp (>4)
Cat (UTI)	Urinary	2022	439	17.3	0.5[a]	0.2	0.9	0	0	1.4[b]
Dog (UTI)	Urinary	2022	956	13.1	1.0[a]	0.5	1.1	0	0.4	5.6[b]
Horse (e.g., endometritis)	Genital tract	2022	282	9.9	0[a]	0	3.9	0		19.5[b]
Calf (enteritis)	Faeces/Post-mortem	2021-22	46	76.1	0[a]	0	0	0		30.4[b]
Dairy cow (mastitis)	Milk	2022	46	10.9	4.3[a]	0	0	0		6.5[b]
Laying hens	Post-mortem	2022	52	0	0[a]	0	1.9	0		0[b]
Pig (enteritis)	Faeces/Post-mortem	2022	61	37.7	0[a]	0	1.6	0		21.3[b]
Broiler (healthy)	Intestinal content	2022	179	19.0	0	0	0	0		9.5
Cattle under 1 year (healthy)	Intestinal content	2020-21	56	1.7	0	0	0	0		1.8
Laying hens (healthy)	Intestinal content	2021-22	110	2.7	0.9	0	0	0		3.6
Pig (healthy)	Intestinal content	2021	175	24.9	0	0	0	0		19.7
Turkey (healthy)	Intestinal content	2022	34	0	0	0	0	0		0
Humans (UTI)	Urinary	2022	223 039	28.8	10.5	4.1[c]			1.2	18.6
Humans (bloodstream infections)	Blood	2022	10 554		13.8	7.3	6.0	0		18.7[b]

[a]Enrofloxacin tested, BP >1mg/L; [b]Trimethoprim-sulphamethoxazole tested, BP >4 mg/L, NordicAST v. 12.0; [c]Data from only five laboratories.

Background data, material, methods and references

Demographics and denominator data

Humans

Table 6.1. Denominator data (population in Sweden per region and age group) for calculation of antibiotic sales in humans, 2022. Data from the eHealth Agency.

	<1 years	1-4 years	5-19 years	20-44 years	45-64 years	65-84 years	≥85 years	All age groups	0-6 years
Blekinge	1 513	6 446	27 648	45 083	39 767	33 292	5 188	158 937	11 479
Dalarna	2 816	12 498	49 325	79 974	71 292	63 450	9 032	288 387	21 923
Gotland	532	2 284	9 769	16 580	15 721	14 166	1 949	61 001	4 043
Gävleborg	2 770	12 176	48 864	80 601	72 905	61 808	8 643	287 767	21 294
Halland	3 597	15 364	62 643	97 536	85 569	65 589	9 945	340 243	27 242
Jämtland Härjedalen	1 343	5 743	22 517	38 505	32 561	27 552	3 833	132 054	10 087
Jönköping	4 054	17 319	67 425	112 611	88 501	66 513	10 641	367 064	30 479
Kalmar	2 486	10 397	41 282	68 328	61 544	54 837	8 301	247 175	18 401
Kronoberg	2 275	9 582	37 103	63 015	47 821	37 434	6 110	203 340	16 876
Norrbotten	2 448	9 811	39 372	73 119	63 377	53 730	7 836	249 693	17 506
Skåne	15 717	65 567	251 960	454 435	338 575	240 654	35 517	1 402 425	115 664
Stockholm	28 880	114 130	434 470	848 859	597 003	345 156	46 641	2 415 139	202 177
Sörmland	3 113	13 934	55 484	86 316	74 209	60 310	8 435	301 801	24 583
Uppsala	4 310	18 037	69 902	138 309	90 503	65 111	8 854	395 026	32 126
Värmland	2 657	11 916	46 454	81 813	71 279	59 612	9 465	283 196	20 894
Västerbotten	2 842	12 057	46 075	90 560	63 777	51 827	7 425	274 563	21 182
Västernorrland	2 393	10 099	41 758	67 572	62 215	52 693	7 463	244 193	17 930
Västmanland	2 870	12 813	49 295	84 281	68 867	52 944	7 897	278 967	22 272
Västra Götaland	19 687	79 225	303 823	572 711	424 482	300 287	44 644	1 744 859	140 146
Örebro	3 297	13 790	53 926	95 834	73 473	58 402	8 070	306 792	24 247
Östergötland	5 063	20 583	82 545	151 158	112 845	84 776	12 734	469 704	36 881
Sweden	**114 663**	**473 771**	**1 841 640**	**3 347 200**	**2 556 286**	**1 850 143**	**268 623**	**10 452 326**	**837 432**

Table 6.2. Denominator data (population in Sweden) for calculation of antibiotic sales in humans, 2000-2022. Data from the eHealth Agency.

Year	Population	Year	Population
2000	8 861 426	2012	9 482 855
2001	8 882 792	2013	9 555 893
2002	8 909 128	2014	9 644 864
2003	8 940 788	2015	9 747 355
2004	8 975 670	2016	9 851 017
2005	9 011 392	2017	9 995 153
2006	9 047 752	2018	10 120 242
2007	9 113 257	2019	10 230 185
2008	9 182 927	2020	10 327 589
2009	9 256 347	2021	10 379 295
2010	9 340 682	2022	10 452 326
2011	9 415 570		

Table 6.3. Number of admissions and patient-days in somatic medical care in Sweden, 2018-2022. Data represent acute care hospitals in all regions except Blekinge 2019 due to a known reporting error at that time.

Year	Admissions	Patient-days
2018	1 296 510	5 507 012
2019	1 265 083	5 346 161
2020	1 220 236	4 960 480
2021	1 241 200	5 158 835
2022	1 202 382	4 902 803

Animals

Official statistics on agriculture in Sweden is provided by the Board of Agriculture. The Board of Agriculture maintains a statistical database accessible online (www.jordbruksverket.se). Annual figures on the number of animals are given in Table 6.4, on animals slaughtered in Table 6.5 and 6.6 and average herd size in Table 6.7. Readers are referred to the Board of Agriculture for further information.

In brief, the number of dairy cows and pigs has decreased notably over the last three decades but herd size has increased. During the same period, the number of beef cows has increased, as well as the number of chickens slaughtered.

Estimates of the number of dogs and cats are available from the Board of Agriculture for 2006 and 2012, and in a study by the company Novus in 2017. In 2012 the numbers of dogs and cats in Sweden were estimated to 784 000 and 1 159 000, respectively. The corresponding figures for 2017 were 881 000 and 1 443 000.

Table 6.4. Number of livestock and horses (in thousands) 1980-2022. From the statistical database of the Board of Agriculture.

Animal Species	1980[a]	1985[a]	1990	1995	2000	2005	2010	2015	2020	2021	2022
Cattle											
Dairy cows	656	646	576	482	428	393	348	338	303	302	297
Beef cows	71	59	75	157	167	177	197	184	207	210	213
Other cattle >1 year	614	570	544	596	589	527	513	487	480	476	482
Calves <1 year	595	563	524	542	500	509	479	466	462	465	458
Total, cattle	1 935	1 837	1 718	1 777	1 684	1 605	1 537	1 475	1 453	1 453	1 449
Sheep											
Ewes and rams	161	173	162	195	198	222	273	289	263	272	264
Lambs	231	252	244	266	234	249	292	306	238	252	245
Total, sheep	392	425	406	462	432	471	565	595	501	523	510
Pigs											
Boars and sows	290	260	230	245	206	188	156	142	131	129	127
Fattening pigs >20 kg	1 254	1 127	1 025	1 300	1 146	1 085	937	830	869	845	895
Piglets <20kg	1 170	1 113	1 009	769	566	539	427	384	368	376	371
Total, pigs	2 714	2 500	2 264	2 313	1 918	1 811	1 520	1 356	1 368	1 351	1 393
Hens for egg production											
Laying hens	5 937	6 548	6 392	6 100	5 670	5 065	6 061	7 571	8 403	6 363	7 919
Chickens reared for laying	2 636	2 159	2 176	1 812	1 654	1 697	1 647	1 842	2 420	2 390	1 722
Total, hens for egg-production	8 573	8 708	8 568	7 912	7 324	6 762	7 707	9 413	10 823	8 753	9 641
Horses											
Total, horses						283[a]	363	356[b]			

[a]Data from 2004; [b]Data for 2016.

Table 6.5. Number of animals slaughtered (in thousands) at slaughterhouses, 1980-2022. From the statistical database of the Board of Agriculture.

Animal Species	1980	1985	1990	1995	2000	2005	2010	2015	2020	2021	2022
Cattle											
Cattle > 1 year	574	584	523	502	490	433	425	406	420	400	401
Calves < 1 year	130	152	70	30	39	33	27	22	13	11	11
Total, cattle	704	736	593	532	529	466	453	428	434	412	412
Sheep	302	328	280	189	202	206	255	256	240	227	227
Pigs	4 153	4 283	3 653	3 743	3 251	3 160	2 936	2 560	2 623	2 651	2 672
Broilers	40 466	36 410	38 577	61 313	68 617	73 458	78 507	95 974	110 335	115 629	112 852
Turkeys							495	475	521	528	533

Table 6.6. Quantity of livestock slaughtered (in 1000 tonnes) at slaughterhouses, 1995-2022. From the statistical database of the Board of Agriculture.

Animal Species	1995	2000	2005	2010	2015	2020	2021	2022
Cattle	142	150	136	138	133	141	136	135
Cattle > 1 year	140	145	131	134	130	138	134	133
Calves < 1 year	3	4	5	4	4	2	2	2
Sheep	4	4	4	5	4	5	5	5
Pigs	309	277	275	264	233	247	253	254
Broilers	74	90	96	112	138	167	180	172
Turkeys				3	4	5	5	5

Table 6.7. Average number of animals per holding 1995-2022. From the statistical database of the Board of Agriculture.

Animal Species	1995	2000	2005	2010	2015	2020	2021	2022
Cattle								
Dairy cows	27	34	46	62	82	98	102	106
Beef cows	9	12	14	16	18	21	21	22
Ewes and rams	20	25	29	32	32	33	32	32
Boars and sows	31	63	156	156	186	185	173	175
Fattening pigs	157	294	471	664	845	945	942	951

Materials and methods, sales of antibiotics

Legal framework and distribution of drugs

Marketing of drugs in Sweden is regulated by the Medicinal Products Act, which applies both to human and veterinary medicinal products. According to this Act, a medicinal product may not be sold until it has been granted marketing authorisation by the Medical Products Agency (MPA). In case there are no authorised medicinal products for a certain condition, the MPA can permit special license prescription for a medicinal product for a specified pharmacy, prescriber or clinic.

Medicinal products in which an antibiotic is the active substance are only dispensed through pharmacies, which are supplied by drug wholesalers or manufacturers. In outpatient care, antibiotic drugs (including premixes for feed for veterinary use) may only be sold on prescriptions, ApoDos (individually packed doses of drugs often dispensed to the elderly) or requisitions. Prescribers (veterinarians or medical doctors) are not permitted to own a pharmacy or to otherwise sell medicinal products for profit. In hospital care, both for humans and animals, antibiotics are usually bought on requisition from pharmacies, although some regions manage drug supplies to human hospitals independently. Veterinarians may deliver products to the animal caretaker in relation to the examination of a case for self-cost (no profit) and such products are also bought on requisition.

All pharmacies in Sweden are required to provide statistics on sales of all products on a daily basis to the Swedish eHealth Agency (eHälsomyndigheten). This agency maintains a national database with sales statistics for all drugs and provides statistics to the competent national and regional authorities and to others on a commercial basis. These data are protected by the Public Access to Information and Secrecy Ordinance and publication of data needs to be carefully reviewed to avoid risk of disclosure of sensitive information. For this publication, measures for protection of information have been taken and for sales of antibiotics for humans, consent has been obtained from the legal entities concerned.

Feed mills may only mix antimicrobials in feed if the mill is controlled and authorised by the Swedish Board of Agriculture (SBA). The feed mills normally acquire the antibiotic products from a pharmacy. The quantities of antibiotic products used by feed mills are reported yearly to the SBA as part of the feed control. Mixing of antibiotics in feed may also take place on farms; provided that the SBA has inspected and authorised the establishment for the purpose. In such cases, the premix is sold by a pharmacy following prescriptions from a veterinarian.

The ATC classification system and defined daily doses (DDD)

Since 1988, the Anatomical Therapeutic Chemical (ATC) and ATCvet classification systems recommended by the WHO are used in Sweden for national drug statistics. For drugs sold for use in humans, to facilitate drug utilisation studies from a medical point of view, the measure defined daily dose (DDD) is used as a unit of comparison in drug statistics. The DDD for a drug is established on the basis of the assumed average dose per day for the drug given to adults for its main indication. If possible, the DDD is given as the amount of active substance. The DDDs are usually equal for all dosage forms of a preparation. The statistical data systems of the Swedish eHealth Agency are upgraded annually according to the recommendations made by the WHO Collaborating Centre for Drug Statistics Methodology in Oslo, Norway. Sales figures are presented as number of DDDs per 1 000 inhabitants per day, which gives an estimate of the proportion of the population daily exposed to a particular drug. This number is a rough estimate and should be interpreted with caution.

All data on the number of DDDs in this report are displayed in the 2023 version of the ATC/DDD index, available at https://www.whocc.no/atc_ddd_index/.

Antibiotic sales in humans

Sales statistics on medications have been monitored and compiled since 1975, initially by the National Corporation of Swedish Pharmacies. The sales are registered as number of DDDs, cash value and number of packages. Outpatient care data include information on the sales of prescribed drugs from all Swedish pharmacies by the prescription survey, running since 1974. The statistical material was until 1995 based on samples of dispensed prescriptions. From 1996 all prescriptions dispensed by pharmacies are included. From 1999, ApoDos (individually packed doses of drugs dispensed e.g. to the elderly) is also included in the survey. Recorded data are trade name, quantity, patient fee, total cost, sex and year of birth of the patient. Data can be expressed as DDD per 1 000 inhabitants per day or number of prescriptions per 1 000 inhabitants per year. Hospital care data include drugs delivered by all hospital pharmacies to the hospital departments (see the section "Completeness of data" below). The sales are expressed as cash value, number of packages and number of defined daily doses.

Following the de-monopolisation of the pharmacy market in Sweden in July 2009, the responsibility for collection of drug statistics was transferred to the core infrastructure supplier for all pharmacies, Apotekens Service. In January

2014, the activities in the state-owned company Apotekens Service were transferred to the Swedish eHealth Agency. The Swedish eHealth Agency aims to contribute to improved health care, improved public health and better caring by pursuing development of a national e-health infrastructure. The agency is also responsible for Sweden's national drug statistics.

Completeness of data

In Sweden, pharmacies are required by law to report sales statistics to the Swedish eHealth Agency. Concerns have been raised that after the re-regulation of the pharmacy market, the statistics on sales of medical products to hospitals in Sweden is less complete than before. However, after the re-regulation, regions can choose to manage drug supplies to hospitals independently. If so, the regions are not required to report data to the national database.

Therefore, no national database with complete sales statistic is currently available. Efforts have been made to complement the data from the Swedish eHealth Agency with data from regions.

Data sources and inclusion criteria

Data on sales of antibiotics in outpatient and hospital care as well as population data are obtained from the Swedish eHealth Agency. For the overall statistics, the data include all antimicrobial products marketed in Sweden in the ATC class J01. The data on sales of antibiotics for humans include all sales, even if the antimicrobial (J01) is prescribed by a veterinarian. Throughout this report, methenamine is excluded in all displays of J01 as a group. Measures used are defined daily dose per 1 000 inhabitants per day (DDD/1 000 inhabitants per day) and prescriptions per 1 000 inhabitants per year. Every purchase of a drug prescribed in outpatient care is also recorded in the Prescribed Drug Register, maintained by the Swedish National Board of Health and Welfare. This register provides the opportunity to link each prescription to an individual, which makes it possible to study the actual number of individuals or the fraction of the population treated with a specific drug. Thus, some of the data are presented as treated inhabitants per 1 000 total inhabitants per year. Data on the age-adjusted average body weight of the population in Sweden were obtained from Statistics Sweden, the agency responsible for official statistics in Sweden.

Antibiotic sales to hospital care are measured in DDD per 1 000 inhabitants per day and DDD per 100 admissions or patient-days. The number of DDDs is obtained from the Swedish eHealth Agency and from local registers in the regions. The Swedish National Board of Health and Welfare has provided data on admissions and patient-days to hospitals. Admission is calculated as number of discharges (one patient can be discharged and admitted multiple times if transferred between wards during one hospital stay). A patient-day is defined as each additional day during one hospital stay. The number of admissions and patient-days includes data on somatic medical care by each region.

For antibiotics sold in Sweden on a special license, information regarding strength and package size may be incomplete, preventing proper DDD calculation. Therefore, when data is obtained from the Swedish eHealth Agency in DDD, these products sold on special license may not be properly included and usage of certain antibiotics could be underestimated. For most antibiotic classes, this difference is negligible. However, for certain antibiotic substances, such as several cephalosporins, this underestimation has a notable effect on data represented in DDD.

Trend analysis

In the report, some general regression models were executed in the section "Sales of antibiotics". Time was used as explanatory variable and the outcome was the sales of antibiotics, adjusted for population size in Sweden, data on population provided by the eHealth Agency. The analyses were executed on a basis of a negative binomial distribution.

The Swedish Prescribed Drug Register

Since July 2005 the National Board of Health and Welfare supplies an individual based register on all drugs prescribed and dispensed in outpatient care. The register includes information on the number of individuals treated with at least one course of antibiotics during a specific period of time, i.e. number of treated inhabitants per 1 000 total inhabitants per year (Inhabitants/1 000/year). It is also possible to follow the number of purchases per person.

Number of admissions and patient-days

The 21 regions in Sweden deliver data annually to the National Patient Register maintained by The National Board of Health and Welfare. Administrative data within hospital care include, among others, date of admission, date of discharge and length of stay. The register is updated annually in autumn with data from the previous year after a process of validation. However, the data are available and can be obtained earlier. Data for 2022 are therefore not yet fully validated by the time this report is published, however the numbers are accurate. The numbers of admissions and patient-days in Swedish somatic medical care (produced by acute care hospitals) 2018-2022 are shown in Table 6.3.

Definitions of DDD 2022

Table 6.8. DDD for all antibiotic substances (J01) registered in Sweden in 2022.

	DDD (g)		DDD (g)
J01AA02- doxycycline	0.1	J01DI54- ceftolozane and enzyme inhibitor	3
J01AA04- lymecycline	0.6	J01EA01- trimethoprim	0.4
J01AA07- tetracycline	1	J01EC02- sulfadiazin	0.6
J01AA08- minocycline	0.2	J01EE01-sulphamethoxazolel and trimethoprim	1.92
J01AA12- tigecycline	0.1	J01FA01- erythromycin	1
J01BA01- chloramphenicol	3	J01FA01- erythromycin erythylsuccinate tablets	2
J01CA01- ampicillin- parenteral	6	J01FA06- roxithromycin	0.3
J01CA01- ampicillin- oral	2	J01FA09- clarithromycin- oral	0.5
J01CA04- amoxicillin	1.5	J01FA10- azithromycin- parenteral	0.5
J01CA08- pivmecillinam	0.6	J01FA10- azithromycin- oral	0.3
J01CA12- piperacillin	14	J01FA15- telithromycin	0.8
J01CA17- temocillin	4	J01FF01- clindamycin- parenteral	1.8
J01CE01- benzylpenicillin	3.6	J01FF01- clindamycin- oral	1.2
J01CE02- phenoximethylpenicillin (penicillin V)	2	J01FG01- pristinamycin	2
J01CE08- benzathine benzylpenicillin	3.6	J01GB01- tobramycin- parenteral	0.24
J01CF01- dicloxacillin	2	J01GB01- tobramycin- oral inhalation solution	0.3
J01CF02- cloxacillin	2	J01GB01- tobramycin- oral inhalation powder	0.112
J01CF05- flucloxacillin	2	J01GB03- gentamicin	0.24
J01CR02- amoxicillin and enzyme inhibitor	1.5	J01GB06- amikacin	1
J01CR05- piperacillin and enzyme inhibitor	14	J01MA01- ofloxacin	0.4
J01DB01- cefalexin	2	J01MA02- ciprofloxacin- parenteral	0.8
J01DB04- cefazolin	3	J01MA02- ciprofloxacin- oral	1
J01DB05- cefadroxil	2	J01MA06- norfloxacin	0.8
J01DC01- cefoxitin	6	J01MA12- levofloxacin- oral/parenteral	0.5
J01DC02- cefuroxime- parenteral	3	J01MA12- levofloxacin- inhalation	0.24
J01DC02- cefuroxime- oral	0.5	J01MA14- moxifloxacin	0.4
J01DC04- cefaclor	1	J01XA01- vancomycin	2
J01DD01- cefotaxime	4	J01XA02- teicoplanin	0.4
J01DD02- ceftazidime	4	J01XA04- dalbavancin	1.5
J01DD04- ceftriaxone	2	J01XB01- colistin- parenteral	9 MU
J01DD08- cefixime	0.4	J01XB01- colistin- oral	3 MU
J01DD14- ceftibuten	0.4	J01XB02- polymyxin B	0.15
J01DD52- ceftazidime and enzyme inhibitor	6	J01XC01- fusidic acid	1.5
J01DE01- cefepime	4	J01XD01- metronidazole	1.5
J01DF01- aztreonam- parenteral	4	J01XE01- nitrofurantoin	0.2
J01DF01- aztreonam- inhalation	0.225	J01XX01- fosfomycin- parenteral	8
J01DH02- meropenem	3	J01XX01- fosfomycin- oral	3
J01DH03- ertapenem	1	J01XX04- spectinomycin	3
J01DH51- imipenem and enzyme inhibitor	2	J01XX05- methenamine- hippurate	2
J01DH52- meropenem and enzyme inhibitor	3	J01XX05- methenamine- mandelate	3
J01DH56- imipenem and enzyme inhibitor	2	J01XX08- linezolid	1.2
J01DI01- ceftobiprolmedocaril	1.5	J01XX09- daptomycin	0.28
J01DI02- ceftarolinfosamil	1.2	J01XX11- tedizolid	0.2

Sales of antibiotics for animals

Data sources, inclusion criteria and analysis

For the overall statistics, the data include all products with antibiotics as active substance marketed in Sweden and sold for use in terrestrial animals in the ATCvet classes QA07, QJ01, QG01A and QJ51. Products that are authorised in other countries and sold on special license are also included. Medicinal products authorised for human use but prescribed for use in animals are not included in the overall statistics.

Data are retrieved as number of packages sold per product-presentation. Calculation to kg active substance is done based on information on strength and package size obtained from the national product register of the MPA, or for products sold on special license from other sources, e.g. pharmacies.

Products sold on special license

Antibiotic products sold with special licence (products prescribed and sold on exemption from Swedish market authorisation) are included in the dataset. However, in 2011 it was noticed that the information on sales of products with special licence was less complete than in previous years. Figures for 2011 are therefore likely to be a slight underestimate. Between 2012 and 2014, efforts were made to obtain sales data for major products on license from pharmaceutical companies to adjust the data on pharmacy sales. The reporting system was adjusted, and it is assumed that from 2015 data from the eHealth Agency on sales of products with special licence is no less complete than for products with general marketing authorisation.

Materials and methods, resistance in bacteria from animals

Isolation and identification of bacteria

Antibiotic resistance as notifiable diseases

ESBL

$ESBL_A$, $ESBL_M$ and $ESBL_{CARBA}$-producing *Escherichia coli* were isolated by culture on MacConkey agar (Oxoid) with cefotaxime (1 mg/L), CHROMID CARBA (CC) agar (bioMérieux) and CHROMID OXA 48 (CO) agar (bioMérieux), with prior enrichment in buffered peptone water (BPW).

Intestinal samples: Shortly, 1 g of intestinal content was diluted in 9 ml BPW and incubated at 37°C overnight. From the BPW solution 10 µl was spread each on a plate of MacConkey agar with cefotaxime (1 mg/L), CC agar and CO agar. The plates were incubated overnight at 44°C (MacConkey agar) or 35°C (CC, CO agar). From MacConkey agar with cefotaxime up to three lactose positive colonies with morphology typical for *E. coli* was sub-cultured on MacConkey agar with cefotaxime and then sub-cultured again on horse-blood agar (5% v/v), after which the isolate was tested for production of tryptophanase (indole). Only lactose and indole positive isolates with typical morphology were selected for susceptibility tests and further tested for ESBL production. Isolates suspected to be Enterobacterales species on CC agar and CO agar were sub-cultured on MacConkeyagar and then sub-cultured again on horse blood agar. These isolates were species identified by MALDI-TOF MS and if positive for any Enterobacterales species the isolate would be further tested for ESBL production.

Meat samples: Briefly, 25 g of surface meat was homogenised in 225 ml BPW and incubated at 37°C overnight. From the BPW homogenisate 10 µl per agar plate was spread on MacConkey agar with cefotaxime (1 mg/L), CC agar and CO agar and incubated overnight at 44°C (MacConkey agar) or 35°C (CC, CO agar). From MacConkey agar with cefotaxime one lactose positive colony with morphology typical for *E. coli* was sub-cultured on MacConkey agar with cefotaxime and then sub-cultured again on horse-blood agar (5% v/v), after which the isolate was tested for production of tryptophanase (indole). Only lactose and indole positive isolates with typical morphology were selected for susceptibility tests and further tested for ESBL production. From MacConkey agar with cefotaxime up to three lactose positive colonies with morphology typical for *E. coli* was sub-cultured on MacConkey agar with cefotaxime and then sub-cultured again. *Escherichia coli* like colonies on CC agar and CO agar were sub-cultured on MacConkeyagar, and if they were lactose positive, they were sub-cultured on horse-blood agar. Lactose positive isolates were species identified by MALDI-TOF MS and if positive for any Enterobacterales species the isolate would be further tested for ESBL production.

Clinical isolates from cats, dogs, and horses were submitted to the Dept. of Animal Health and Antimicrobial Strategies, SVA as bacterial strains. Isolates were species identified by MALDI-TOF MS.

MRSA and MRSP

Isolates were species identified by MALDI-TOF MS and tested for presence of *mecA* and *mecC* with PCR (see below, Genotyping). Isolates were susceptibility tested using microdilution (see below, Susceptibility testing).

Zoonotic pathogens

Salmonella

Salmonella was isolated and identified at the Dept. of Microbiology, SVA or at regional laboratories in accordance with standard procedures. All samples within official control programmes are cultured according to the procedures detailed by the MSRV (ISO 6579-1:2017). Confirmatory identification and serotyping were performed according to the procedures of White-Kauffmann-Le Minor. For certain isolates, the serovar was verified by whole genome sequencing.

Campylobacter

Campylobacter jejuni and *Campylobacter coli* were isolated and identified at the Dept. of Microbiology, SVA, from caecal content from healthy broilers sampled at slaughter within the Swedish Campylobacter programme. Ten whole caeca were collected from each batch of broilers slaughtered and pooled at analyse. In 2022, 165 flocks were positive for *C. jejuni* and 17 for *C. coli*, from these 163 *C. jejuni* and 16 *C. coli* were susceptibility tested. Samples were cultured according to ISO 10272-1:2017 for detection of thermophilic *C. jejuni* and *C. coli* by direct cultivation on mCCDA and Butzler agar followed by incubation at 41,5°C for 44 h in a microaerophilic environment. Identification was based on colony morphology, microscopic appearance including motility. All isolates were species identified by MALDI-TOF MS. The isolates were stored in -70°C until tested.

Clinical isolates from animals

Clinical isolates were isolated and identified with accredited methodology following standard procedures at SVA.

Indicator bacteria

Escherichia coli

After the initial dilution in BPW and incubation (see screening for ESBL above), 10 µL was spread on MacConkey agar and incubated overnight at 44°C.

Up to three lactose positive colonies with morphology typical for *E. coli* was sub-cultured on horse-blood agar (5% v/v), after which the isolate was tested for production of tryptophanase (indole). Only lactose and indole positive isolates with typical morphology were selected for susceptibility tests.

Susceptibility testing

Microdilution

At SVA, fast growing aerobic bacteria, *Campylobacter* and bacteria from fish are tested for antibiotic susceptibility with accredited methodology using dilution methods in cation adjusted Mueller-Hinton broth (CAMHB) (Difco). Tests are performed following the standards for microdilution of the Clinical and Laboratory Standards Institute (CLSI, 2018). The microdilution panels used are produced by Trek diagnostics LTD (Sensititre) and for *Brachyspira* spp. the panels are produced at Section of Substrate, SVA (VetMIC). Different panels are used depending on the bacterial species tested and the purpose of the investigation (monitoring or clinical diagnostics). Minimum inhibitory concentration (MIC) is recorded as the lowest concentration of an antibiotic that inhibits bacterial growth.

Some adaptations from the CLSI standard are employed. For *Pasteurella* spp. the tests are made by dilution in CAMHB supplemented with 5-10% horse serum followed by incubation in CO_2, 37°C for 16-18 hours. For testing of *A. pleuropneumoniae* dilution in HTM broth was used and with incubation in CO_2 at 37°C for 18-24 hours. *Streptococcus* spp. were tested using CAMHB supplemented with 5-10% horse serum followed by incubation at 35°C for 16-18 hours.

Susceptibility of *C. jejuni* and *C. coli* was tested according to the CLSI standard M45-^{3rd} ed. for fastidious bacteria (CLSI, 2015).

Susceptibility of *Brachyspira hyodysenteriae* and *B. pilosicoli*, was tested by a broth dilution method described by Karlsson et al. (2003), in tissue culture trays with 48 wells per plate. The wells were filled with 0.5 ml of a suspension of bacteria ($1x10^6$-$5x10^6$ CFU/ml) in brain heart infusion broth (BHI) with 10% foetal calf serum and incubated in an anaerobic atmosphere at 37°C for four days on a shaker.

Bacteria from fish are tested for antibiotic susceptibility by broth microdilution adapted for aquatic bacteria according to CLSI (2020a).

Phenotypic confirmatory tests for production of extended spectrum beta-lactamases (ESBLs) in Enterobacterales were performed with and without clavulanic acid in Sensititre EUVSEC2 microdilution panels and interpreted according to EUCAST.

Genotyping

Suspected isolates of MRSA and MRSP were confirmed by detection of the *mecA* and *mecC* genes applying real-time PCR as described by Pichon et al. (2012). *Spa*-typing, a single locus sequence typing method using the polymorphic region X of the protein A gene, was performed on all isolates confirmed as MRSA, according to Harmsen et al. (2003) and the specific *spa*-type was determined using BioNumerics® (Applied Maths). ST types were found in confirmed MRSP isolates using Ridom SeqSphere+ software (Ridom GmbH, Germany).

Isolates of Enterobacterales confirmed as $ESBL_A$ phenotypically or suspected being $ESBL_{CARBA}$ were subjected to genome sequence analyses (see below). Isolates suspected of being $ESBL_M$ based on phenotype was first subjected to PCR detecting genes encoding $ESBL_M$ (Perez-Perez and Hanson, 2002) and $ESBL_A$ (Woodford et al., 2006 and Fang et al., 2008). After confirmation of suspected transferable genes these isolates were subjected to genome sequencing.

DNA from confirmed ESBL-producing Enterobacterales, MRSA and MRSP was extracted from overnight cultures on horse-blood agar using Qiagen EZ1 DNA tissue kit, according to the recommendations of the manufacturer. For a subset of ESBL-producing Enterobacterales DNA was extracted by using IndiMag® Pathogen Kit (Indical Bioscience) in a Maelstrom 9600 (TANBead). DNA concentrations were determined using Qubit HS DNA-kit (Life technologies). DNA was sent to Clinical genomics Stockholm, SciLifeLab (Solna, Sweden) for library preparation and paired-end sequencing using Illumina technologies. The specific ESBL-gene was determined using "Antimicrobial Resistance Identification By Assembly (ARIBA)" (Hunt et al., 2017) against the Resfinder database (https://cge.cbs.dtu.dk/services/ResFinder/). Reads were then trimmed with Trimmomatic and genome assembly was performed with SPAdes with the careful parameter, followed by Pilon with default settings to correct assemblies (Bankevich et al., 2012; Bolger et al., 2014; Walker et al., 2014). Using the assembled contigs the isolates were assigned an MLST, when available, using Ridom SeqSphere+ software (Ridom GmbH, Germany).

Quality assurance system

Laboratories performing antibiotic susceptibility testing at SVA are accredited according to SS-EN ISO/IEC 17025 by the Swedish Board for Accreditation and Conformity Assessment (SWEDAC) to perform antibiotic susceptibility tests with microdilution methods. In addition, Dept. of Microbiology is accredited for isolation and identification of animal pathogens and of *Salmonella* according to the same standard.

For susceptibility tests of zoonotic, pathogenic and indicator bacteria, *Escherichia coli* ATCC 25922, *Enterococcus faecalis* ATCC 29212, *Staphylococcus aureus* CCUG 15915 (analogue to ATCC 29213), *Actinobacillus pleuropneumoniae* ATCC 27090, *Trueperella pyogenes* CCUG 13230, *Acinetobacter baumannii* 2012-70-100-69 - EURL 69 (used for control of higher concentrations of cephalosporins and carbapenems), *Aeromonas salmonicida* subsp. *salmonicida* CCUG 2116 (analogue to ATCC 14174) and *Campylobacter jejuni* CCUG 11284 (analogue to *Campylobacter jejuni* ATCC 33560) were included as quality controls. When testing animal pathogens relevant control strains were included and evaluated at least once weekly. For testing of *Brachyspira*, the *B. hyodysenteriae* type strain $B78^T$ ATCC 27164^T was used for quality control. Dept. of Animal Health and Antimicrobial Strategies participate once a year in two proficiency tests for antibiotic susceptibility testing, one for isolation and antibiotic susceptibility testing and one comparative test for antibiotic susceptibility testing. These are arranged by the European Union Reference Laboratory - Antimicrobial Resistance and as a national ring trial. We also participate in DTU genomic proficiency test once a year. Likewise, Dept. of Microbiology participates in proficiency tests concerning isolation and identification of *Salmonella* and general clinical veterinary bacteriology and susceptibility tests.

Data handling

Records such as source of cultured sample, identification results, antibiotic susceptibility etcetera were registered in a laboratory information management (LIM) system at SVA.

Cut-off values for resistance

For interpretation of MICs from susceptibility testing of zoonotic bacteria (*Salmonella* and *Campylobacter*) and indicator bacteria (*Escherichia coli* and enterococci) epidemiological cut-off values (ECOFFs) issued by EUCAST (www.eucast.org) or values suggested by the European Food Safety Authority are used. For some antibiotics, values based on MIC distributions obtained in Svarm are used.

ECOFFs are used when available also for clinical isolates from animals. When ECOFFs are not available, or the range of concentrations tested precludes use of a recommended value, values based on MIC distributions obtained in Svarm are used, but clinical breakpoints issued by CLSI (CLSI, 2023) or epidemiological cut-offs (ECVs) issued by CLSI (CLSI, 2020b) are also taken into consideration.

ECOFFs and ECVs classify isolates with acquired reduced susceptibility as non-wild type. In Svarm, non-wild type isolates are called resistant. This classification is relevant for monitoring purposes, but it should be understood that resistance defined in this manner not always implies clinical resistance.

Svarm 2000–2022

The number of isolates of different matrices reported in Svarm since 2000 is available as supplementary material on the SVA web page (www.sva.se/svarm).

Table 6.9. Cut-off values (mg/L) for resistance. Values in red are current EUCAST epidemiological cut-off values (ECOFFs), values in blue are CLSI ECVs, black underlined values deviate from ECOFFs and ECVs, and for values in black, ECOFFs or ECVs are not defined.

Antibiotic	*Actinobacillus pleuropneumonia*	*Brachyspira hyodysenteriae*	*Campylobacter jejuni*	*Campylobacter coli*	*Escherichia coli* (indicator)	*Escherichia coli* (pathogen)	*Flavobacterium psychrophilum*	*Klebsiella pneumoniae*	*Pasteurella multocida*	*Pseudomonas aeruginosa*	*Salmonella enterica*	*Staphylococcus hyicus*	*Staphylococcus pseudintermedius*	*S. felis, S. schleiferi*	*Staphylococcus aureus*	*Streptococcus suis*	*Streptococcus zooepidemicus*
Amikacin					>8						>4						
Ampicillin	>0.5				>8	>8			>0.5		>4						
Azithromycin					>16						>16						
Cefalexin						>32											
Cefepime					>0.25												
Cefotaxime					>0.25	>0.25		>0.25			>0.5						
Cefoxitin															>4		
Ceftazidime					>1						>2						
Ceftiofur									0.12								
Cephalothin													>1	>1	>1		>2
Chloramphenicol			>16	>16	>16						>16				>16		
Ciprofloxacin			>0.25	>0.5	>0.06						>0.12				>2		
Clindamycin												>0.5	>0.5	>0.5	>0.5[c]	>0.5	>0.5
Colistin					>2	>2		>2		>4							
Doxycycline	>2	>0.5															
Enrofloxacin	>0.12				>0.12	>0.12		>0.12	>0.06	>2		>0.25	>0.5	>0.5	>0.5		
Ertapenem			>0.5	>0.5	>0.03												
Erythromycin			>4	>8								>1	>0.5	>0.5	>1	>0.5	>0.5
Florfenicol	>1						>2		>1								
Fusidic acid												>0.5	>0.5	>0.5	>0.5		
Gamithromycin	>4								>4								
Gentamicin			>2	>2	>2	>2		>2		>8	>1		>1	>1	>2		
Imipenem					>0.5												
Linezolid															>4		
Meropenem					>0.12	>0.12					>0.12						
Nalidixic acid					>8						>8						
Neomycin						>8		>8									
Nitrofurantoin						>64							>32 (UTI)	>32 (UTI)	>32 (UTI)		
Oxacillin												>1	>0.25	>1			
Oxolinic acid							>0.25										
Oxytetracycline							>0.25										
Penicillin	>1								>0.5			>0.06	[b]	[b]	[b]	>0.12	>0.06
Sulphamethoxazole					>64						>256						
Temocillin					>16												
Tetracycline	>2		>1	>2	>8	>8	>0.12	>8	>2		>8	>1	>0.5	>0.5	>1	>0.5	
Tiamulin		>0.25															
Tigecycline					>0.5						>0.5						
Trimethoprim					>2						>2				>2		
Trim & sulpha[a]	>0.25					>1		>0.5	>0.12			>0.25	>0.5	>0.5	>0.25	>0.25	>0.5
Tylosin		>16															
Tylvalosin		>1															
Valnemulin		>0.12															

[a]Concentration of trimethoprim given, tested with sulphamethoxazole in concentration ratio 1/20; [b]beta-lactamase production; [c]EUCAST ECOFFs are used for MRSA (clindamycin >0.25).

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SWEDRES|SVARM 2022

This annual report describes the monitoring of antibiotic resistance and antibiotic sales in human and veterinary medicine in Sweden in 2022.

From an international perspective, the situation in Sweden regarding antibiotic resistance in bacteria from humans and animals is favourable. In spite of this, there are still problems with cross infection and increasing resistance. Thus, the preventive efforts must continue, and in some instances be intensified.

The total sales of antibiotics for both humans and animals have decreased continually from a long-term perspective, and prescribers' choices of antibiotics are broadly in line with policies and recommendations.

The number of cases of $ESBL_{CARBA}$ in humans is low in Sweden. Still, 240 cases were reported during 2022, compared to 137 in 2021. The risk of introducing $ESBL_{CARBA}$ among vulnerable patients is very concerning as this could have serious consequences for these patients. So far, $ESBL_{CARBA}$ has never been confirmed in samples from domestic animals in Sweden.

For humans, the COVID-19 pandemic had considerable impact on notifiable antibiotic resistance. During 2022, as the pandemic receded, the number of cases for most types of notifiable resistance increased compared to previous levels. In contrast, resistance in clinical cultures, such as for *Escherichia coli* isolated from blood, generally followed the previous trends during the pandemic.

Work against antibiotic resistance has naturally been hampered during the pandemic. The efforts to optimise antibiotic use, prevent infections, and minimise dissemination of antibiotic resistance are now back at pre-pandemic levels. It is increasingly important to address the slow pandemic that antibiotic resistance constitutes.

Focus areas:
- Medicinal shortages – the role of the Swedish Medical Products Agency
- Swedish antibiotic prescribing according to the WHO AWaRe classification
- Antibiotics in digital health
- SvarmPat – monitoring of resistance in pathogens from farm animals
- Interpretation of antibiotic susceptibility for topical treatment

The Public Health Agency of Sweden (PHAS) has a national responsibility for public health issues. The Agency promotes good public health by generating and disseminating knowledge to professionals involved in the field of public health, including infectious disease prevention.

The National Veterinary Institute (SVA) is an expert authority within the field of risk assessment and diagnostics, as well as the prevention and control of infectious animal diseases. The Institute strives for good animal and human health through research, contingency planning and communication of knowledge.