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SWEDRES | SVARM

Sales of antibiotics and occurrence of antibiotic resistance in Sweden

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

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Public Health Agency of Sweden and National Veterinary Institute

Editors:

Olov Aspevall, Ragda Obeid and Wenjing Tao
Public Health Agency of Sweden
Oskar Nilsson and Märit Pringle,
National Veterinary Institute

Addresses:

The Public Health Agency of Sweden
Solna. SE-171 82 Solna, Sweden
Östersund. Box 505, SE-831 26 Östersund, Sweden
Phone: +46 (0) 10 205 20 00
Fax: +46 (0) 8 32 83 30
E-mail: info@folkhalsomyndigheten.se
www.folkhalsomyndigheten.se

National Veterinary Institute
SE-751 89 Uppsala, Sweden
Phone: +46 (0) 18 67 40 00
E-mail: svarm@sva.se
www.sva.se

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Preface

For almost two decades, the Swedres-Svarm report on the monitoring of antibiotic resistance and antibiotic sales in human and veterinary medicine has been published as a joint venture by the Swedish veterinary and public health sectors. Data from humans, animals, and food have been analysed and presented in a comprehensive manner - a pure One Health output - with Sweden leading the way in interdisciplinary work to mitigate the effects of antibiotic resistance.

Two years with a pandemic crisis has exposed many societal vulnerabilities and at the time when this preface is written, we are facing yet another crisis with global repercussions. We have war in our direct vicinity, with millions of Ukrainians seeking refuge in the European Union, for themselves and for some also for their pets. These very different events again underline the importance of international cooperation to, with joint efforts improve public health and living conditions in all countries, which also applies to a great extent to the problem of antibiotic resistance.

However, this report focuses on 2021, which was also the first year where the harmonised monitoring of antimicrobial resistance in animals followed the new Commission Implementing Decision (EU) 2020/1729 of 17 November 2020. Through the new act, food products imported into the Union are now also subjected to monitoring requirements. This gives an opportunity to gain a deeper understanding of the exposure and transmission of resistance, and it also acknowledges the global nature of antimicrobial resistance as a threat. In addition, a new and improved method to culture *Campylobacter* has been introduced in the monitoring of resistance in animals and food.

As in 2020, the COVID-19 pandemic has meant that both antibiotic sales and the number of cases of notifiable antibiotic-resistance bacteria in humans have been lower than usual. Fewer cases of most communicable diseases in humans have been reported during the pandemic. Resistance levels among clinical isolates from humans, however, were relatively unaffected by the COVID-19 pandemic. The pandemic has had an extensive impact on society and healthcare and has also affected the sampling for bacteriological culture, the number of health care visits, and the nature of the visits within healthcare in general. The impact of the COVID-19 pandemic is described in a section directly after the summary.

Internationally the high level of activity regarding antimicrobial resistance has continued during 2021 despite the COVID-19 pandemic. In April, a high level meeting, the 3rd High Level Technical Consultation and Meeting on Surveillance of Antimicrobial Resistance and Use for Concerted Actions, was held in Sweden. The aims were to improve the WHO Global Antimicrobial resistance and use Surveillance System (GLASS), and to support countries in implementing national surveillance systems.

On the veterinary side, Sweden is still in the forefront as overall sales of antibiotics continue to decrease at the EU level, as shown in the latest ESVAC report. Also, the new regulation on veterinary medicinal products that came into effect early this year reinforces Swedish standpoints regarding prudent and responsible use of antimicrobials in animals, including reserving certain antimicrobials for the treatment of infections in people. It prohibits the use of antibiotics in farm animals to compensate for poor animal husbandry, and will hopefully be a driver to further reduce the use of antibiotics in animals in the EU.

The general COVID-19 restrictions are presently lifted in Sweden, vaccination is easily available, and incidence has decreased significantly. Still, the pandemic has shown us how infectious diseases can impact societies if there is no treatment available. Following that line of thought, it should also be a reminder of how we rely on antibiotics to make full use of the progress made in many fields of medicine, and also how good health in people and animals is the best way to save our antibiotics for the future.

Solna and Uppsala, June 2022

Karin Tegmark Wisell

Director General
The Public Health Agency of Sweden

Ann Lindberg

Director General
National Veterinary Institute

Contributors and participants

Editors

Olov Aspevall, Ragda Obeid and Wenjing Tao,
Public Health Agency of Sweden
Oskar Nilsson and Märit Pringle,
National Veterinary Institute, Sweden

Project Manager

Oskar Nilsson, National Veterinary Institute, Sweden

Authors Swedres

Public Health Agency of Sweden
Olov Aspevall, Hanna Billström, Stefan Börjesson
Jessica Darenberg, Petra Edquist, Nazanin Hashemi,
Jenny Hellman, Jerker Jonsson, Caroline Kaipe,
Eva Morfeldt, Barbro Mäkitalo, Ragda Obeid,
Kristina Rizzardi, Karin Westmo, Gunilla Skoog Ståhlgren,
Johan Struwe, Tomas Söderblom, Wenjing Tao,
Anders Ternhag

Strama Stockholm
Annika Hahlin

National Reference Laboratory for Sexually Transmitted Infections & National Reference Laboratory for *Neisseria meningitidis*
Magnus Unemo, Hans Fredlund and Susanne Jacobsson

Department of Clinical Microbiology, Karolinska University Hospital, Stockholm
Eva-Lena Ericson and Nora Vestberg

Authors Svarm

National Veterinary Institute
Annette Backhans, Karin Bergström, Christina Greko,
Annica Landén, Mattias Myrenås, Oskar Nilsson,
Karl Pedersen and Märit Pringle

Swedish Board of Agriculture
Kinfe Girma

Other contributors in Svarm

National Veterinary Institute
Boel Harbom, Paulina Hysing, Ellinore Jansson
and Karin Lindgren

Farm & Animal Health
Maria Lindberg and Frida Matti

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Content

Sammanfattning/Summary

Sammanfattning

År 2021 har covid-19 pandemin medfört att både antibiotikaförsäljning och anmälningar av antibiotikaresistenta bakterier hos människor varit lägre än vanligt, liksom 2020. Det har också rapporterats färre fall av de flesta anmälningspliktiga sjukdomarna hos människor under pandemin, även anmälningspliktig antibiotikaresistens. För anmälningspliktiga sjukdomar är skillnaden mot före pandemin mindre 2021 än 2020, medan däremot MRSA och ESBL inom anmälningspliktig antibiotikaresistens fortsatt minska under 2021. I övervakningen av resistensnivåer bland kliniska isolat från människor ses däremot inte denna påverkan av pandemin, utan trenderna är relativt opåverkade. Covid-19 pandemin har haft en omfattande påverkan på samhället och sjukvården och även påverkat provtagningen för resistenta bakterier, antalet vårdtillfällen, antalet besök samt karaktären på besöken inom sjukvården i stort.

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 smittspridning och ökande antibiotikaresistens, vilket motiverar fortsatt förebyggande arbete. Viktiga exempel är de återkommande utbrotten av vankomycinresistenta enterokocker på sjukhus och ett ökande antal vårdrelaterade kluster av ESBL-CARBA.

Antibiotikaförsäljningen inom humanmedicinen i Sverige fortsatte att minska under 2021, efter att ha minskat kraftigt under 2020.

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 2021

- Den totala antibiotikaförsäljningen inom humanmedicinen i Sverige minskade med 3 procent under 2021 jämfört med 2020. Det återspeglas inom både recept och rekvisitioner, med undantag av akutsjukhusen där försäljningen ökade markant. Försäljningen av antibiotika inom tandvården ökade med 3 procent under samma period.
- Antibiotikaförsäljningen inom öppenvården ökade under andra till fjärde kvartalet jämfört med samma period året innan. Framför allt förskrivning av luftvägsantibiotika till barn bidrog till denna ökning.
- Andelen MRSA bland Staphylococcus aureus från blododling har minskat till 2,0 procent, från 2,3 procent 2020.
- Inga nya vårdrelaterade kluster av ESBL-CARBA rapporterades under 2021.
- Under pandemin har antalet fall minskat av flertalet typer av anmälningspliktig antibiotikaresistens. Denna påverkan ses däremot inte på resistensnivåer bland kliniska isolat från människor, utan trenderna är relativt opåverkade.
- 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. Med selektiva metoder kunde dock ESBL-bildande E. coli isoleras från 12 procent av tarmproven från nötkreatur under ett år. Antalet prov från nötkreatur under ett år som undersökts är dock begränsat.
- 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 minskade med 3 procent under 2021 och ligger nu på 9,4 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 230 recept per 1 000 invånare, en minskning med 3 procent jämfört med 2020. Bland landets 21 regioner uppnådde 19 regioner det nationella målet på högst 250 recept per 1 000 invånare och år även under 2021. Försäljningen minskade i samtliga åldersgrupper, med undantag av barn i åldern 0–4 år där den ökade med 11,4 procent jämfört med året innan. Tydligast var ökningen under det fjärde kvartalet, där antibiotikaförsäljning till barn ökade med 143 procent jämfört med samma period 2020. Denna ökning bestod framför allt av antibiotika som ofta används vid luftvägsinfektioner.

Försäljningen av antibiotika på recept inom tandvården ökade med 3 procent under 2021 jämfört med året innan, och utgör 7 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 var 1,3 DDD per 1 000 invånare och dag under 2021, en minskning med 5 procent jämfört med 2020. Antibiotikaförsäljningen till akutsjukhusen ökade däremot 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, medan försäljningen av betalaktamaskänsliga penicilliner och makrolider minskade. Liksom tidigare år fanns stora regionala variationer i användningen av bredspektrumantibiotika vid akutsjukhusen.

Antibiotikaförsäljning inom veterinärmedicin

Försäljningen av antibiotika för djur uppgick 2021 till 9 129 kilogram, varav 57 procent var penicillin med smalt spektrum. Motsvarande värden för 2012 var 11 385 kilogram och 53 procent. Försäljningen av antibiotika som bör användas särskilt restriktivt (fluorokinoloner, tredje generationens cefalosporiner och polymyxin) har minskat kraftigt sedan 2012 (84–95 procent). 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 2021 såldes 53,3 ton antibiotika för behandling av människor och 9,0 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 79,3 milligram per kilogram för människor och 11,8 milligram per kilogram för djur. Försäljning inom humanmedicin dominerade för alla antibiotikaklasser utom aminoglykosider.

Anmälningspliktig resistens

ESBL-bildande Enterobacterales (tidigare Enterobacteriaceae)

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

Resultat 2021, Enterobacterales (tidigare Enterobacteriaceae) med ESBL

- Antal rapporterade fall: 7 860 (föregående år 8 230), relativ förändring: 4 procent minskning.
- Antal fall med blodförgiftning: 719 (föregående år 727).
- Som tidigare år var E. coli den vanligaste arten, 85 procent, följt av Klebsiella pneumoniae, 9 procent.
- Andelen E. coli från blododling som är resistenta mot tredje generationens cefalosporiner har minskat till 7 procent, från 8 procent 2020.

Resultat 2021, Enterobacterales (tidigare Enterobacteriaceae) med ESBL-CARBA

- Antal rapporterade fall: 137 (föregående år 128), relativ förändring: 7 procent ökning.
- Antal fall med blodförgiftning: 7 (föregående år 11).
- E. coli var den vanligaste arten, 58 procent, följt av K. pneumoniae, 31 procent.
- Andelen E. coli från blododling som är resistenta mot meropenem är 0,1 procent, jämfört med 0 procent 2020.

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 2021 undersöktes förekomsten av ESBL-bildande E. coli i tarm- och köttprov från gris och nöt samt i tarmprov från slaktkyckling med selektiva metoder.

Sådana bakterier hittades i 1 procent av tarmproven från gris, 12 procent av tarmproven från nötkreatur under ett år och 1 procent av tarmproven från slaktkyckling. Antalet prov från nötkreatur under ett år som undersökts är dock begränsat. Vidare hittades sådana bakterier i mindre än 1 procent respektive 0 procent av nöt- och grisköttsproven med svenskt ursprung. 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 33 procent respektive 16 procent av fallen.

Resultat 2021

- Antal rapporterade fall: 2 895 (föregående år 3 112), relativ förändring: 7 procent minskning.
- Antal fall med blodförgiftning: 97 (föregående år 98).
- Andelen MRSA bland S. aureus från blododling har minskat till 2,0 procent, från 2,3 procent 2020.

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 och katt. Hos hundar och katter dominerar samma typer av MRSA som hos människor, vilket tyder på att människor är smittkällan. Hos hästar rapporterades under året 23 fall av MRSA, vilket är i nivå med 2020 (27 fall), och fortsatt fler jämfört med tidigare högsta noteringen, 9 fall år 2014. En del av det ökande antalet under 2021 (8 fall) beror på ett MRSA-utbrott på hästsjukhus av en spa-typ, t034, som inte tidigare påvisats hos hästar i Sverige.

Staphylococcus pseudintermedius resistenta mot meticillin (MRSP)

Under 2021 var antalet anmälda fall av meticillinresistenta Staphylococcus pseudintermedius (MRSP) hos djur på samma nivå som de senaste åren. Totalt anmäldes 43 fall av MRSP till Jordbruksverket, varav 41 fall från hund samt ett från katt och ett från häst. 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). Numera förekommer flera olika sekvenstyper.

MRSP är inte anmälningspliktig vid förekomst hos människor.

Streptococcus pneumoniae med nedsatt känslighet för penicillin (PNSP)

Resultat 2021

- Antal rapporterade fall: 92 (föregående år 112), relativ förändring: 17 procent minskning.
- Antal fall med blodförgiftning: 3 (föregående år 4).
- Andelen S. pneumoniae med nedsatt känslighet för penicillin (PNSP) från blododling har minskat till 6,3 procent, från 8,3 procent 2020.

Enterococcus faecium och Enterococcus faecalis resistenta mot vankomycin (VRE)

Resultat 2021

- Totalt antal rapporterade fall: 209 (föregående år 79), relativ förändring: 64 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: 204 (föregående år 77), relativ förändring: 65 procent ökning.
- Antal rapporterade fall av E. faecalis med vankomycinresistens: 1 (föregående år 4).
- Tre fall av VRE rapporterades med både E. faecium och E. faecalis.
- Antal fall med blodförgiftning: 2 (föregående år 4).
- Elva smittspridningar rapporterades under året med 2-36 fall. Av dessa var fem större sjukhusrelaterade utbrott med 11-36 fall vardera. År 2020 rapporterades åtta 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 antibiotikagruppen fluorokinoloner är ovanlig.

För salmonellaarter var resistensen bland faecesisolat från människor högst mot fluorokinoloner, 17 procent. Ingen resistens mot meropenem 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 45 procent och mot tetracyklin 17 procent 2021. En 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 6–7 procent. Antalet anmälningar av E. coli ESBL från blod 2021 var 575. 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 6–7 procent. Antalet anmälningar av K. pneumoniae ESBL från blod 2021 var 97. Liksom för E. coli är resistensen mot ciprofloxacin nu relativt hög, 11 respektive 8 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 2,0 procent respektive 1,9 procent. Antalet anmälningar av MRSA från blod 2021 var 97.
- Enterococcus faecalis och Enterococcus faecium: Vankomycin-resistensen hos isolat från blod är fortsatt låg (0,1 respektive 0,3 procent) och för höggradig aminoglykosidresistens ses en gradvis minskning sedan 2017.
- Clostridioides difficile: Incidensen har legat relativt stabilt sedan 2018, och är nu 61 fall per 100 000 invånare och år. Antibiotikaresistens har inte undersökts 2021.

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. Penicillinresistens är däremot vanligt hos Staphylococcus pseudintermedius från hundar 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 72 respektive 64 procent av E. coli från friska slaktkycklingar och slaktgrisar i de senast gjorda undersökningarna känsliga för alla testade substanser.

Summary

Similar to 2020, the COVID-19 pandemic has meant that both antibiotic sales and the number of cases of notifiable antibiotic-resistance bacteria in humans have been lower than usual. Fewer cases of most communicable diseases in humans have been reported during the pandemic, including cases of notifiable antibiotic resistance. For notifiable infections, the difference from before the pandemic was smaller in 2021 than in 2020, while MRSA and ESBL continued to decrease in 2021. Resistance levels among clinical isolates from humans, however, were relatively unaffected by the COVID-19 pandemic. The COVID-19 pandemic has had an extensive impact on society and healthcare and has also affected the sampling for bacteriological culture, the number of health care visits, and the nature of the visits within healthcare in general.

The situation in Sweden regarding antibiotic resistance in bacteria from humans has been, and still is, favourable from an international perspective. One contributing factor is that our strategies to promote the responsible use of antibiotics and to limit the spread of antibiotic resistance are effective. Despite our relatively good situation, there are problems with cross infection and increasing antibiotic resistance, which calls for continued efforts in preventive work. Important examples are the recurrent outbreaks of vancomycin-resistant enterococci in hospitals, and an increasing number of health care related clusters of $ESBL_{CARBA}$.

Antibiotic sales for humans continued to decrease in 2021, after a considerable reduction in 2020. During the past decades, consumption of broadspectrum antibiotics has shifted towards narrow-spectrum antibiotics. However, this development seems to have gradually reversed 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 2021

- Total sales of antibiotics for humans in Sweden decreased by 3% in 2021 compared to 2020, as measured in DDD per 1 000 inhabitants per day. The decrease was reflected in both outpatient and inpatient care, with the exception of acute care hospitals where antibiotic sales increased considerably. Antibiotic sales in dentistry increased with 3% in 2021.
- Antibiotic sales in outpatient care increased between the second and fourth quarter of 2021 compared to the same time period in 2020. In particular, sales of antibiotics commonly used for respiratory tract infections in children contributed to this increase.
- The proportion of MRSA among *Staphylococcus aureus* isolated from blood has decreased to 2.0%, compared to 2.3% in 2020.
- No new clusters of health care-related $ESBL_{CARBA}$ were reported in 2021.
- During the pandemic, the number of cases has decreased for most types of notifiable antibiotic resistance. However, this effect is not seen in resistance levels among clinical isolates from humans, which are relatively unaffected.
- 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. However, using selective methods, such bacteria could be isolated from 12% of caecal samples from bovines under one of age. The number of samples is, however, limited.
- $ESBL_{CARBA}$-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 were 3% lower in 2021 and were estimated at 9.7 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 2021, 230 prescriptions per 1 000 inhabitants were dispensed at pharmacies in Sweden, a decrease of 3% compared to 2020. Among the 21 regions in Sweden, 19 regions achieved the national long-term target of 250 or fewer prescriptions per 1 000 inhabitants and year. Antibiotic sales decreased in all age groups with the exception of children aged 0-4 years, where sales increased by 11.4% compared to the year before. The most substantial increase occurred during the fourth quarter of 2021, where sales of antibiotics to children increased by 143% compared to the same time period in 2020. This increase consisted primarily of antibiotics commonly used against respiratory tract infections.

The sales of antibiotics in dentistry increased by 3% in 2021, and accounted for 7% of all antibiotic prescriptions during the year. Since 2007, antibiotics prescribed by dentists have decreased by half.

Hospitals and other health and social care facilities

In 2021, the sales of antibiotics on requisition decreased with 5% to 1.3 DDD per 1 000 inhabitants per day. This includes all antibiotics sold to hospitals and other health- and social care facilities. Antibiotic sales to acute care hospitals increased during 2021, as measured both in DDD per 100 admissions and per 100 patient days, and reached its highest values in a five-year period. In particular, sales of broad-spectrum antibiotics increased, whereas sales of beta-lactamase-sensitive

penicillins and macrolides decreased. Large regional variations were observed in the use of broadspectrum antibiotics, which is consistent with previous years.

Sales of antibiotics for animals

In 2021, reported sales of antibiotics for animals were 9 129 kg, of which 57% were narrow-spectrum penicillins. The corresponding figures for 2012 were 11 385 kg and 53%, respectively. Sales of antibiotics that should be used with special restrictions (fluoroquinolones, third generation cephalosporins and polymyxins) have decreased considerably since 2012 (by 84-95%). 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 2020, a total of 53.3 tonnes of antibiotics were sold for human use and 9.0 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 79.3 and 11.8 milligrams per kilogram, respectively. Antibiotic sales for humans still dominate for all included classes of antibiotics except for aminoglycosides.

Notifiable resistance

ESBL-producing Enterobacterales (previously Enterobacteriaceae)

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

Results 2021, Enterobacterales (previously Enterobacteriaceae) with ESBL

- Number of reported cases: 7 860 (previous year 8 230), relative change –4%.
- Number of bloodstream infections: 719 (previous year 727).
- As in previous years, *Escherichia coli* was the most common species, (85%), followed by *Klebsiella pneumoniae*, (9%).
- The proportion of *E. coli* from blood cultures that are resistant to third-generation cephalosporins has decreased to 7%, from 8% in 2020.

Results 2021, Enterobacterales (previously Enterobacteriaceae) with $ESBL_{CARBA}$

- Number of reported cases: 137 (previous year 128), relative change +7%.
- Number of bloodstream infections: 7 (previous year 11).
- Among Enterobacterales (previously Enterobacteriaceae) with $ESBL_{CARBA}$, *E. coli* was the most common species, (58%) followed by *Klebsiella pneumoniae* (31%).

The proportion of *E. coli* from blood cultures resistant to meropenem was 0.1%, compared to 0% in 2020.

ESBL-producing Enterobacterales (previously Enterobacteriaceae) 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 2021, the occurrence of ESBL-producing *E. coli* in intestinal samples from pigs, cattle under one year, and broilers, as well as samples of pig and bovine meat was investigated with selective methods. Such bacteria were isolated from 1% of the intestinal samples from pigs, 12% of the intestinal samples from cattle under one year, and 1% of the intestinal samples from broilers. The number of samples from cattle under one year is however limited. Furthermore, such bacteria were isolated from <1% and 0% of bovine and pig meat of Swedish origin.

$ESBL_{CARBA}$-producing bacteria has 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/household-related infections and community-acquired infections accounted for 33% and 16% of the cases, respectively.

Results 2021

- Number of reported cases: 2 895 (previous year 3 112), relative change -7%.
- Number of bloodstream infections: 97 (previous year 98).
- The proportion of MRSA among *Staphylococcus aureus* isolated from blood has decreased to 2.0%, compared to 2.3% in 2020.

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 and cats. In horses the number of MRSA cases in 2021 (n=23) was, as in 2020 (n=27) higher than in previous years. The previous highest figure was in 2014 (n=9). The increase could partly be explained

by an outbreak in an equine hospital with eight cases. The outbreak in horses was caused by a, for horses in Sweden new *spa*-type, t034, belonging to the livestock-associated MRSA clonal complex 398. 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 2021, the number of reported cases of methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) in animals was around the same level as in previous years. In total 43 cases of MRSP were notified to the Swedish Board of Agriculture, including 41 from dogs, one from a cat and one from a horse. 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 2021

- Number of reported cases: 92 (previous year 112), relative change –17%.
- Number of bloodstream infections: 3 (previous year 4).
- The proportion of *S. pneumoniae* with reduced susceptibility to penicillin (PNSP) among bloodstream infections decreased to 6.3% from 8.3% 2020.

Vancomycin-resistant enterococci (VRE)

Results 2021

- Total number of reported cases: 209 (previous year: 79), relative change +64%.
- 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: 204 (previous year: 77), relative change +65%
- Number of reported cases of *E. faecalis* with vancomycin resistance: 1 (previous year: 4)
- There were three cases infected with both *E. faecium* and *E. faecalis*.
- Number of bloodstream infections: 2 (previous year: 4)
- Eleven clusters were reported during the year with 2-36 cases each. Out of these, five were large hospital-related outbreaks with 11-36 cases each. In 2020, eight 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.

For *Salmonella* species isolated from human faeces, the highest occurrence of resistance was to fluoroquinolones, (17%). No resistance to meropenem 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 45% and resistance to tetracycline was 17% 2021, and 1% 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 6-7%. The number of reported *E. coli* ESBL from blood was 575 cases in 2021. 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 6-7%. The number of reported *K. pneumoniae* ESBL from blood was 97 cases in 2021. As for *E. coli*, resistance to ciprofloxacin is now relatively high at, 8-11% 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 2.0% and 1.9% respectively. The number of reported MRSA from blood was 97 cases in 2021.
- *Enterococcus faecalis* and *Enterococcus faecium*: Vancomycin resistance in isolates from blood remains low (0.1% and 0.3%, respectively) and the high-level aminoglycoside resistance has gradually decreased since 2017.
- *Clostridioides difficile*: The incidence is now 61 cases per 100 000 inhabitants and has remained rather stable since 2018. No isolates were tested for antibiotic resistance in 2021.

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 penicillin resistance is common in *Staphylococcus pseudintermedius* from dogs 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, 72% and 64% respectively, were suseptible to all tested substances.

Effects of the COVID-19 pandemic

The pandemic, and the actions to handle it, have had enormous impact on the whole of society, especially on public health and the health care sector. Here we summarise and discuss these effects, and some factors contributing to them, from the point of view of antibiotic resistance and antibiotic use. This is also commented on, where relevant, in each separate section of the report.

Summary of COVID-19 during 2021

The year 2021 began with a high incidence of the alpha variant of SARS-CoV-2. The summer months were characterised by low spread of infection with levels similar to those during the summer of 2020. In the autumn of 2021, the spread of infection increased again when a new virus variant of SARS-CoV-2, the delta variant, spread in Sweden and in other parts of the world. From December, another new variant, omicron, spread rapidly and the number of cases increased sharply. Both virus variants, delta and omicron, were found to be more contagious than previous variants.

Vaccinations against COVID-19 began at the turn of the year 2020/2021, and since then the number of seriously ill and deceased from COVID-19 has gradually decreased.

In total 881 853 cases were reported 2021, and this corresponds with an incidence of 437 per 100 000 inhabitants. The mean age was 37 years, and 50% of the cases were men. During the year, 3 926 cases were admitted to intensive care, and 4 494 persons died with COVID-19. The mean age of the deceased were 80 years, and 57 % was men.

Effect in human medicine

The total sales of antibiotics continued to decrease in 2021, and were 3% lower compared to 2020 as measured in DDD per 1 000 inhabitants per day. This decrease in antibiotic sales was observed in both outpatient and inpatient, albeit to a lesser extent than during the first year of the pandemic. However, sales of antibiotics commonly used to treat respiratory tract infections started increasing from the second quarter of 2021 compared to 2020, especially in children aged 0-6 years - the same group that experienced the greatest decrease in antibiotic sales during 2020. The national long-term target of 250 or fewer antibiotic prescriptions per 1 000 inhabitants per year was achieved nationally for the first time in 2020, and this national average decreased further in 2021.

The number of cases of infections caused by the antibiotic-resistant bacteria ESBL and MRSA decreased compared to 2020, while the cases of $ESBL_{CARBA}$ were largely unchanged. All of these diseases had fewer cases compared with the year before the pandemic (2019), which may be due to reduced international travel, measures against the spread of COVID-19 and changes in health care seeking behaviour as well as healthcare delivery. Resistance proportions in clinical cultures, such as resistance in *E. coli* from blood cultures, were not affected by the pandemic.

Several outbreaks of VRE in hospitals led to an increase in the number of disease cases compared to 2020. For PNSP and *Clostridioides difficile*, the situation was stable, and no clear impact of the pandemic on these diseases can be seen.

The total number of cultures increased by 5% between 2020 and 2021. For blood cultures the increase was 4%, and for urine cultures 7%. Nasopharyngeal cultures and throat cultures continued to decrease by 23% and 17% respectively.

Recommendations issued to reduce the spread of COVID-19 have resulted in changed behaviour in the general population, which in turn has led to a reduced spread of communicable diseases in general. Also health care seeking behaviour appears to have been affected. Further, the management of the COVID-19-pandemic has forced health care to reprioritise resources, leading to, for example, cancelling or postponing some planned health care visits and elective surgeries.

The incidence of many of the surveyed communicable diseases decreased when the pandemic started, and this continued during 2021. Both respiratory infections, like influenza and respiratory syncytial virus infections, and directly travel-related infections, such as *Salmonella* and $ESBL_{CARBA}$, have been markedly affected and decreased substantially during 2020 and 2021 as compared to previous years.

Effect on veterinary medicine

Because COVID-19 is primarily a human pandemic, its consequences on animal health and veterinary medicine are less pronounced. However, in 2021 it continued to affect these sectors. Especially indirect consequences, for example due to shortage of personnel and consumables, were at times problematic.

Guidance for readers

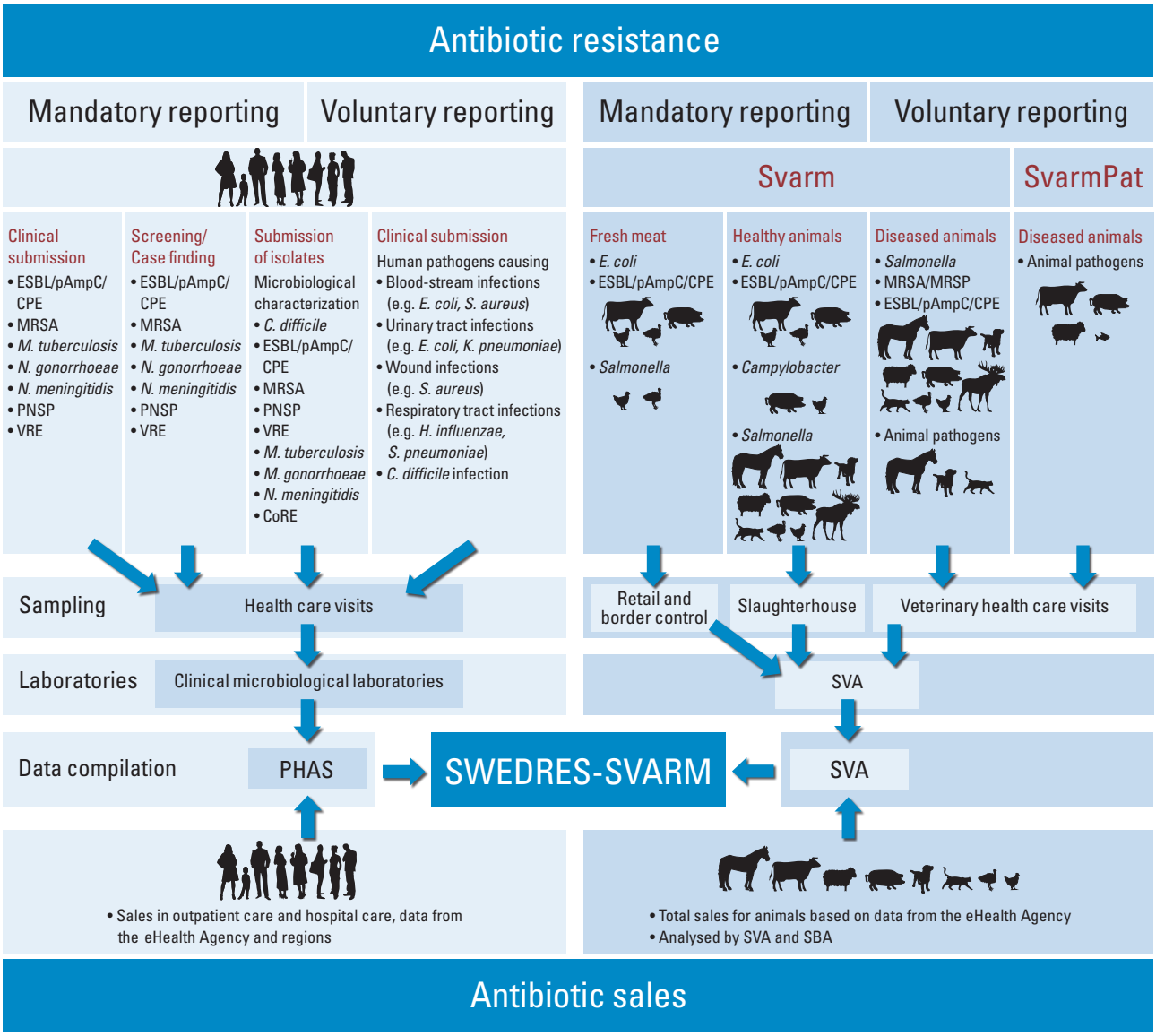
The Swedres-Svarm report is the result of a cooperation between the Public Health Agency of Sweden and the National Veterinary Institute with the aim to present data relating to both humans and animals on the sales of antibiotics and on antibiotic resistance in a joint report.

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 Background data, material, methods and references.

Schematic view of antimicrobial sales and resistance monitored in Sweden 2021.

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 health care providers from all 21 regions in Sweden and encompasses primary health care 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 for all regions with the exception of Dalarna. 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 sales of antibiotics 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, with the exception of Dalarna, 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.

Example of a table with MIC distributions.

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	Penicillin non-susceptible *Streptococcus pneumoniae*
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 following the COVID-19 pandemic. Most notably, considerable decreases were observed in prescriptions to children, especially of antibiotics commonly used for respiratory tract infections. Several factors were suggested to have contributed to the drop in sales, including decreased health care consumption in outpatient care and fewer planned surgeries, lower spread of communicable diseases, and behavioural changes in the general population in accordance with COVID-19 restrictions.

Total sales of antibiotics have continued to decrease during 2021, although to a considerable lesser extent than the year before. A breakdown of sales by quarter indicates higher sales of antibiotics in outpatient care during the second to fourth quarter compared to 2020. This increase was most noticeable for antibiotics commonly prescribed for respiratory tract infections to children. Although lower than the pre-pandemic years, sales data from the fourth quarter demonstrates that antibiotic sales are slowly moving towards the levels observed prior to 2020. The same factors that contributed to a decline in antibiotic sales during the first year of the pandemic are likely behind this increase. More social interactions, made possible by the introduction of COVID-19 vaccines, may have contributed to greater spread of communicable diseases as evidenced by surveillance data on common viral infections; surges in infections with respiratory syncytial virus and influenza virus were reported during the third and fourth quarter of 2021, while these seasonal infections were hardly detected during the previous year (Public Health Agency, 2021a and 2021b). Health care consumption have been fluctuating during the year and some sectors, such as day surgery and outpatient specialist care, have partially resumed their activities (National Board of Health and Welfare, 2022).

It is reasonable to expect an increase in antibiotic prescribing as COVID-19 restrictions are relaxed and society gradually returns to normal. However, if antibiotic sales will return to the levels observed prior to the pandemic remains to be seen. To what extent the increased antibiotic prescribing observed in outpatient care during the latter part of 2021 were appropriate cannot be elucidated from sales data alone, and merits further studies with other data sources. Continued antimicrobial stewardship efforts are needed to ensure that appropriate prescribing is maintained, especially as primary care contacts has increasingly shifted form 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 and further discussed in *Guidance for readers.*

Total sales of antibiotics

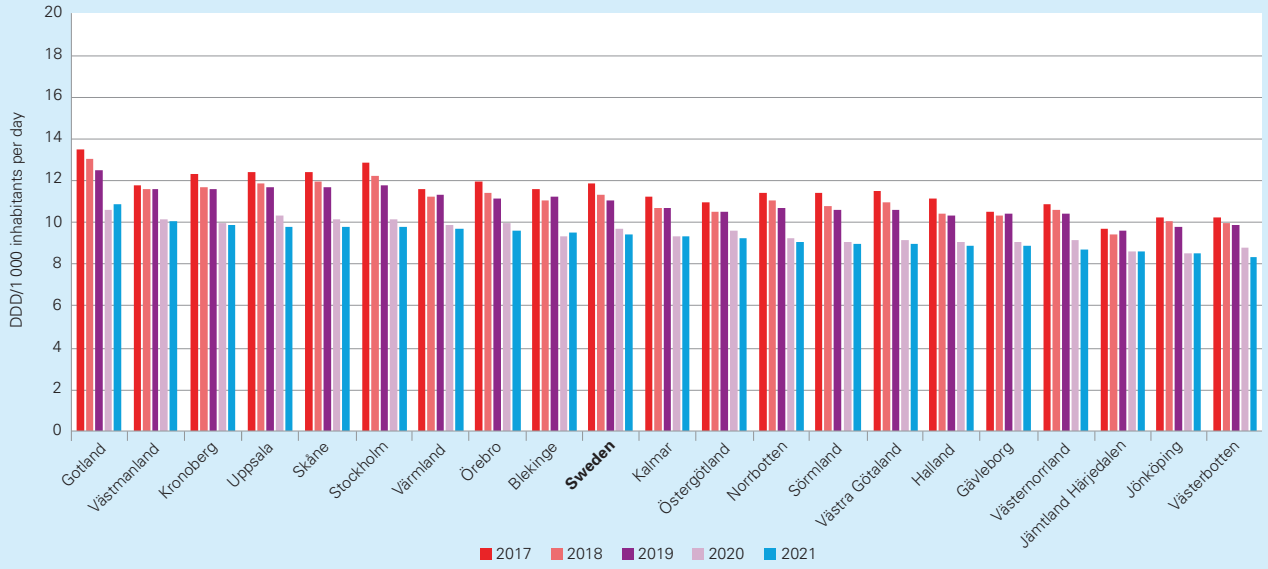
Results

- The total sales of antibiotics (J01 excl. methenamine) decreased by 2.9% compared to 2020 (from 9.7 DDD to 9.4 DDD per 1 000 inhabitants per day), Figure 1.1.
- The sales of cephalosporins continued to decrease while the sales of carbapenems and combinations of penicillins increased, Figure 1.2.
- Beta-lactamase sensitive penicillins and tetracyclines were the two most sold antibiotic classes in Sweden during 2021, despite decreased sales, Figure 1.2.
- Total sales of antibiotics varied between regions, ranging from 8.4 DDD per 1 000 inhabitants per day in Västerbotten region to 10.9 DDD per 1 000 inhabitants per day in Gotland region, Figure 1.1.

Comments

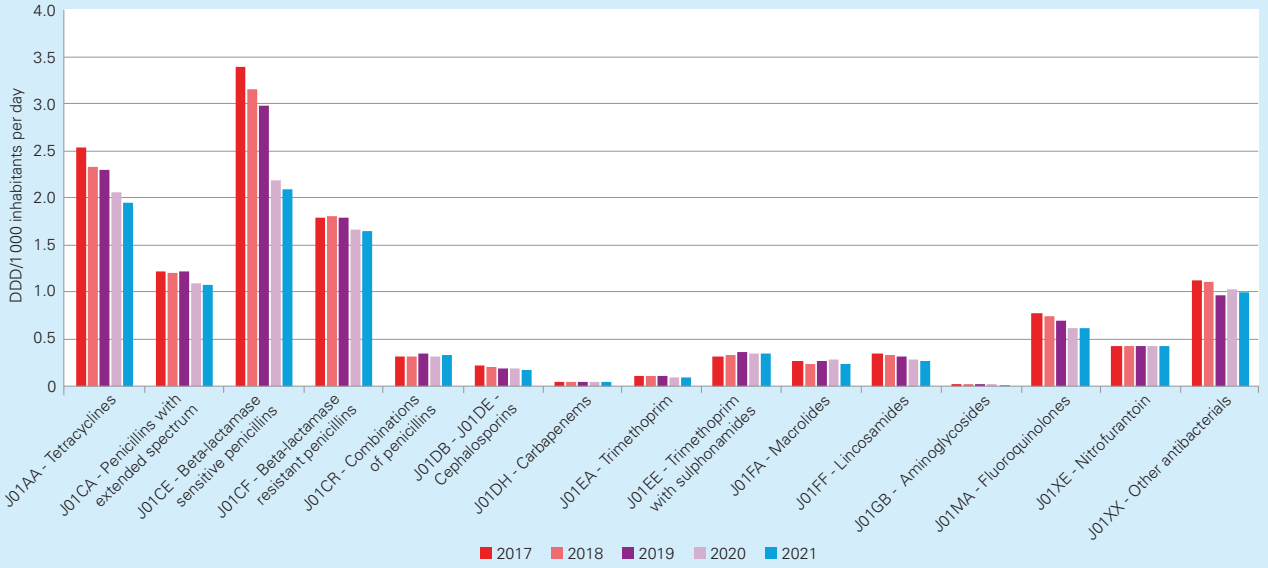
The sales of antibiotics continued to decrease in 2021, albeit to a lesser extent than the previous year. The decrease add to a continuous downward trend in Sweden. A comparison with the population-weighted mean in the EU/EEA countries from 2016-2020 (ECDC, 2021) confirms Sweden's restrictive position regarding antibiotic prescribing.

Figure 1.1. Total sales of antibiotics (J01 excl. methenamine) in 2017-2021, by region.



Source: The Public Health Agency of Sweden

Figure 1.2. Total sales of selected antibiotic classes (ATC level 4) between 2017 and 2021.



Source: The Public Health Agency of Sweden

Antibiotics in outpatient care

Total sales in outpatient care

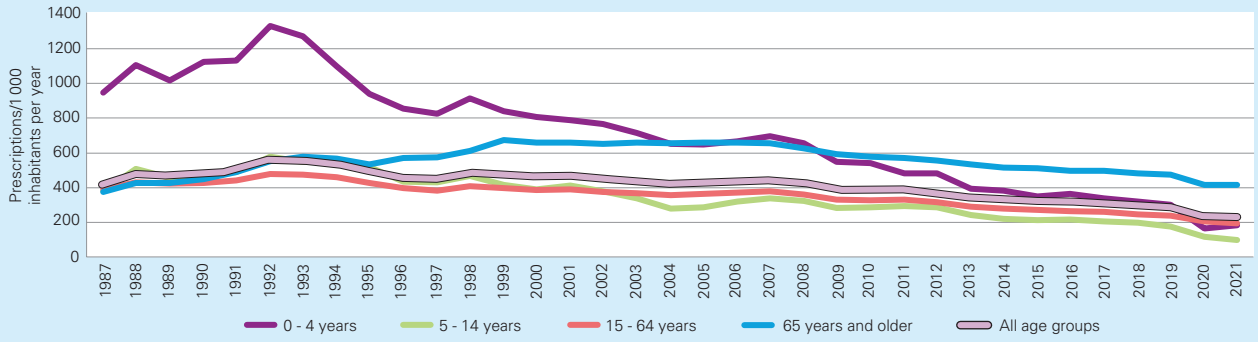
Results

- In 2021, 230 prescriptions per 1000 inhabitants were sold in Sweden – a decrease by 3.0% compared to 2020.
- Sales of antibiotics decreased for all age groups in 2021, with the exception of children aged 0-4 years where the sales increased by 11.4% compared to the year before, Figure 1.3.
- A decrease in sales were observed for most antibiotic classes in 2021, but a slight increase was observed for combinations of penicillins, cephalosporins, trimethoprim with sulphonamides, and nitrofurantoin, Figure 1.4.
- Beta-lactamase sensitive penicillins (J01CE) and beta-lactamase resistant penicillins (J01CF) were the most commonly sold antibiotics in 2021 measured in the number of prescriptions. Measured in DDD, beta-lactamase sensitive penicillins (J01CE) and tetracyclines (J01AA) were the most commonly sold antibiotics, Table 1.1.
- The number of prescriptions per 1 000 inhabitants varied between 189 in Västerbotten region to 254 in Gotland region in 2021. In 18 out of 21 regions, antibiotic sales decreased during 2021, while no difference or a slight increase in antibiotic sales were observed in the remaining three regions, Figure 1.5.
- In 2021, 13.4% of the Swedish population was treated with at least one course of antibiotics, ranging from 10.6% in Västerbotten region to 14.7% in Skåne region, Figure 1.6.

Comments

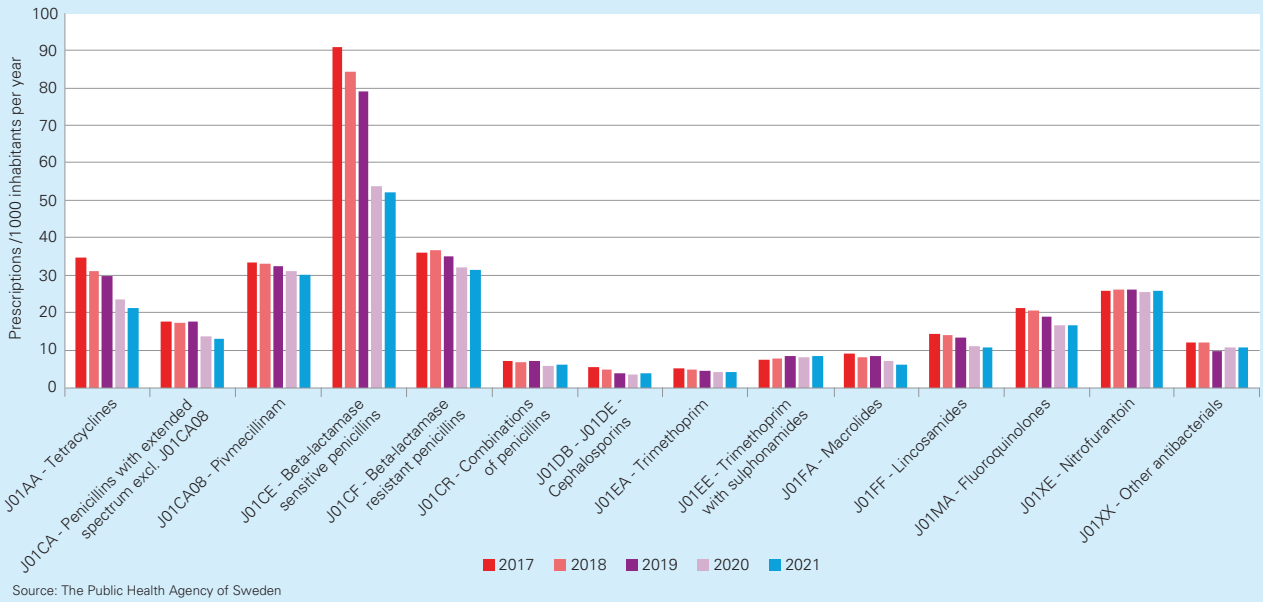
The sales of antibiotics have decreased with 59% since 1992, when the prescription of antibiotics peaked. The greatest decrease during this time period was observed in children aged 0-4 years, dropping from 1 328 prescriptions per 1 000 inhabitants in 1992 to 184 in 2021. The COVID-19 pandemic led to a steep decrease in sales of antibiotics in 2020, which was most noticeable for children aged 0-4 years. This decrease became less substantial in 2021, and for children aged 0-4 years an increase was observed during 2021.

Figure 1.3. Sales of antibiotics (J01 excl. methenamine) in outpatient care by age group in 1987-2021.



Source: The Public Health Agency of Sweden

Figure 1.4. Sales of selected antibiotic classes (ATC level 4) in outpatient care between 2017 and 2021.



Source: The Public Health Agency of Sweden

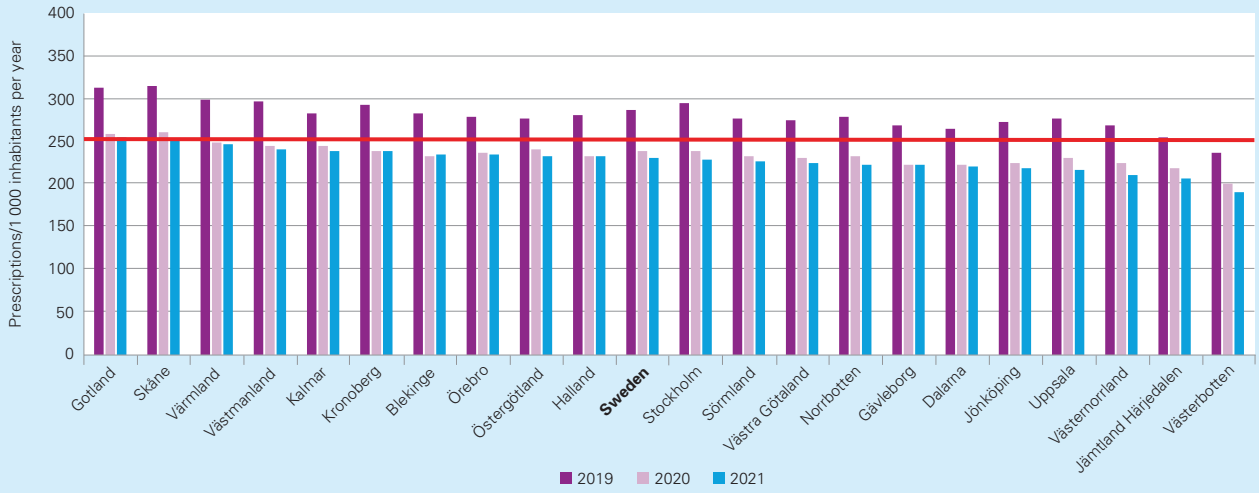
In 2018, the national annual average sales of antibiotics were below 300 prescriptions/1 000 inhabitants for the first time since national monitoring started. The trend has continued downwards and in 2020 the national long-term target of 250 prescriptions per 1 000 inhabitants per year was achieved nationally (Strama, 2016). This target was also achieved in 19 out of 21 regions in 2021. The decrease in antibiotic sales in outpatient care is, however, considerably less pronounced in 2021 compared to the previous year, and there are continued large regional variations in antibiotic prescribing.

Monthly and quarterly sales in outpatient care

Results

- During the second, third and fourth quarter of 2021, the sales of antibiotics in outpatient care increased by 3%, 7% and 15%, respectively, compared to the same quarters in 2020, Figure 1.7.
- Starting from the second quarter of 2021, sales of antibiotics commonly prescribed against respiratory tract infections (RTIs) increased. Sales of antibiotics commonly prescribed for urinary tract infections (UTIs), skin- and soft tissue infections (SSTIs) and acne hardly changed during 2020-2021, Figure 1.8.

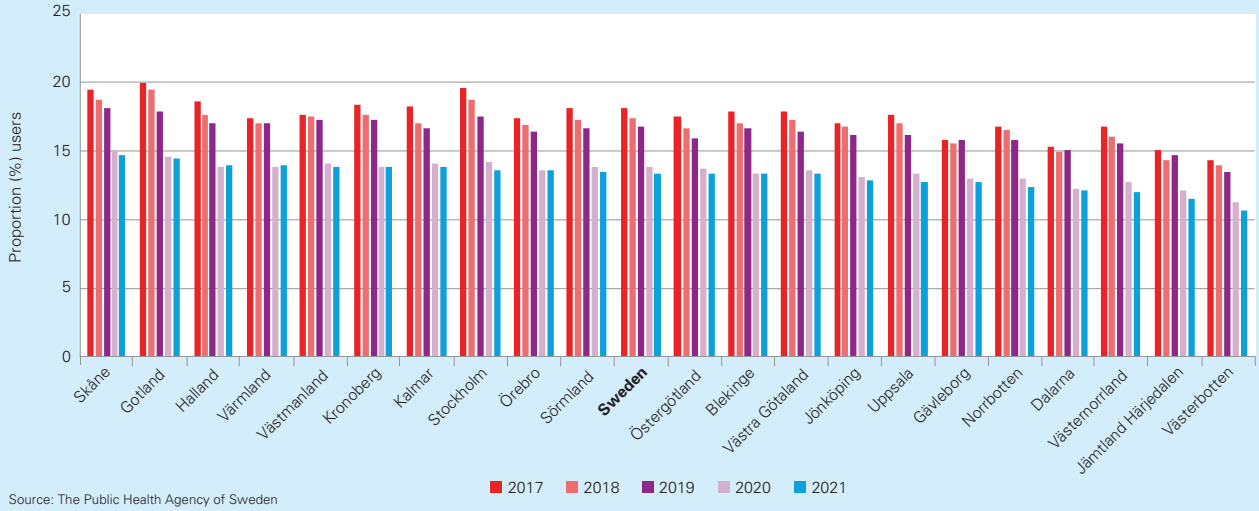
Figure 1.5. Sales of antibiotics (J01 excl. methenamine) in outpatient care in 2019-2021, by region[a].



[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. Proportion (%) of the population treated with at least one course of antibiotics (J01 excl. methenamine) in outpatient care from 2017 to 2021, by region.



Source: The Public Health Agency of Sweden

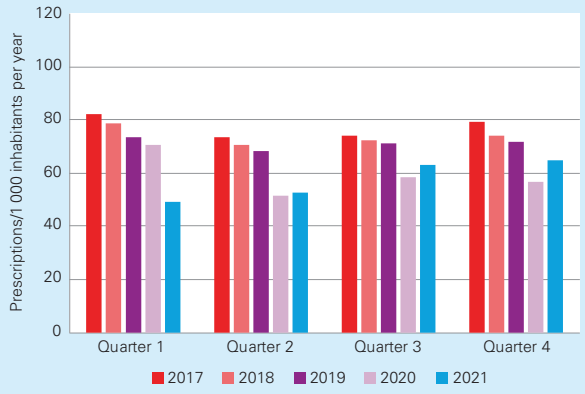
- The increase in antibiotic sales was mainly observed in children aged 0-6 years where the sales increased with 143% in the fourth quarter of 2021 compared to 2020, and reached similar levels to the pre-pandemic years. This increase is primarily reflected in the sales of antibiotics commonly prescribed against RTIs in this age group, where the sales more than doubled (233%) in the fourth quarter, Figure 1.9-1.10.

Comments

The rapidly declining sales of antibiotics observed during the first year of the COVID-19 pandemic slowed down during 2021. Over the course of the year, sales of antibiotics in outpatient care decreased by 3% compared to 2020. In contrast, sales of antibiotics in outpatient care dropped by 17% in 2020 compared to the year before. Prior to the pandemic, the annual decrease of antibiotic sales varied between 1-5%.

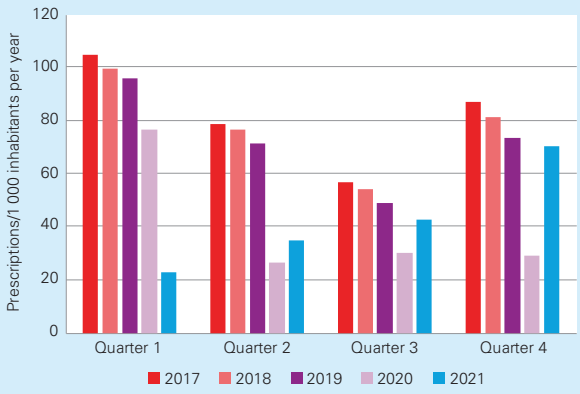
Starting from the second quarter of 2021, the sales of antibiotics gradually increased compared to the same time period in the previous year. This increase was particularly observed in children aged 0-6 years and for antibiotics commonly used to treat RTIs, which experienced the greatest decrease in antibiotic sales during 2020.

Figure 1.7. Sales of antibiotics (J01 excl. methenamine) in outpatient care from 2017 to 2021, by quarter.



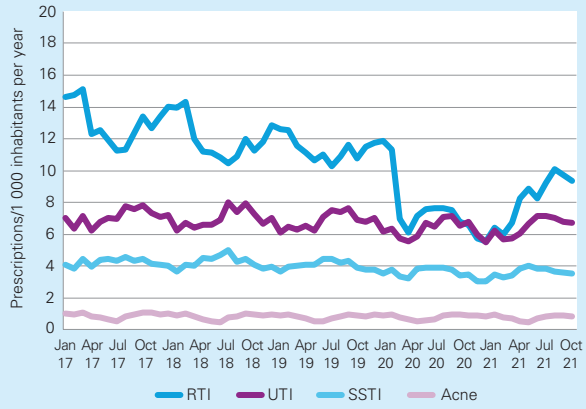
Source: The Public Health Agency of Sweden

Figure 1.9. Sales of antibiotics (J01 excl. methenamine) in children aged 0-6 years in outpatient care from 2017 to 2021, by quarter.



Source: The Public Health Agency of Sweden

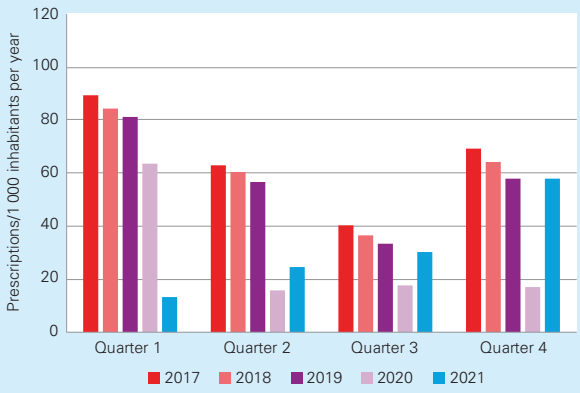
Figure 1.8. Sales of antibiotics commonly used to treat respiratory tract infections (RTI), urinary tract infections (UTI), skin and soft tissue infections (SSTI) and acne vulgaris in outpatient care from 2017 to 2021, by month[a].



[a]RTI: doxycycline (J01AA02; excluding packages larger than 50 tablets), penicillin V (J01CE02), amoxicillin (J01CA04), amoxicillin with enzyme inhibitor (J01CR02), 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 1.10. Sales of antibiotics commonly used to treat respiratory tract infections[a] in children aged 0-6 years in outpatient care from 2017 to 2021, by quarter.



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

Source: The Public Health Agency of Sweden

Table 1.1. Sales of antibiotics in outpatient care by antibiotic class or substance and age groups between 2017 and 2021.

Age groups (years)	DDD/1000 and day					Prescriptions/1000 and year					User/1000 and year				
	2017	2018	2019	2020	2021	2017	2018	2019	2020	2021	2017	2018	2019	2020	2021
Tetracyclines (J01AA)															
0-6	0.01	0.01	0.01	0.01	0.01	0.28	0.30	0.31	0.33	0.37	0.22	0.23	0.23	0.23	0.25
7-19	2.65	2.59	2.72	2.74	2.75	22.77	21.24	21.96	21.37	21.16	15.04	14.09	14.59	14.12	13.99
20-64	2.47	2.26	2.21	2.01	1.92	35.75	32.00	30.47	24.98	22.51	27.84	25.09	23.98	19.11	17.11
65-79	2.82	2.54	2.44	1.82	1.62	54.90	49.12	45.74	30.26	25.40	42.27	38.10	35.45	22.76	19.28
80-	2.05	1.90	1.80	1.29	1.18	46.88	42.47	40.11	25.96	21.70	37.41	34.25	32.19	19.93	16.55
All age groups	2.35	2.16	2.14	1.92	1.84	34.59	31.06	29.69	23.50	21.24	26.27	23.77	22.72	34.78	31.13
Penicillins with extended spectrum (J01CA) excl. pivmecillinam (J01CA08)															
0-6	0.63	0.65	0.61	0.30	0.33	37.56	38.73	35.82	17.58	19.78	28.35	29.08	27.07	13.66	15.00
7-19	0.21	0.21	0.20	0.14	0.12	7.81	7.89	7.22	4.78	4.03	6.06	6.08	5.63	3.74	3.11
20-64	0.34	0.34	0.36	0.32	0.31	11.75	11.36	11.96	10.68	10.01	9.25	8.90	9.39	7.98	7.56
65-79	0.96	0.95	0.99	0.80	0.80	31.02	30.01	30.71	23.43	22.89	24.11	23.14	23.67	17.48	17.24
80-	1.24	1.23	1.36	1.11	1.17	37.65	37.04	39.09	29.93	30.75	29.99	29.45	30.54	22.89	23.44
All age groups	0.49	0.49	0.51	0.41	0.41	17.69	17.34	17.70	13.53	13.12	13.63	13.31	13.49	19.98	19.53
Pivmecillinam (J01CA08)															
0-6	0.02	0.02	0.02	0.02	0.02	1.42	1.71	1.60	1.34	1.28	1.28	1.56	1.47	1.23	1.18
7-19	0.19	0.19	0.18	0.18	0.15	12.89	12.71	12.36	12.00	10.53	11.24	11.13	10.86	10.49	9.30
20-64	0.47	0.46	0.45	0.43	0.41	29.12	28.80	28.30	27.21	25.65	24.04	23.84	23.57	22.61	21.42
65-79	1.00	1.00	0.98	0.92	0.93	58.28	58.31	56.68	53.66	53.58	43.27	43.37	42.26	40.02	40.13
80-	1.92	1.92	1.90	1.86	1.88	113.02	112.75	111.29	107.57	108.15	81.04	80.78	80.17	76.62	76.70
All age groups	0.55	0.54	0.53	0.51	0.49	33.33	33.07	32.42	31.07	30.06	25.99	25.87	25.48	48.82	47.24
Beta-lactamase sensitive penicillins (J01CE)															
0-6	2.68	2.53	2.33	1.13	1.23	196.07	185.01	171.14	82.12	89.98	147.11	139.97	130.92	66.45	71.44
7-19	2.63	2.43	2.20	1.34	1.13	92.47	86.04	76.35	45.35	36.58	73.43	68.72	61.39	36.91	29.64
20-64	3.17	2.93	2.76	2.06	1.98	75.78	70.27	66.47	49.11	47.15	64.67	59.89	56.69	41.97	40.18
65-79	3.61	3.36	3.26	2.63	2.70	83.98	77.92	75.51	59.59	61.09	70.50	65.60	63.41	49.70	51.05
80-	3.10	3.05	2.97	2.38	2.42	74.34	72.69	70.74	55.00	55.13	63.46	62.12	59.69	45.68	46.03
All age groups	3.15	2.93	2.76	1.99	1.94	90.77	84.43	79.09	53.58	52.01	73.67	68.84	64.71	89.12	86.09
Beta-lactamase resistant penicillins (J01CF)															
0-6	0.27	0.28	0.24	0.19	0.16	27.26	28.35	24.06	18.62	15.91	21.61	22.27	18.94	14.54	12.09
7-19	0.72	0.73	0.72	0.62	0.60	25.20	26.24	24.97	21.25	20.28	20.04	20.95	19.88	16.72	15.90
20-64	1.21	1.22	1.20	1.11	1.07	29.57	29.98	29.14	27.16	26.24	23.43	23.87	23.14	21.30	20.72
65-79	2.54	2.60	2.54	2.42	2.41	51.95	53.19	51.03	47.93	47.51	34.39	35.67	33.92	31.22	31.40
80-	5.23	5.21	5.13	4.89	5.06	99.14	98.77	94.99	90.41	92.84	59.86	60.88	58.73	54.89	56.56
All age groups	1.48	1.49	1.46	1.36	1.34	36.05	36.61	35.06	32.18	31.41	26.25	26.92	25.71	46.53	45.51
Combinations of penicillins (J01CR)															
0-6	0.13	0.10	0.12	0.08	0.08	12.85	9.25	10.98	6.98	6.85	7.68	5.70	6.45	3.87	3.94
7-19	0.11	0.11	0.11	0.08	0.08	4.76	4.07	4.42	3.32	3.18	2.81	2.56	2.56	1.90	1.86
20-64	0.18	0.19	0.19	0.16	0.17	5.59	5.71	5.80	4.99	5.13	4.45	4.54	4.66	3.96	4.11
65-79	0.33	0.35	0.38	0.33	0.33	9.90	9.96	10.57	9.08	9.06	7.15	7.23	7.57	6.27	6.27
80-	0.35	0.39	0.42	0.41	0.45	10.14	10.97	12.19	11.23	12.16	7.46	8.03	9.01	7.80	8.34
All age groups	0.20	0.21	0.22	0.18	0.19	7.02	6.72	7.12	5.87	5.98	5.03	4.92	5.15	8.36	8.60
Cephalosporins (J01DB-DE)															
0-6	0.03	0.01	0.01	0.01	0.03	2.94	1.03	0.74	1.99	4.80	2.55	0.81	0.54	1.63	3.89
7-19	0.05	0.04	0.03	0.02	0.02	3.73	2.62	1.84	1.46	1.68	3.11	2.20	1.53	1.21	1.31
20-64	0.08	0.07	0.06	0.05	0.05	5.09	4.61	3.82	3.36	3.26	4.09	3.71	3.01	2.66	2.55
65-79	0.12	0.10	0.09	0.08	0.08	7.48	6.67	5.83	5.30	5.09	5.57	4.92	4.20	3.78	3.68
80-	0.21	0.19	0.16	0.14	0.15	13.61	12.54	10.54	9.79	10.27	10.39	9.65	8.15	7.33	7.53
All age groups	0.08	0.07	0.06	0.05	0.05	5.55	4.76	3.94	3.61	3.82	4.36	3.72	3.02	5.54	5.80

Age groups (years)	DDD/1000 and day					Prescriptions/1000 and year					User/1000 and year				
	2017	2018	2019	2020	2021	2017	2018	2019	2020	2021	2017	2018	2019	2020	2021
Trimethoprim (J01EA)															
0-6	0.06	0.06	0.05	0.04	0.04	7.80	8.22	7.00	6.16	6.12	5.80	6.15	5.22	4.44	4.11
7-19	0.03	0.03	0.02	0.02	0.02	1.87	1.73	1.50	1.40	1.26	1.39	1.29	1.14	1.01	0.87
20-64	0.06	0.06	0.05	0.05	0.05	2.22	2.02	1.88	1.75	1.59	1.65	1.49	1.37	1.25	1.12
65-79	0.24	0.23	0.22	0.21	0.21	8.95	8.26	8.36	7.99	7.97	5.91	5.57	5.55	4.88	4.81
80-	0.58	0.54	0.55	0.52	0.53	28.37	26.38	27.70	26.63	27.08	12.92	12.36	12.78	11.76	11.34
All age groups	0.11	0.10	0.10	0.09	0.09	4.98	4.67	4.54	4.29	4.21	3.16	3.00	2.86	5.12	4.82
Trimethoprim with sulphonamides (J01EE)															
0-6	0.09	0.09	0.09	0.08	0.07	10.32	10.96	10.12	8.91	8.34	6.60	7.03	6.46	5.12	4.64
7-19	0.11	0.11	0.11	0.10	0.10	4.62	4.77	4.72	4.26	3.89	2.25	2.29	2.22	1.95	1.76
20-64	0.20	0.21	0.22	0.20	0.20	5.11	5.32	5.67	5.49	5.44	2.78	2.89	3.15	2.90	2.92
65-79	0.62	0.67	0.73	0.69	0.71	14.53	15.57	17.82	17.66	18.13	9.23	9.81	11.15	10.57	10.83
80-	0.54	0.62	0.74	0.70	0.77	14.92	16.74	20.87	20.22	22.01	10.68	11.51	13.84	13.05	14.40
All age groups	0.26	0.28	0.30	0.28	0.28	7.44	7.86	8.55	8.22	8.27	4.37	4.61	5.01	9.21	9.33
Macrolides (J01FA)															
0-6	0.26	0.24	0.19	0.10	0.10	12.45	11.55	9.89	5.41	5.16	9.54	8.61	7.23	3.52	3.23
7-19	0.22	0.19	0.18	0.15	0.12	9.35	7.79	7.06	5.40	3.88	6.49	5.13	4.71	3.14	2.12
20-64	0.21	0.19	0.23	0.24	0.22	8.23	7.48	7.86	7.04	6.14	6.30	5.66	6.10	5.41	4.71
65-79	0.32	0.28	0.35	0.38	0.35	9.04	8.33	9.18	8.71	7.53	5.65	4.98	5.80	5.20	4.65
80-	0.22	0.21	0.27	0.31	0.29	6.61	6.40	7.63	7.45	6.80	4.45	3.87	4.91	4.63	4.41
All age groups	0.24	0.22	0.25	0.25	0.22	9.19	8.16	8.35	7.15	6.11	6.41	5.63	5.88	9.69	8.35
Lincosamides (J01FF)															
0-6	0.04	0.03	0.04	0.01	0.01	7.66	7.07	7.76	3.21	2.19	5.70	5.40	6.01	2.32	1.59
7-19	0.12	0.11	0.11	0.09	0.08	7.72	7.37	7.26	5.26	4.30	6.00	5.75	5.61	4.06	3.25
20-64	0.29	0.28	0.26	0.23	0.21	13.64	13.06	12.34	10.61	9.99	10.80	10.28	9.78	8.25	7.69
65-79	0.56	0.53	0.48	0.45	0.43	21.94	21.39	19.54	17.81	17.65	15.10	14.56	13.51	12.03	12.06
80-	0.75	0.72	0.71	0.66	0.66	29.99	29.39	28.37	26.19	27.27	18.48	18.15	17.62	16.09	16.59
All age groups	0.31	0.30	0.28	0.25	0.23	14.48	13.90	13.20	11.16	10.62	10.70	10.24	9.80	16.19	15.28
Fluoroquinolones (J01MA)															
0-6	0.02	0.02	0.02	0.02	0.02	0.98	1.09	0.99	1.00	1.05	0.55	0.64	0.60	0.48	0.49
7-19	0.10	0.09	0.10	0.08	0.08	3.47	3.30	3.27	2.92	2.63	2.69	2.56	2.52	2.21	1.97
20-64	0.52	0.49	0.45	0.38	0.37	16.78	16.07	14.71	12.68	12.25	12.24	11.69	10.71	9.13	8.80
65-79	1.47	1.41	1.31	1.15	1.16	49.97	48.17	44.49	39.53	39.30	33.97	32.59	30.15	26.55	26.37
80-	1.82	1.83	1.70	1.55	1.61	67.28	67.51	62.76	57.10	58.84	47.22	46.72	43.38	39.12	40.65
All age groups	0.63	0.60	0.56	0.49	0.48	21.20	20.49	18.93	16.65	16.47	14.84	14.28	13.19	23.03	22.75
Nitrofurantoin (J01XE)															
0-6	0.06	0.07	0.07	0.06	0.06	8.04	7.49	8.66	8.50	8.33	6.11	6.11	6.80	6.47	6.36
7-19	0.12	0.11	0.11	0.10	0.10	9.21	8.71	8.85	8.35	7.94	7.83	7.41	7.50	7.10	6.67
20-64	0.32	0.33	0.32	0.32	0.32	21.51	21.86	21.70	21.40	21.78	17.22	17.45	17.29	17.00	17.32
65-79	0.78	0.80	0.81	0.78	0.78	45.72	46.23	46.58	44.10	44.10	32.42	32.53	32.29	30.47	30.56
80-	1.44	1.46	1.49	1.47	1.52	90.38	91.64	93.85	92.56	95.32	53.66	53.61	54.07	50.85	50.82
All age groups	0.40	0.40	0.41	0.40	0.40	25.86	26.02	26.24	25.56	25.93	19.01	19.08	19.05	36.80	37.09
All agents (J01 excl. methenamine)															
0-6	4.30	4.13	3.80	2.06	2.18	325.85	310.94	289.25	162.33	170.34	200.20	193.33	181.09	105.93	109.35
7-19	7.29	6.97	6.83	5.69	5.38	206.47	194.98	182.28	137.85	121.95	133.58	127.80	118.96	89.34	79.00
20-64	9.54	9.04	8.78	7.59	7.30	260.87	249.19	240.72	207.10	197.78	164.83	158.05	152.70	130.27	125.67
65-79	15.44	14.88	14.62	12.73	12.55	449.06	434.48	423.12	366.17	360.52	236.19	228.14	221.15	189.67	189.07
80-	19.50	19.32	19.25	17.33	17.75	634.08	626.87	621.40	561.21	569.77	301.50	298.15	293.00	258.98	261.18
All age groups	10.28	9.81	9.58	8.20	8.01	308.95	295.86	285.50	237.08	229.94	180.70	173.97	167.30	275.17	267.62

Antibiotics commonly used to treat respiratory tract infections and urinary tract infections

Respiratory tract infections (RTIs)

Results

- Overall sales of antibiotics commonly prescribed against RTIs decreased by 4.9% in 2021 compared to 2020.
- Beta-lactamase sensitive penicillins (J01CE), was the most frequently prescribed antibiotic in outpatient care in 2021, and decreased by 2.9% compared to 2020, Figure 1.11.
- The greatest relative decrease in 2021 was observed for doxycycline (J01AA02) and macrolides (J01FA), i.e. 15.0% and 14.5% respectively compared to 2020.

Comments

The recommended first-line treatment for lower RTIs in Sweden is beta-lactamase sensitive penicillin (J01CE) (Medical Products Agency, 2008). In 2021 the sales of antibiotics commonly used to treat RTIs were lower than in 2020, except for amoxicillin with enzyme inhibitor (J01CR02) and cephalosporines (J01DB-DE). 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 slight increase since 2019.

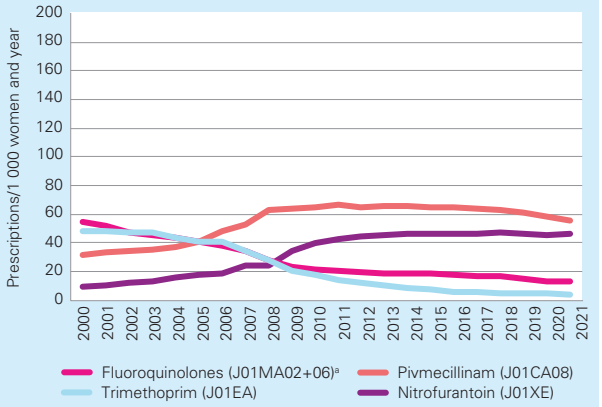
Shortages of specific antibiotics may impact the patterns of antibiotic sales, possibly resulting in prescription of broader spectrum antibiotics. Especially oral solutions commonly prescribed to children have been particularly exposed to shortages. In 2021, shortages were observed for erythromycin and some penicillins and cephalosporins in Sweden, and there was a notable decrease in sales of erythromycin compared to previous years.

Urinary tract infections (UTIs)

Results

- Total sales of antibiotics commonly used to treat UTIs decreased by 2.2% in 2021 among women aged 15-79. Sales of pivmecillinam (J01CA08) and trimethoprim (J01EA) decreased by 5.0% and 4.7%, respectively, whereas nitrofurantoin (J01XE) increased by 1.3%, Figure 1.12.
- In men aged 65 or older, the sales of antibiotics against UTIs increased by 1.7% in 2021 compared to 2020. The greatest relative change was observed for trimethoprim with sulphonamides (J01EE), which increased by 5.4%, Figure 1.13.
- At the national level, 9.5% of the antibiotics commonly prescribed for UTIs in women aged 15-79 consisted of ciprofloxacin in 2021. This proportion ranged from 7.3% in Jönköping region to 12.8% in Västmanland region, Figure 1.14.

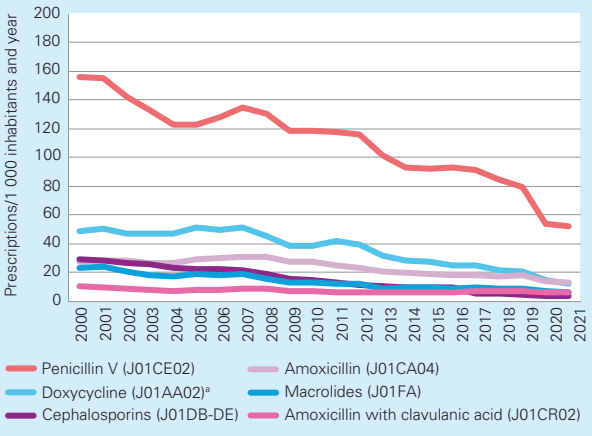
Figure 1.12. Sales of antibiotics commonly used to treat urinary tract infections in women aged 15-79 years in outpatient care between 2000 and 2021.



aFrom 2021 only ciprofloxacin (J01MA02) is included in fluoroquinolones

Source: The Public Health Agency of Sweden

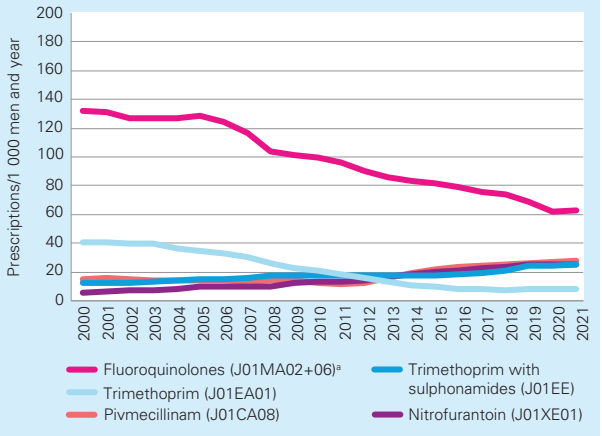
Figure 1.11. Sales of antibiotics commonly used to treat respiratory tract infections in outpatient care between 2000 and 2021.



aDoxycycline (J01AA02) excl. packages with more than 50 tablets.

Source: The Public Health Agency of Sweden

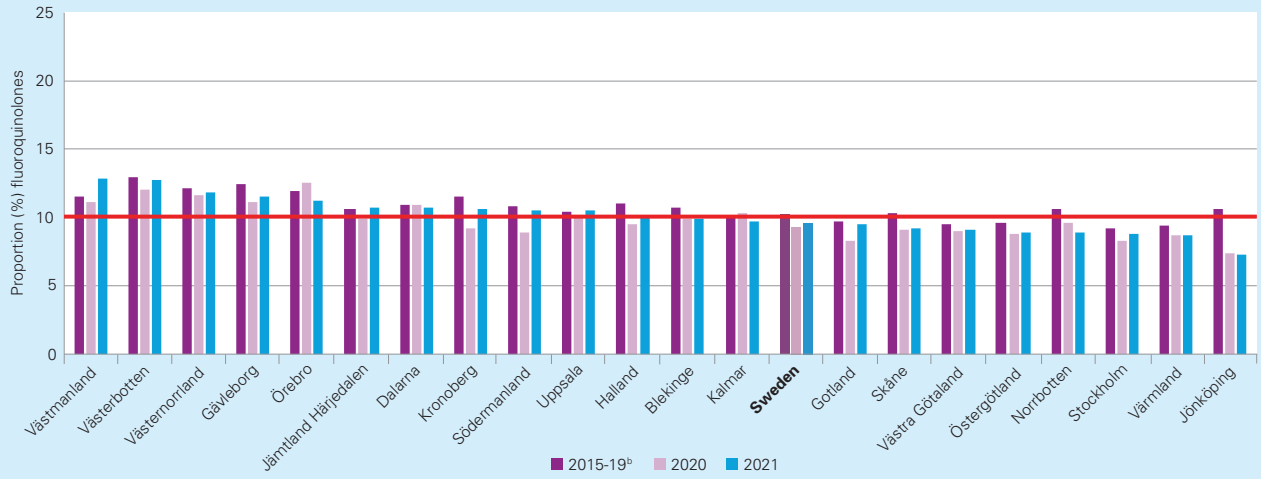
Figure 1.13. Sales of antibiotics commonly used to treat urinary tract infections in men aged 65 years or older in outpatient care between 2000 and 2021.



aFrom 2021 only ciprofloxacin (J01MA02) is included in fluoroquinolones

Source: The Public Health Agency of Sweden

Figure 1.14. 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 2021, by region.



[a]Pivmecillinam (J01CA08), trimethoprim (J01EA01), ciprofloxacin (J01MA02), norfloxacin (J01MA06) until 2020, and nitrofurantoin (J01XE01).
[b]Average 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

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 2021 consisted of these two antibiotics. In men aged 65 or older, flouoroquinolones made up 42% of the UTI antibiotics in 2021, but trend analysis indicate decreasing sales of fluoroquinolones and increasing sales of pivmecillinam and nitrofurantoin since ten or more years in this population. Note that since 2021, norfloxacin (J01MA06) has been removed from the market and only ciprofloxacin (J01MA02) is included among the fluoroquinolones.

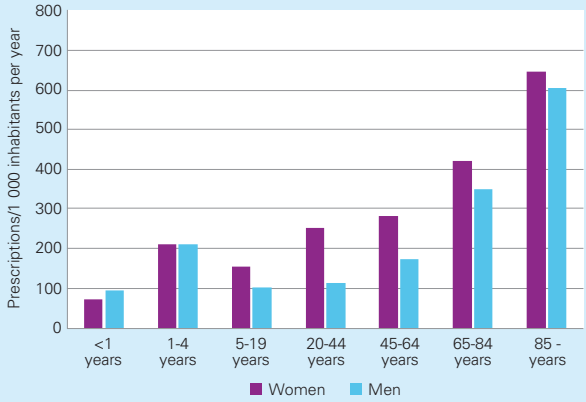
Strama has proposed a number of quality indicators in outpatient care; one of them being that maximum 10% of antibiotics prescribed for UTIs in women aged 18-79 years consists of fluoroquinolones (Strama, 2016). This target was achieved at the national level and by 10 out of 21 regions in 2021, which is a decrease compared to 2020 when 14 out of 21 regions achieved this target.

Age and gender comparisons

Results

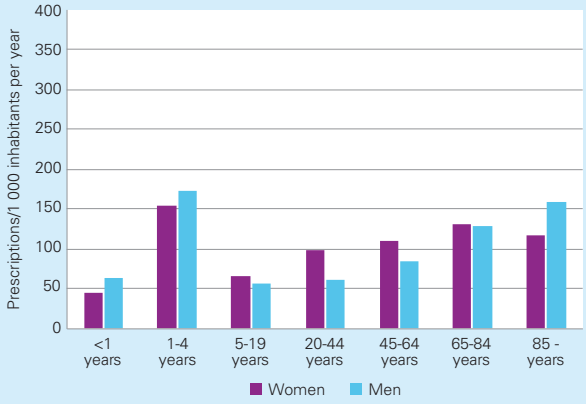
- The rate of antibiotic prescriptions in outpatient care were highest for people aged 85 years or older; 643 prescriptions per 1 000 inhabitants in women and 603 prescriptions per 1 000 inhabitants in men in 2021, Figure 1.15. 61% of all antibiotic prescriptions during 2021 were issued to women.
- The most frequently prescribed antibiotics to children aged 0-4 were antibiotics commonly used to treat RTIs, representing 78% of the total antibiotic sales in this age group. RTI antibiotics were prescribed more to women than to men, except in the youngest and the oldest age groups, Figure 1.16.

Figure 1.15. Sales of antibiotics (J01 excl. methenamine) in outpatient care in 2021, by age and gender.



Source: The Public Health Agency of Sweden

Figure 1.16. Sales of antibiotics commonly used to treat respiratory tract infections (RTIs)[a] in outpatient care in 2021, 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), and macrolides (J01FA)

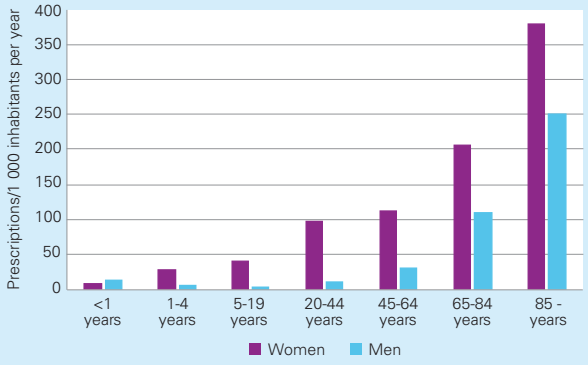
Source: The Public Health Agency of Sweden

- Antibiotics commonly used to treat UTIs are mostly prescribed to women, and the prescription rate increases with higher age, Figure 1.17.
- Sales of antibiotics commonly used to treat SSTIs were highest for the oldest age groups, and the prescriptions to men exceeds that of women in these age groups, Figure 1.18.
- Antibiotics commonly used to treat acne are mainly used in the age groups 5-44 years and predominately by women, Figure 1.19. 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 use of antibiotics is highest in the oldest age group. As mentioned in the *Guidance for readers*, parts 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 data. Therefore a possible underestimation in the oldest age groups cannot be ruled out.

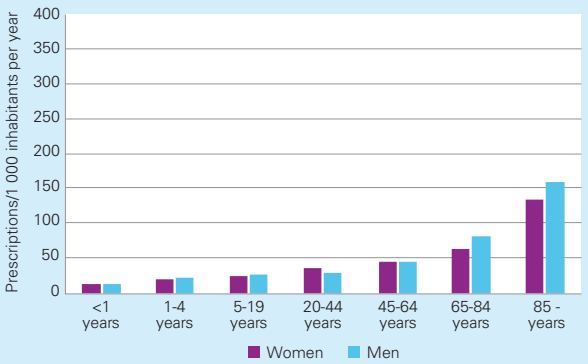
Figure 1.17. Sales of antibiotics commonly used to treat urinary tract infections[a] in outpatient care in 2021, by age and gender.



[a]Pivmecillinam (J01CA08), trimethoprim (J01EA01), ciprofloxacin (J01MA02), norfloxacin (J01MA06) until 2020, and nitrofurantoin (J01XE01)

Source: The Public Health Agency of Sweden

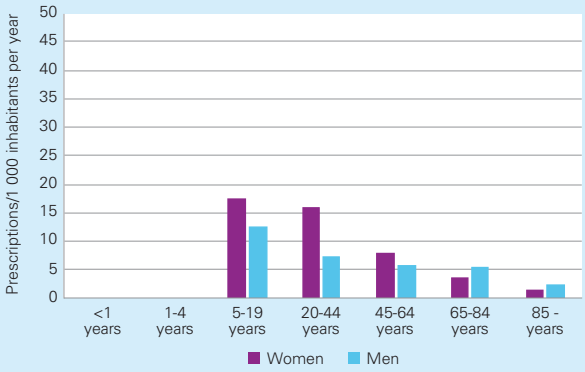
Figure 1.18. Sales of antibiotics commonly used to treat skin and soft tissue infections[a] in outpatient care in 2021, by age and gender.



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

Source: The Public Health Agency of Sweden

Figure 1.19. Sales of antibiotics commonly used to treat acne vulgaris[a] in outpatient care in 2021, by age and gender.



[a]Doxycycline (J01AA02; packages over 50 tablets), lymecycline (J01AA04), oxytetracycline (J01AA06) and tetracycline (J01AA07)

Source: The Public Health Agency of Sweden

Antibiotic sales in children

Results

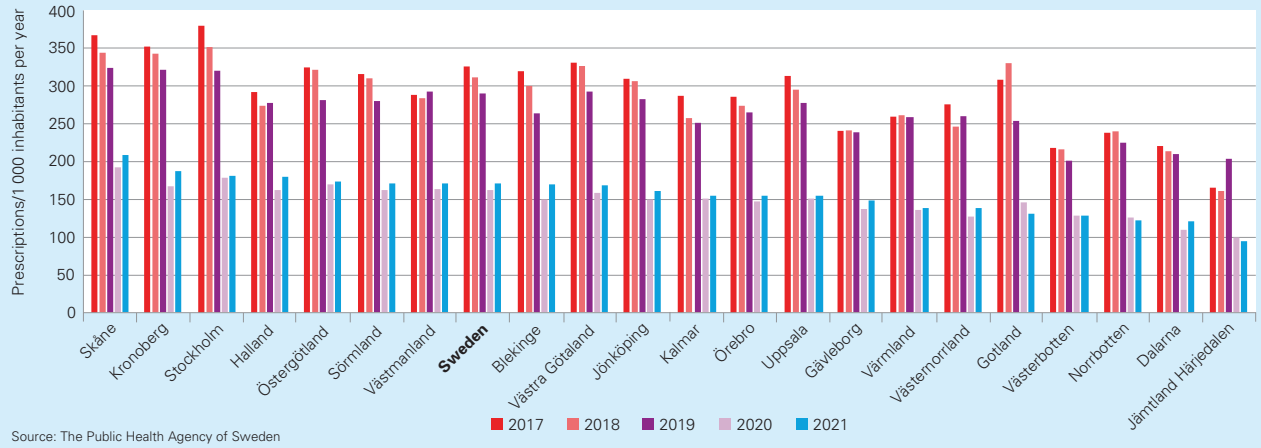
- Sales of antibiotics for children aged 0-6 years were 4.9% higher in 2021 than in 2020.
- The sales of antibiotics for children aged 0-6 years increased in 17 out of 21 regions in Sweden. There were large variations between regions; from 209 prescriptions per 1 000 children in Skåne region to 95 in Jämtland Härjedalen region in 2021, Figure 1.20.
- The most sold antibiotic for children aged 0-6 years was beta-lactamase sensitive penicillin (J01CE), which constituted 53% of the sales, Table 1.1.
- The proportion of children aged 0-6 years treated with at least one course of antibiotics increased in 2021 compared to 2020 and was estimated to 11%, Figure 1.21.
- At the national level, 72% of antibiotics commonly prescribed against RTIs in children aged 0-6 consisted of penicillin V. This proportion ranged from 62% in Gotland region to 80% in Jämtland Härjedalen region, Figure 1.22.

Comments

While sales of antibiotics to children aged 0-6 years have increased in most regions in Sweden during 2021 compared to 2020, the prescriptions rates are well below the levels observed prior to the COVID-19 pandemic.

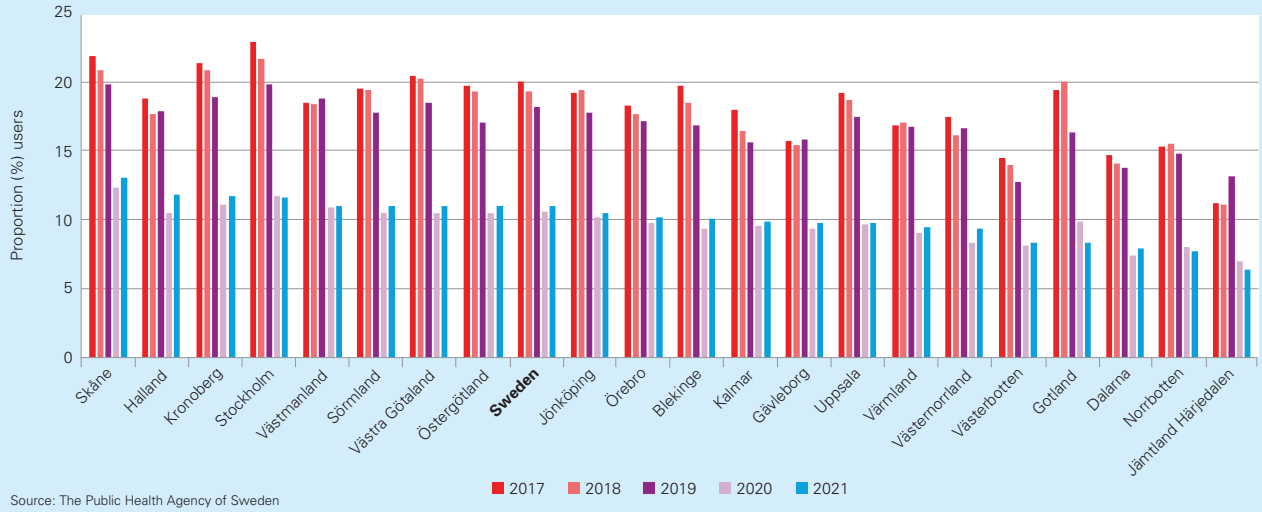
According to Strama's proposed quality indicator for outpatient care, 80% of antibiotics prescribed for RTIs in children aged 0-6 years should consist of penicillin V (Strama, 2016). To calculate this indicator, the following antibiotics are included in the denominator: amoxicillin (J01CA04), penicillin V (J01CE02), amoxicillin with clavulanic acid (J01CR02), cephalosporins (J01DB-DE excl. ceftibuten J01DD14) and macrolides (J01FA). In 2021, 2 out of 21 regions achieved this target, but it is yet to be achieved at the national level.

Figure 1.20. Sales of antibiotics (J01 excl. methenamine) to children aged 0-6 years in outpatient care between 2017 and 2021, by region.



Source: The Public Health Agency of Sweden

Figure 1.21. Proportion (%) of children aged 0-6 years treated with at least one course of antibiotics (J01 excl. methenamine) in outpatient care between 2017 and 2021, by region.



Source: The Public Health Agency of Sweden

Figure 1.22 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 2021, by region.

[a]Doxycycline (J01AA02; excluding packages larger than 50 tablets), penicillin V (J01CE02), amoxicillin (J01CA04), amoxicillin with enzyme inhibitor (J01CR02), cephalosporins (J01DB-DE), and macrolides (J01FA). [b]Average proportion is presented for the time period 2015-19. The red line indicates Strama's target of at least 80% penicillin V.

Source: The Public Health Agency of Sweden

Antibiotics in dentistry

Results

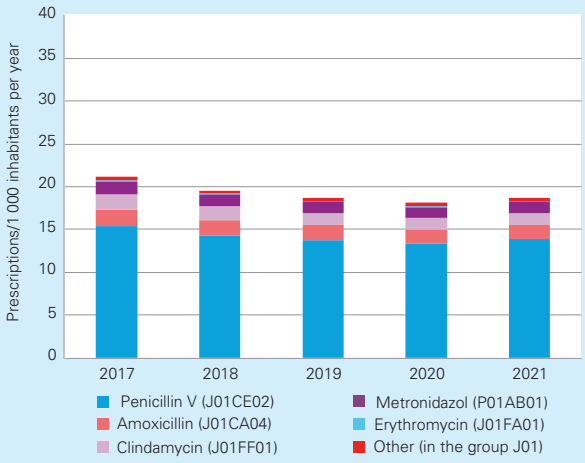
- Dentists accounted for 7.1% of all systemic antibiotics (J01 excl.methenamine) prescribed in Sweden in 2021, an increase from 6.6% in 2020.
- Antibiotics (J01 excl.methenamine; metronidazole P01AB01) prescribed by dentists in 2021 was estimated to 19 prescriptions per 1 000 inhabitants, an increase by 3.0% compared to the year before, Figure 1.23.
- The most commonly prescribed antibiotic by dentists was penicillin V (74% of total sales), Figure 1.23. Compared to 2020, the sales of amoxicillin and penicillin V increased by 7.1% and 3.8%, respectively, whereas the sales of other antibiotics decreased.
- Sales of antibiotics increased in 16 of 21 regions during 2021. There were notable regional differences; dentists in Skåne region issued 24 prescriptions per 1 000 inhabitants, twice as many as dentists in Västerbotten region who prescribed the least (11 prescriptions per 1 000 inhabitants), Figure 1.24.
- The increase in prescribing was most prominent in the population aged 65 years and older. Most antibiotics were prescribed in the age group 65-84 years, followed by the age group 45-64 years, Figure 1.25.

Comments

The decrease in prescribing of antibiotics observed between 2019 and 2020 seems to have resumed in 2021. This increase is most clearly observed in the oldest age groups; in fact, the number of antibiotic prescriptions issued by dentists to the population aged 85 years or older in 2021 exceeded the estimates from 2019. The decline in antibiotic prescriptions observed in 2020 may be the result of fewer dental care visits, especially among the elderly (National Board of Health and Welfare, 2020a). It is possible that this decline has started to resume in 2021.

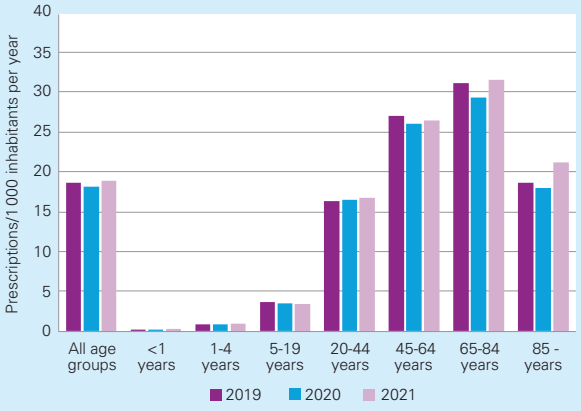
Penicillin V was the most commonly prescribed antibiotic by dentists and made up 74% of the total sales, which is in line with treatment recommendations (Medical Products Agency, 2014). In combination with or as a complement to penicillin V, metronidazole is also recommended as first-line treatment to attain a broader anaerobic spectrum; metronidazole is therefore included in the measure of sales.

Figure 1.23. Antibiotics prescribed by dentists in outpatient care between 2017 and 2021.



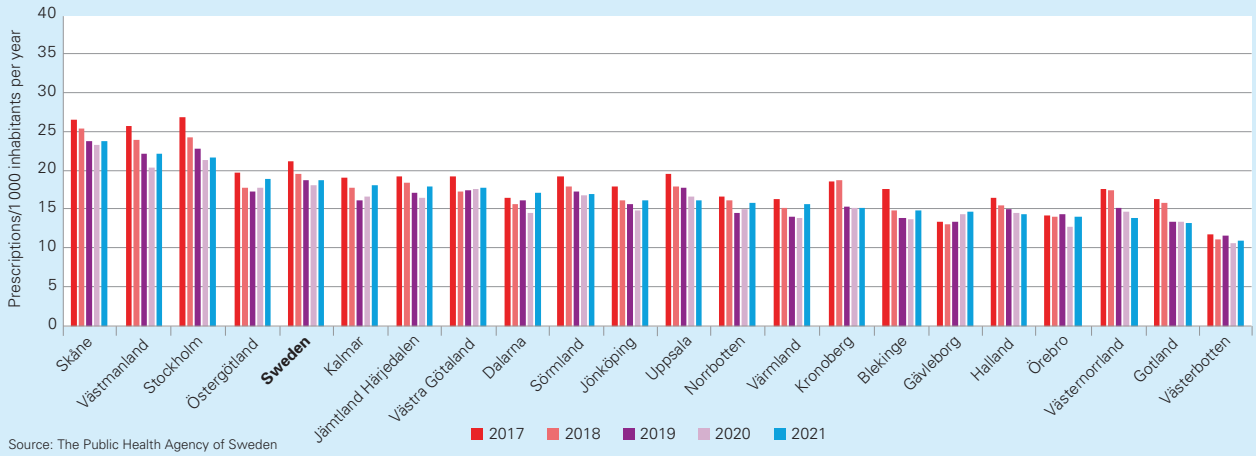
Source: The Public Health Agency of Sweden

Figure 1.25. Antibiotics (J01 incl. methenamine; metronidazole P01AB01) prescribed by dentists in outpatient care between 2019 and 2021, by age group.



Source: The Public Health Agency of Sweden

Figure 1.24. Antibiotics (J01 incl. methenamine; metronidazole P01AB01) prescribed by dentists in outpatient care between 2017 and 2021, by region.



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 is estimated to 74% at the national level, and varies from region to region. Some challenges associated with this procurement data are further described in *Guidance to readers*.

To present statistics on antibiotic use 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*.

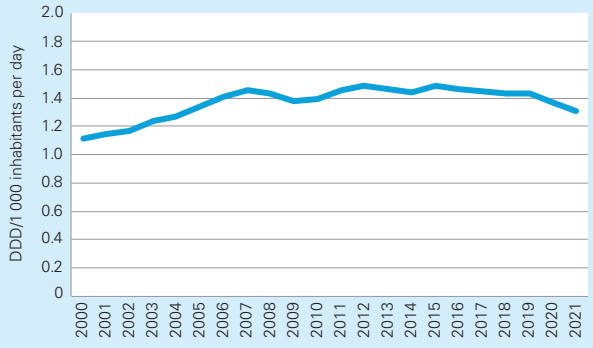
The Dalarna region is not included in either of the data sources used in this section, and data from acute care hospitals in Jönköping region from 2014 are incomplete.

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 1.3 DDD/1 000 inhabitants per day in 2021, which is a 4.7% decrease compared to 2020, Figure 1.26.
- Sales of beta-lactamase sensitive penicillins (J01CE) and cephalosporins (J01DB-DE) decreased in 2021, while combinations of penicillins (J01CR) increased. The sales of other antibiotic classes and substances commonly used in hospital care remained unchanged, Figure 1.27.

Figure 1.26. Sales of antibiotics (J01 excl. methenamine) to hospitals and other health and social care facilities between 2000 and 2021.



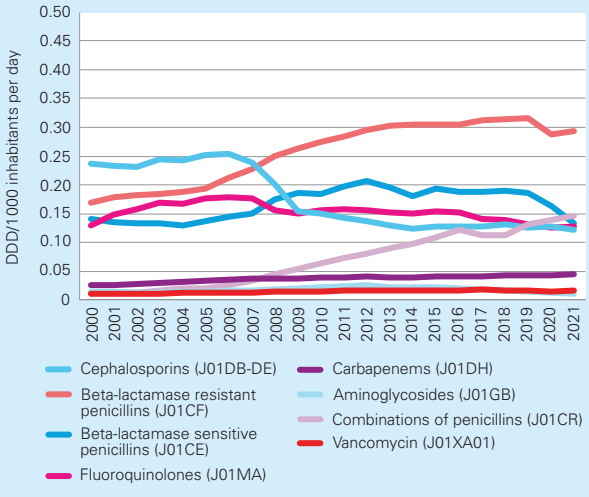
Source: The Public Health Agency of Sweden

Comments

There has been several modifications to antibiotic prescribing in the past years that explains some of the observed changes in Figure 1.27. The dip in sales of cephalosporins around 2006-2009 can be attributed to a shift in the choice of cephalosporin prescribed, leading to lower numbers of DDDs. However, since then the continued decreased sales of cephalosporin is a result of altered prescribing behaviour with beta-lactamase sensitive penicillins (J01CE) and combinations of penicillins (J01CR), mainly piperacillin-tazobactam (J01CR05), gradually replacing cephalosporins. Variations in the availability of antibiotic substances can also cause fluctuations in the data, such as the global shortage of piperacillin-tazobactam in 2016/17 which led to decreased sales of combinations of penicillins (J01CR). A reason behind the decreased sales of penicillins (J01CE and J01CF) in 2020 might be due to a decreased number of surgeries during the COVID-19 pandemic (National Board of Health and Welfare, 2020b), as these substances are often used as prophylaxis (Skoog et al., 2016).

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 cefiderokol did not have any impact on the estimates in this report.

Figure 1.27. Sales of selected classes of antibiotics (ATC level 4 and 5) to hospitals and other health and social care facilities between 2000 and 2021.



Source: The Public Health Agency of Sweden

Antibiotic sales in acute care hospitals

Results

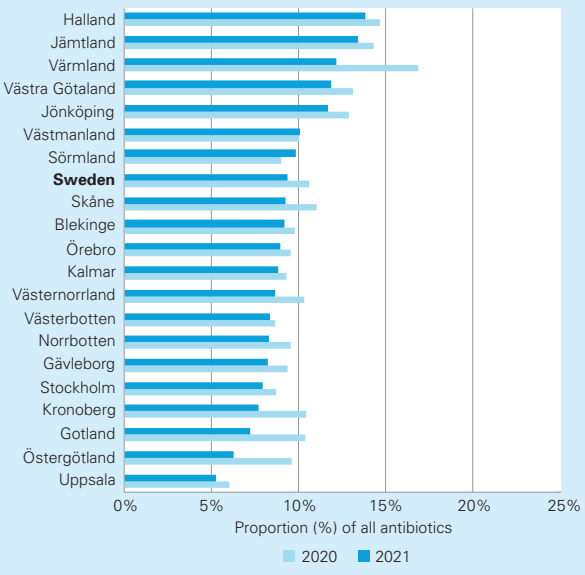
- Data from acute care hospitals show that sales of antibiotics increased in 2021 compared to 2020 measured in both DDD per 100 admissions and in DDD per 100 patient-days, Table 1.2.
- Beta-lactamase resistant penicillins (J01CF) are the most commonly prescribed antibiotics, making up 23% of the sales.
- The proportion of beta-lactamase sensitive antibiotics (penicillin V and G J01CE01-02) sold during 2021 decreased in 18 of 20 regions compared to 2020, Figure 1.28.
- 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 2021 – a marginal change compared to 2020 (35%). The proportions ranged from 18% in the Jämtland Härjedalen region to 41% in Gävleborg region, Figure 1.28.
- Notable regional variations were also observed for the individual classes of broad-spectrum antibiotics; 4% to 16% for cephalosporins, 6% to 13% for fluoroquinolones, 4% to 15% for piperacillin-tazobactam, and 2% to 5% for carbapenems, Figure 1.29.

Comments

The main antibiotic classes used in acute care hospitals are beta-lactamase resistant penicillins, combinations of penicillins that mainly consist of piperacillin-tazobactam, cephalosporins (J01DB-DE), beta-lactamase sensitive penicillins (J01CE), and fluoroquinolones (J01MA). Accounting for hospital activity (admissions and patient days), the use of beta-lactamase resistant pencillins, piperacillin-tazobactam, and cephaloporins seem to have increased during the past five years.

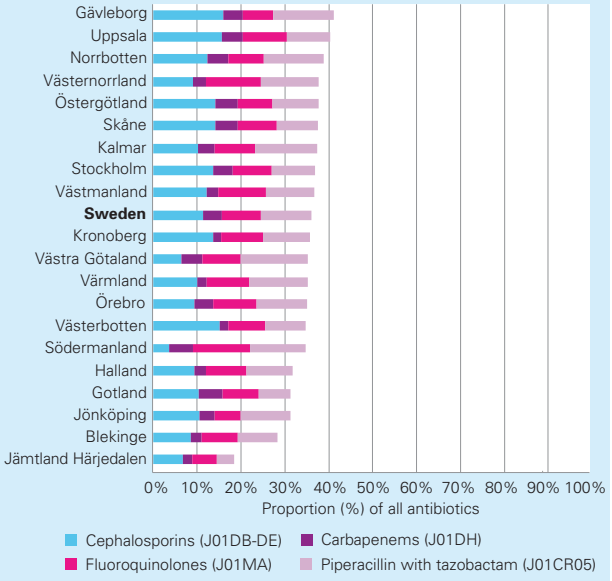
There are substantial regional variations in sales of antibiotics to Swedish acute care hospitals, both in number of DDD/1 000 inhabitants per day and in the proportion and distribution of the different antibiotic classes, Figure 1.28 and Figure 1.29. These differences can be partially attributed to the type of hospitals, case mix and patient demographics in the region, and 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.

Figure 1.28. Proportion (%) of beta-lactamase sensitive penicillins (penicillin V and G, J01CE01-02) out of all antibiotics sold to Swedish acute care hospitals in 2020 and 2021, by region.



Source: The Public Health Agency of Sweden

Figure 1.29. Proportion (%) of selected broad-spectrum antibiotics out of all antibiotics sold to Swedish acute care hospitals in 2021, by region.



Source: The Public Health Agency of Sweden

Table 1.2. Sales of selected classes of antibiotics (ATC level 4 and 5) to acute care hospitals between 2017 and 2021.

	DDD/100 admissions					DDD/100 patient-days				
	2017	2018	2019	2020	2021	2017	2018	2019	2020	2021
Tetracyclines (J01AA)	21.5	20.3	19.6	18.3	17.2	4.8	4.6	4.6	4.4	4.1
Penicillins with extended spectrum (J01CA)	23.8	23.6	23.4	22.9	25.3	5.3	5.4	5.5	5.5	6.1
Pivmecillinam (J01CA08)	8.3	8.3	7.8	8.0	9.0	1.9	1.9	1.8	1.9	2.2
Betalactamase sensitive penicillins (J01CE)	35.1	35.5	34.8	31.0	29.5	7.9	8.1	8.2	7.4	7.1
Benzylpenicillin. PcG (J01CE01)	21.3	21.9	22.1	20.1	19.1	4.8	5.0	5.2	4.8	4.6
Phenoximethylpenicillin. PcV (J01CE02)	13.7	13.6	12.7	10.9	10.5	3.1	3.1	3.0	2.6	2.5
Betalactamase resistent penicillins (J01CF)	61.4	64.4	64.7	63.2	71.3	13.7	14.7	15.1	15.1	17.1
Combinations of penicillins (J01CR)	28.1	28.8	33.4	38.7	44.3	6.3	6.6	7.8	9.2	10.6
Piperacillin and tazobactam (J01CR05)	22.8	23.2	27.2	31.0	36.4	5.1	5.3	6.4	7.4	8.7
Cephalosporins (J01DB-DE)	31.2	32.5	31.2	34.0	36.1	7.0	7.4	7.3	8.1	8.7
Carbapenems (J01DH)	10.1	10.7	10.9	11.9	13.4	2.3	2.4	2.5	2.8	3.2
Trimethoprim (J01EA)	0.7	0.7	0.7	0.6	0.8	0.2	0.2	0.2	0.2	0.2
Trimethoprim with sulphonamides (J01EE)	11.3	11.8	12.8	13.0	14.9	2.5	2.7	3.0	3.1	3.6
Macrolides (J01FA)	5.6	5.1	5.5	7.1	5.2	1.2	1.2	1.3	1.7	1.2
Lincosamides (J01FF)	8.6	8.5	7.8	7.4	7.9	1.9	1.9	1.8	1.8	1.9
Aminoglycosides (J01GB)	4.7	4.0	3.7	3.6	3.2	1.1	0.9	0.9	0.9	0.8
Fluoroquinolones (J01MA)	27.1	27.0	25.6	25.3	28.3	6.1	6.1	6.0	6.0	6.8
Moxifloxacin (J01MA14)	2.2	1.9	1.7	1.6	2.1	0.5	0.4	0.4	0.4	0.5
Glycopeptides (J01XA)	4.7	4.8	4.6	4.7	5.6	1.0	1.1	1.1	1.1	1.4
Imidazole derivates (J01XD)	4.6	4.7	4.2	4.3	5.0	1.0	1.1	1.0	1.0	1.2
Nitrofurantoin (J01XE)	2.3	2.3	2.1	2.2	2.4	0.5	0.5	0.5	0.5	0.6
Other ATC classes										
Vancomycin (A07AA09)	0.3	0.4	0.4	0.5	0.5	0.1	0.1	0.1	0.1	0.1
Methenamine (J01XX05)	1.9	1.8	1.5	1.3	2.4	0.4	0.4	0.4	0.3	0.6
Linezolid (J01XX08)	0.8	0.8	1.0	1.2	1.8	0.2	0.2	0.2	0.3	0.4
All agents (J01)	**284.4**	**288.5**	**289.3**	**292.5**	**316.4**	**63.6**	**65.7**	**67.8**	**69.8**	**75.9**

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 health care professionals and patients. Adverse reactions related to antibiotics between 2016 and 2021 were analysed for various classes of agents.

There were 3 246 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=1,436), gastrointestinal disorders (n=768), nervous system disorders (n=468), general disorders (n=453), respiratory disorders (n=219), musculoskeletal disorders (n=210), immune system disorders (n=149), investigations (n=138), hepatobiliary disorders (n=142), renal and urinary disorders (n=127), psychiatric disorders (n=108) and reproductive system and breast disorders (n=101). 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 five years, unadjusted for sold substances and regardless of the cause of the report, are presented in Table 1.3.

Table 1.3. Substances most commonly associated with adverse reactions reported to the Swedish Medical Products Agency 2017-2021.

Antibiotic	Total number of adverse drug reaction reports 2017-2021	Number of 'serious' reports	Number of fatal cases
Phenoxymethylpenicillin (J01CE02)	435	127	0
Flucloxacillin (J01CF05)	303	155	6
Ciprofloxacin (J01MA02)	298	197	6
Nitrofurantoin (J01XE01)	243	93	2
Clindamycin (J01FF01)	244	97	4
Sulfamethoxazole and trimethoprim (J01EE01)	227	141	3
Amoxicillin (J01CA04)	165	58	0
Doxycycline (J01AA02)	150	40	0
Piperacillin-tazobactam (J01CR05)	115	72	3
Metronidazole (P01AB01)	107	57	0

Swedish antibiotic prescribing according to the WHO AWaRe classification

WHO AWaRe classification

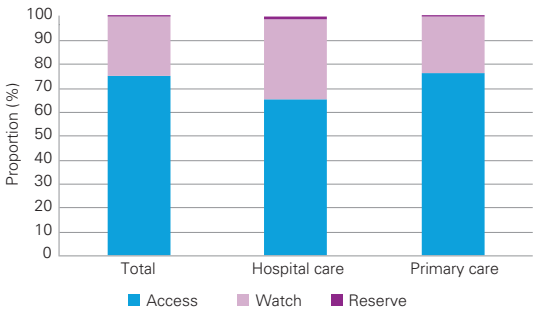
The World Health Organization (WHO) introduced the AWaRe Classification of Antibiotics in 2017 as a tool to support antibiotic stewardship efforts locally and globally. Since then, it has been updated twice and most recently in 2021.

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 where other treatments have failed (World Health Organization, 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, 60% of all antibiotics consumed in countries should belong to the Access group by 2023. There are no separate targets for consumption in the hospital and primary care sector based on the AWaRe classification.

Consumption of Access, Watch, and Reserve antibiotics in Sweden from 2001-2021

Based on data from electronic prescribing (primary care) and requisitions (hospital care), 75% of antibiotics sold in 2021 were Access antibiotics according to the most recent version of the AWaRe classification. Watch group antibiotics made up 24.7% of all antibiotics sold, and the remaining 0.3% consisted of Reserve group antibiotics. As expected, the proportion of Watch antibiotics were higher in hospitals than in primary care, i.e. 34% versus 23% (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 nursing homes and dental care. According to 2021 data, 26% of the antibiotic requisitions belonged to these other care providers. 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.

Figure 1. Relative sales of Access, Watch and Reserve antibiotics in Sweden in 2021 according to health care sector and total.



A review of 20 years of historical data indicates that the proportion of Access antibiotics has stayed stable around 80%, but a drop was observed during the COVID-19 pandemic in both primary care and hospitals (Figure 2a). Simultaneously, the proportion of Watch antibiotics has increased; in hospital care, the relative consumption has returned to the same level as in the beginning of the observation period. In primary care, the proportion of Watch antibiotics prescribed has been higher than ever before (Figure 2b). Prescribing of Reserve antibiotics has increased gradually since the beginning of the observation period, but escalated during the pandemic (Figure 2c). It is important to note, however, that the total consumption of antibiotics has decreased during the COVID-19 pandemic, but the antibiotics prescribed seem to have shifted towards a broader spectrum.

There are no updated numbers to compare with from other EU/EEA countries at the time of writing. Previous publications have indicated a median proportion of 35% for Watch antibiotics and 1.7% for Reserve antibiotics in the European region (Schweickert et al., 2018) However, a direct comparison of the current Swedish data with these numbers is not appropriate due to differences in the year of analysis and the version of the AWaRe classification used.

In conclusion, Sweden exceeds the 60% Access antibiotic target set by the WHO. Although the consumption of Reserve group antibiotics seems to be low by international standards, the prescribing of these substances in primary care merits further review.

Figure 2A. Relative consumption of Access antibiotics in Sweden between 2001-2021 according to health care sector and total.

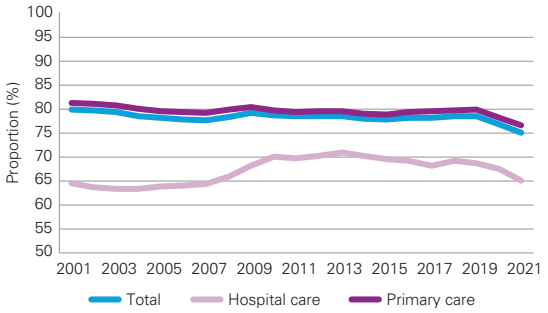


Figure 2B. Relative consumption of Watch antibiotics in Sweden between 2001-2021 according to health care sector and total.

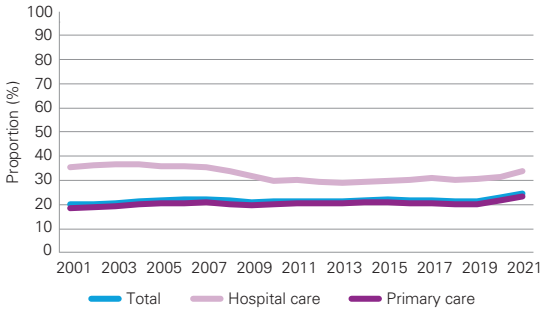
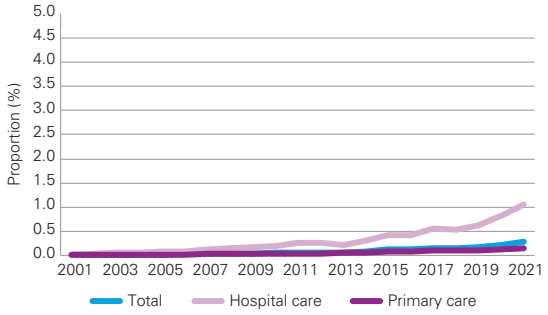


Figure 2C. Relative consumption of Reserve antibiotics in Sweden between 2001-2021 according to health care sector and total.



References

Schweickert B, Feig M, et al. 2018, Antibiotic consumption in Germany: first data of a newly implemented web-based tool for local and national surveillance. *J Antimicrob Chemother*, 73: 3505–3515

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

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

In Sweden, unique prescription codes are issued to all health care providers and provide the opportunity to monitor prescriptions. Prescriptions issued by health care centres that provide both physical and digital health care 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 the physical visits. Therefore, providing a comprehensive picture of prescribing patterns in digital health is not possible at this point in time.

The Swedish strategic programme against antibiotic resistance (Strama) published treatment guidelines for diagnosis-linked antibiotic prescribing in digital health in 2019 (Strama, 2019). 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 is complicated or impossible to establish for the majority of the regions in Sweden. Due to the above mentioned challenges, data presented in this section do not present a fully accurate reflection of prescription patterns in digital care, but they do give an indication of the situation in 2021.

For the purpose of this report, data were collected from five regions (Kalmar, Västmanland, Sörmland, Dalarna and Stockholm) that were able to extract prescription from digital consultations. The data does not include all prescriptions due to multiple reasons, such as inability to collect data from health care centres that use different medical record systems and inability to collect data from health care centres which do not have an agreement with the region to provide health care. Thus, the numbers reflect a small proportion of the digital consultations and are likely higher in reality.

Prescriptions of antibiotics in digital health in Stockholm region

The total number of prescriptions in digital health during 2021 from the five regions was 123 957 prescriptions. Stockholm region accounted for 51% of the prescriptions, and was the only region able to establish a diagnostic connection to the prescription data. Therefore, the data presented in this section is limited to Stockholm region.

According to data from Stockholm region, antibiotics were prescribed in 12% of the digital consultations. These do not include health care providers that only provide digital care. Most antibiotic prescriptions were issued to patients aged 15-64 years, which might indicate that this age group seeks digital health care to a higher extent. Among patients aged 65+, only 3% received an antibiotic prescription, which might be due to the reason for seeking digital care (Table 1). A greater proportion of the prescriptions were issued to females than males.

Out of the 63 489 antibiotic prescription issued through digital care in Stockholm region in 2021, almost half of them were linked to common infection diagnoses (Table 2). The most common diagnosis for antibiotic prescribing in digital care was acute cystitis followed by lyme borreliosis, tonsillitis and upper respiratory tract infection. According to Strama guidelines, only four types of infections can be diagnosed and prescribed antibiotics through digital consultations, i.e. acute cystitis, lyme borreliosis, impetigo and acne. 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.

This sample of data from Stockholm region show that the prescribing of antibiotics in digital health can be improved, and more work needs to be done in this area. It is therefore important to be able to collect and analyse data from digital health in the same manner as outpatient care, dentistry and hospital care. Prescription data from digital health helps identify the gaps and the interventions needed to promote responsible use of antibiotics.

Table 1. The number of prescriptions in Stockholm region outpatient care and digital health care, by age group, in 2021.

Age	Total digital	Total outpatient	Proportion digital
0-6	6 750	36 922	18%
7-14	3 557	22 451	16%
15-64	48 374	317 590	15%
65+	4 808	162 812	3%
Total	63 489	544 788	12%

Table 2. Diagnostic groups connected to the number of prescriptions in Stockholm region digital health care by age group in 2021.

Diagnostic group	All ages	0-6	7-14	15-64	65+
Acute bronchitis	186	21	4	136	25
Acute cystitis	1 2061	166	158	10 475	1 262
Acute otitis media	472	300	55	109	8
Acute sinusitis	1416	<3	14	1311	89
Lyme borreliosis	5 530	701	459	3 815	555
Erysipelas	277	8	8	215	46
Tonsillitis	3 476	217	282	2 937	40
Cough	927	253	34	550	90
Imeptigo	1 153	516	259	372	6
Carbuncle , furuncle, abscess, atheroma	284	16	18	237	13
Ingrown toenail	548	45	104	388	11
Nonspecific skin infections	1 815	229	232	1 263	91
Pneumonia	90	6	<3	54	30
Upper respiratory tract infections	2 482	703	111	1 562	106
Total	**30 717**	**3 183**	**1 738**	**23 424**	**2 372**

References

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

Strama. 2019, Rekommendationer för kvalitetsindikatorer vid digitala vårdmöten [Recommendations for quality indicitators in digital health]. https://strama.se/wp-content/uploads/2019/10/Kvalitetsindikatorer-f%C3%B6r-digitala-v%C3%A5rdm%C3%B6ten-191031.pdf

Clinical trial – comparing the effect of temocillin versus cefotaxime on the intestinal microbiota

This clinical trial showed that treatment with temocillin resulted in fewer resistant bacteria in the intestinal microbiota in patients with febrile urinary tract infection compared to treatment with cefotaxime. Non-inferiority was shown regarding clinical and bacteriological effects.

Introduction

Increasing antibiotic resistance and the shortage of new antimicrobial agents highlights the importance of optimising the use of existing antibiotics. In 2014, the Public Health Agency of Sweden (PHAS) was commissioned by the government to evaluate the use of currently available antibiotics. In collaboration with Swedish hospitals, a study was conducted to investigate whether temocillin, compared to cefotaxime, leads to less resistance in the intestinal microbiota in patients with suspected or diagnosed febrile urinary tract infection (UTI). The study also examined safety and efficacy of these antibiotic treatments. Patients with febrile UTI constitute a large group of patients treated with antibiotics in hospital care.

Temocillin has been used since the 1980s in some European countries, but not in Sweden. Temocillin is a narrow-spectrum penicillin with activity against gram-negative intestinal bacteria (Enterobacterales), including against most strains producing extended-spectrum beta-lactamases (ESBL). It lacks activity against gram-positive and anaerobic bacteria as well as against *Pseudomonas aeruginosa*.

Intervention

Patients were randomized to receive either temocillin (2 grams every 8 hours) or cefotaxime (1-2 grams every 8 hours) intravenously for at least three days. Thereafter, doctors could choose to switch to oral antibiotic therapy. Treatment with antibiotics lasted for 7-10 days, up to 14 days if the patient had bacteremia at the start of treatment.

Patients had rectal swabs taken for microbiota analyses thrice; at baseline, at the end of study drug treatment, and 7-10 days after discontinuation of antibiotic treatment.

Method

The study was a randomized, controlled, superiority study. The trial was open-label for investigators and patients, but masked for the laboratory personnel who analysed the primary outcome. Analyses of urine and blood cultures were performed at the local microbiological laboratories. Analyses of rectal swabs were performed at PHAS.

Outcome measures

The primary outcome was a composite endpoint evaluating disturbances in the intestinal microbiota after at least three days of treatment with the study drug. To fulfill this, at least one of the following two events would occur; colonization with (presence of) Enterobacterales with reduced susceptibility to third generation cephalosporins and/or colonization with toxin-producing Clostridoides difficile. Secondary variables were clinical and bacteriological responses, evaluated as early response (day 3-4), and late response 7-10 days after completion of antibiotic treatment. All patients were followed up during the study period for adverse events. The primary outcome was evaluated for superiority, ie we tested whether our hypothesis that temocillin would cause less disturbances in the microbiota compared to cefotaxime was true. The secondary efficacy variables were evaluated for non-inferiority, ie tested whether temocillin was non-inferior compared to cefotaxime. The non-inferiority margin was set to minus 10 percentage points.

Inclusion criteria

The study included women and men from 18 years of age with fever (>38.0°C), positive urine dipstick and at least one sign or symptom of febrile UTI (flank pain, costovertebral angle tenderness and changes in urinary frequency, urgency or dysuria). Participants should also have an indication for intravenous antibiotic treatment.

Results

A total of 152 patients were included from 12 hospitals between May 2016 and July 2019 (Figure 1). The study showed that treatment with temocillin led to a lower degree of disturbance in the microbiota, mainly due to fewer antibiotic-resistant bacteria in the intestines; 18/68 (26%) in the temocillin group and 30/62 (48%) in the cefotaxime group (risk difference –22% [95% confidence interval –42% to –3%]) fulfilled the criteria for the primary endpoint. Clinical and bacteriological effect, both at early and late response were comparable (non-inferior) between the treatment groups (Figure 2). The number of reported adverse events was similar in the two interventions. Most events were of mild to moderate severity.

Figure 1. Flow chart of enrollment, randomization and outcomes in the clinical trial.

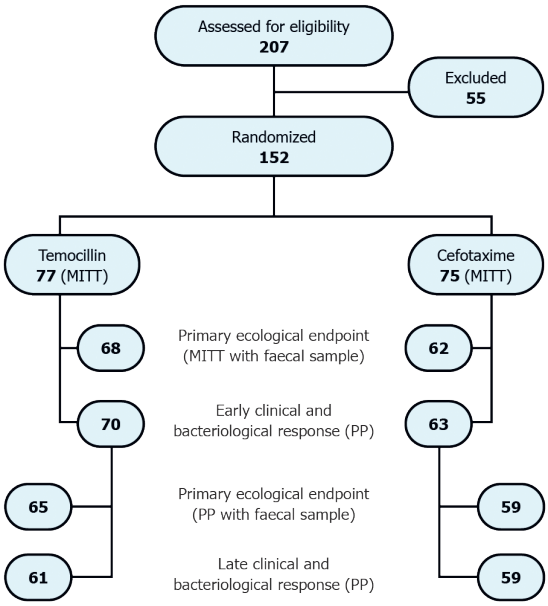
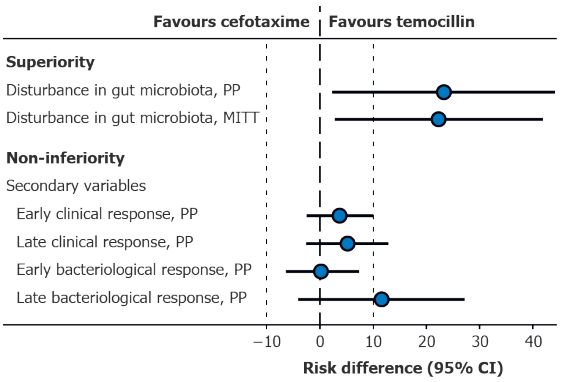


Figure 2. Results of primary and secondary effect variables.



MITT = modified-intention-to-treat population (patients who have received at least one dose of study drugs); PP = per-protocol population (patients who followed the protocol)

Conclusion

In conclusion, we found that temocillin resulted in less disturbance of the intestinal microbiota compared with cefotaxime, and the drugs was shown to be comparable regarding safety, clinical and bacteriological efficacy. There are several potential benefits for both patients and society if using a drug with a favorable ecological profile. A lower incidence of resistant intestinal bacteria can reduce the risk of healthcare-related infections caused by these bacteria. Since temocillin has activity against most ESBL-producing strains, it may also be possible to replace so-called last-line antibiotics in certain situations.

Reference

Edlund C, Ternhag A, et al. 2022, The clinical and microbiological efficacy of temocillin versus cefotaxime in adults with febrile urinary tract infection, and its effects on the intestinal microbiota: a randomised multicentre clinical trial in Sweden. *Lancet Infect Dis*, 22:390-400.

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.

Sales 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, and information is given under Comments by animal species, Aquaculture.

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 benzylpenicillins 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.

Completeness of data

In 2011, it was noted that the information on sales of products with special license were less complete than in previous years and between 2012 and 2014, efforts were made to obtain sales data for the main products sold with special license also from pharmaceutical companies. The system for data-collection has been adjusted and from 2015, it is assumed that the sales of this type of products are no less complete than before the reregulation.

Between 2010 and 2015, there has also been a lack of completeness in the sales of products with general marketing authorisation. For further information on the lack of completeness of data from recent years, see Swedres-Svarm 2015 p. 109.

Trends in animal populations

Changes in the numbers of animals may affect trends in statistics on sales of antibiotics. Compared to 2012, the number of pigs slaughtered in 2021 was approximately the same, while the number of broilers has increased by 48%. 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.

Overall sales

The total yearly sales of antibiotics for animals over the last decade are presented in Table 2.1. The potencies of different antibiotics are not equal and therefore, each class should be evaluated separately.

Of the overall sales expressed as kg active substance, more than 90% are products formulated for treatment of individual animals (injectables, tablets, intramammaries) and less than 10% for treatment of groups or flocks (premixes, oral powders, solutions for in water medication). In 2021, the total reported sales from Swedish pharmacies of antibiotics authorised for veterinary use were 9 129 kg, of which 57% was benzylpenicillin. The corresponding figures for 2012 were 11 385 kg and 53%, respectively.

Since 2012, sales of all classes of antibiotics except aminopenicillins have decreased notably. The sales of aminopenicillins increased slightly in 2020, but in 2021 sales decreased to about the same level as before 2020 (Table 2.1). In addition, in the past five years sales of aminoglycosides have increased. This is explained by a shift from polymyxins (colistin) to aminoglycosides for treatment of weaning diarrhoea in pigs. Sales of tetracyclines have also increased over the last years but are still lower than in 2012. The sales of remaining classes have decreased also over the last five-years period.

The sales of products on special license have increased from 3% of the total sales in kg active substance in 2017 to 10% in 2021. The Swedish market for veterinary antibiotics is small, and for some substance-formulation types there is only one or two products with general marketing authorisation, or a special type of product is lacking. An example of the latter is aminoglycosides for treatment of weaning diarrhoea in piglets via water. Such products have almost entirely replaced sales of colistin, and they are exclusively sold with special license. In recent years, there have also been shortages (sometimes very longlasting) on the Swedish market of products with general marketing authorisation, resulting in situations where special licenses to sell products authorised in other countries are granted.

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

ATCvet code		2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
QJ01AA, QG01A	Tetracyclines	881	935	787	685	515	529	516	522	609	708
QJ01CE, -R, QJ51	Benzylpenicillin[b]	5 983	5 592	5 148	5 479	5 620	5 553	5 594	5 242	5 006	5 242
QJ01CA, QJ01CR	Aminopenicillins	649	645	635	642	677	640	683	648	765	651
QJ01D	Cephalosporins	410	330	299	267	242	210	187	161	162	163
QA07AA, QJ01G, -R, QJ51R	Aminoglycosides	408	264	300	322	312	302	376	343	393	347
QA07AB, QJ01E	Sulphonamides	1 812	1 707	1 699	1 634	1 643	1 678	1 539	1 445	1 462	1 266
QJ01E	Trimethoprim & derivatives	329	320	314	313	318	326	297	281	285	248
QJ01F	Macrolides & lincosamides	632	564	484	485	472	515	578	486	447	410
QJ01MA	Fluoroquinolones	106	52	45	34	30	25	29	20	25	19
QA07AA,QJ01BA, QJ01XQ	Others[c]	174	205	201	224	337	147	237	115	151	75
Total sales		**11 385**	**10 614**	**9912**	**10 086**	**10 165**	**9 925**	**10 037**	**9 263**	**9 306**	**9 129**

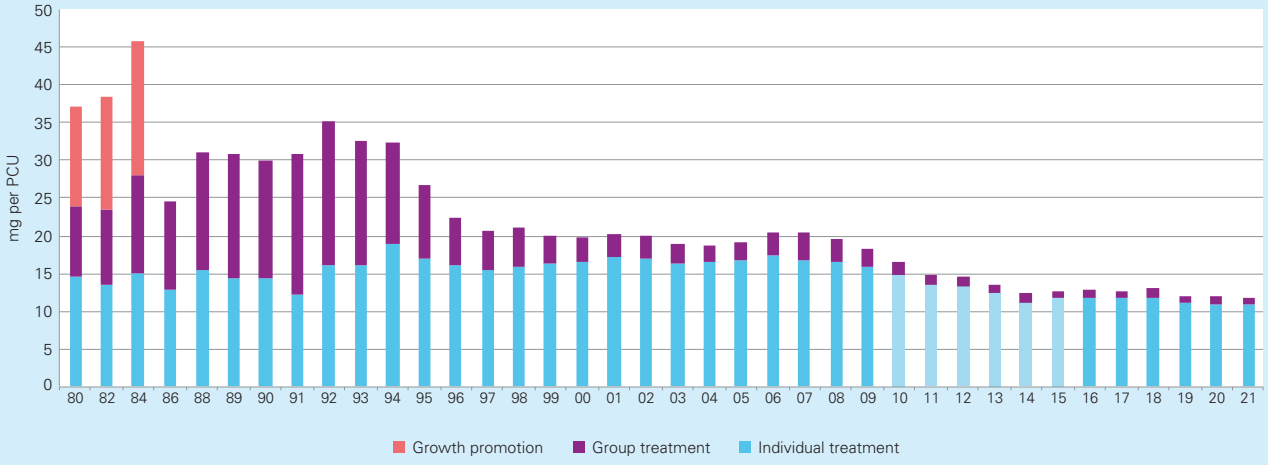
[a]Data from 2010-2015 are uncertain because of a lack of completeness mainly affecting injectable products. [b]Also includes small amounts of phenoxymethylpenicillin and penicillinase stable penicillins. [c]Others include: amphenicols, pleuromutilins and polymyxins, aggregated for confidentiality reasons.

Population corrected 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 2020 as a proxy for PCU in 2021. 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 2021 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].



[a]Data from 2010-2015 are uncertain because of a lack of completeness mainly affecting injectable products. 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.

The Antimicrobial ad hoc expert group (AMEG) of the European medicines agency considers 3rd generation cephalosporins, fluoroquinolones and polymyxins as classes of antibiotics for which there should be special restrictions regarding their use in animals (category B, restrict) (EMA, 2019a). Since 2012, the sales of these antibiotics, expressed as mg/PCU, have decreased by 85%, 84% and 95%, respectively. For the 3rd generation cephalosporins and fluoroquinolones, the decrease is partly explained by a Swedish regulation that since 2013 is limiting veterinarians' rights to prescribe these types of antimicrobials (SJVFS 2019:32). As to polymyxins, the findings of transferable resistance to colistin were communicated to stakeholders during 2016 and onwards. An awareness among prescribers of the importance of this class of antimicrobials for public health, and of the potential consequences of transferable resistance, is a probable explanation for the observed decrease. Use of colistin has, when needed, increasingly been replaced with use of antibiotics in other classes, e.g. aminoglycosides.

Comments on trends by animal species

Dairy cows

Växa (an organisation providing animal health services for dairy cattle) publishes a yearly report related to the livestock organisatiońs work to improve animal health and welfare in dairy cows. For statistics on incidence of antibiotic treatments of dairy cows enrolled in the Swedish milk recording scheme, data are retrieved from a database with veterinary reported disease events and treatments (Jansson Mörk, 2010).

According to Växa (2022), the by far most common indication for treatment of dairy cattle with antibiotics is mastitis. In Sweden, mastitis is generally treated systemically and any changes in treatment incidence, treatment length or choice of antibiotic for this condition will have a noticeable influence on the statistics on sales of antibiotics. The reported incidence of systemic treatments of dairy cows has decreased from 20.4 recorded treatments per 100 completed/interrupted lactations in 2011 to 12.2 in 2020. Of all recorded treatments, benzylpenicillin was by far the most common (89% of reported systemic treatments). Treatment of dairy cows with fluoroquinolones for any indication has decreased from 10% of recorded treatments 2011 to 1% in 2020.

Pigs

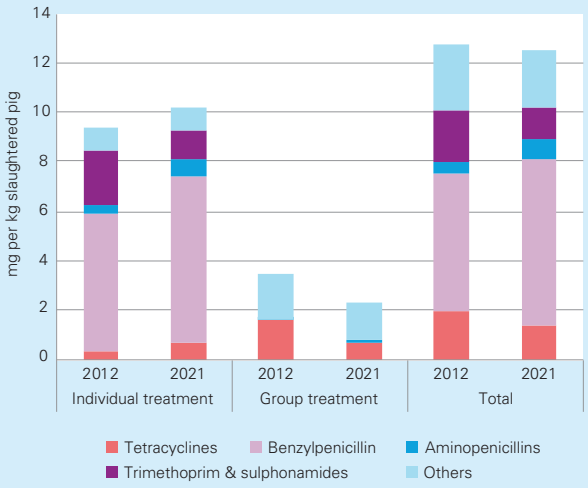
Antibiotics for pigs are mostly sold on veterinary prescription by pharmacies to the animal owner, and the species is recorded by the pharmacy. Sales reported as "for pigs" is therefore believed to closely reflect sales in commercial herds.

In 2012 and 2021 the total sales of antibiotics on prescription for pigs were 2 978 and 3 162 kg active substance, respectively, or 12.8 and 12.5 mg/kg per slaughtered pig. Of the total sales in kg active substance in 2021, 81% were products formulated for use in individual animals, and 65% of that subset were products containing benzylpenicillin.

Sales of fluoroquinolones for use in pigs were negligible, and no cephalosporins were sold for pigs in 2021. In Sweden, polymyxins (colistin) are only used for pigs. As noted under Population corrected overall sales, a marked decrease in sales can be noted over the past ten years.

In Figure 2.2, the sales for pigs are presented as mg/kg pig slaughtered. A shift from products for medication of groups of animals via feed or water towards medication of individual animals, preferably with narrow-spectrum substances such as benzylpenicillin is observed over the period. This is well in line with national guidance on prudent use of antibiotics (Medical Products Agency, 2022).

Figure 2.2. Sales of antibiotics for pigs in 2012 and 2021 expressed as mg active substance per kg slaughtered pig[a].



[a]Others include all classes not given separately, mainly aminoglycosides, macrolides, pleuromutilins and polymyxins.

Poultry

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.

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.

The use in 2021 corresponds to 0.19 mg active substance/kg slaughtered chicken. Of the 13 flocks reported as treated, 12 were administered phenoxymethylpenicillin for necrotic enteritis, and the remaining flock received trimethoprim-sulphonamides for colibacillosis. In addition, 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.

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
2012	2 853	1
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

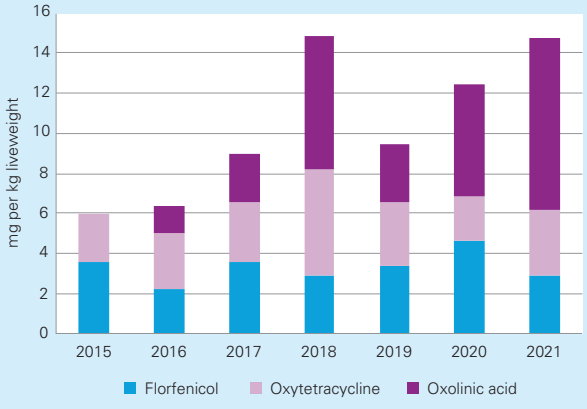
Fish

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. In 2021, a total of 146 kg of antibiotics were prescribed for fish for consumption, compared to 165 kg in 2018, a year with unusually high temperatures. As in previous years, antibiotics prescribed in 2021 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*, respectively. 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.

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



Horses

In 2021, sales of trimethoprim-sulphonamides formulated for oral use in horses (paste or powder) was 12% of the total sales, and 74% of the sales of all products with trimethoprim-sulphonamides. Since 2012, there has been a decrease in sales of trimethoprim-sulphonamides formulated for oral use in horses by 14%, measured as kg active substance. In 2013, guidelines for use of antibiotics in horses were published by the Swedish Veterinary Association and in 2015, this guidance was supplemented by guidance from the Medical products agency (Medical Products Agency, 2015). It is possible that the guidance, together with an overall strong focus on the need for antibiotic stewardship in human and veterinary medicine has also contributed to the observed decrease.

The sales of other antibiotics for horses are difficult to estimate, as such products are frequently sold on requisition and administered by the veterinarian in connection with a clinical examination, in ambulatory practice, in clinics or in hospitals.

Dogs

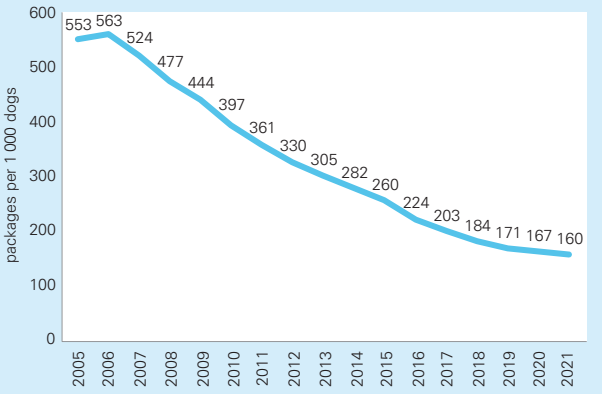
In 2021, the overall sales of veterinary medicinal products for oral medication of dogs were 574 kg compared to 1 071 kg in 2012. As in previous years, aminopenicillins (with and without clavulanic acid), first generation cephalosporins and lincosamides were by far the classes with largest sales in 2021.

The figures above refer to sales of veterinary products only. In 2006, the total number of packages of antibiotics dispensed for oral use in dogs, i.e. both veterinary antibiotics and those authorised for use in humans, corresponded to 563 packages per 1000 dogs. Since then, the number has decreased to 160 packages per 1000 dogs (-72%) (Figure 2.4). The latest estimate of number of dogs is from 2017, and population growth thereafter has been estimated based on rate of change since the previous estimate in 2012. The overall opinion as reported by Swedish media is that there has been a dramatic increase not just in an interest in dog ownership but also in de facto sales of dogs, including illegal imports, during the COVID-19 pandemic. Examples of sources for this information are breeding organisations, organisations that for animal welfare purposes monitor sales of dogs on the internet, including social media, as well as the Swedish Customs authority. The population estimate for 2020 and 2021 used here does not reflect that, and it is possible that the number of packages per 1000 individuals for these years in figure 2.4 is an overestimate.

The most prominent changes relative to 2006 are noted for first generation cephalosporins (-89%), fluoroquinolones (-94%) and aminopenicillins with clavulanic acid (-78%).

As described in Svarm 2008, the emergence of infections with multiresistant methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) and methicillin-resistant *S. aureus* (MRSA) triggered several national and local initiatives. This has most likely led to changes in prescribers' behaviour, which in turn explains the downward trends in sales of antibiotics for dogs shown in Figure 2.4.

Figure 2.4. Sales of the antibiotics for oral medication of dogs expressed as packages per 1 000 dogs. Data include antibiotics authorised for veterinary use as well as antibiotics for human use.



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.

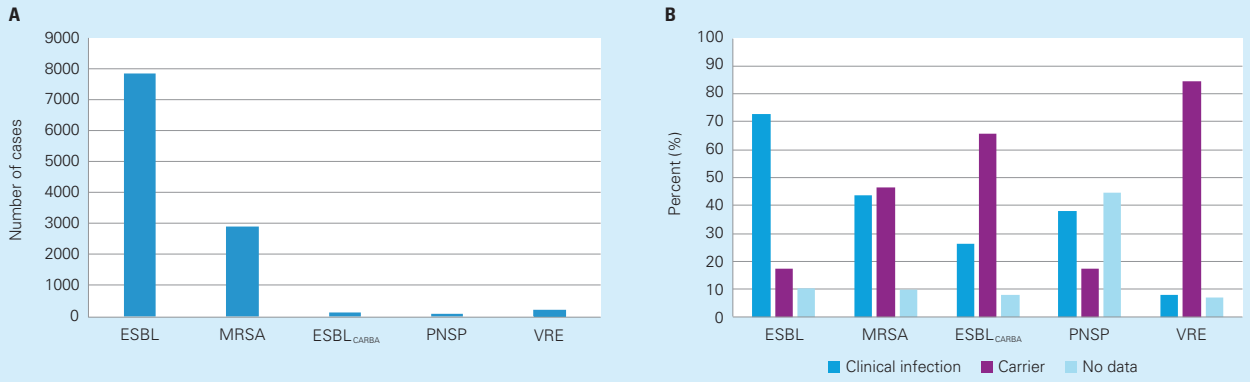
Species, group or type	Sampling
Mandatory reporting (SmiNet)	
Enterobacterales (previously Enterobacteriaceae) with ESBL Enterobacterales (previously Enterobacteriaceae) with $ESBL_{CARBA}$ *Staphylococcus aureus* resistant to methicillin *Streptococcus pneumoniae* non-susceptible to penicillin *Enterococcus faecium* and *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 pneumoniae	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 influenzae	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 (previously Enterobacteriaceae)	All isolates from clinical, screening or case finding samples with reduced susceptibility to colistin.
Enterobacterales (previously Enterobacteriaceae) 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 non-susceptible to penicillin (MIC ≥ 0.5)	All isolates from clinical, screening or case finding samples.
Enterococcus faecium or *Enterococcus faecalis* resistant to vancomycin	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.
Escherichia coli and *Klebsiella pnemoniae* resistant to cefadroxil	Consecutive samples from urine during one month every third year, 600-800 isolates.

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

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 (previously Enterobacteriaceae) 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 A and B. Number of mandatory reported cases during 2021 (A) and the proportion of clinical infection versus carriers (B). ESBL data, based on sample types, clinical infection (blood, urine, CSF), carrier (faeces, rectum, perineal), No data (other sample materials or not specified).



Source: The Public Health Agency of Sweden

Table 3.2. Summary of results for mandatory reported antibiotic resistance 2021.

	ESBL	$ESBL_{CARBA}$	MRSA	PNSP	VRE
Number of cases (inc)	7 860 (75)	137 (1.3)	2 895 (28)	92 (0.9)	209 (2.0)
Proportion clinical infection	73%	26%	44%	38%	10%
Gender	67% women	50% men	52% women	59% men	57% men
Median-age (range)	57 year (0-100+)	53 year (0-87)	33 year (0-100+)	49 year (0-94)	63,5 year (2-99)
Proportion of domestic cases	no information	23% (14% no data)	59% (17% no data)	47% (49% no data)	62% (9% no data)
Short epidemiological information	Community and health-care	Hospital abroad	Community	Community	Hospital, domestic spread
Bloodstream infections	719 (514 new cases 2021, 205 cases known from previous years)	7 (4 new cases 2021, 3 cases known from previous year)	97 (71 new cases 2021, 26 cases known from previous years)	3	2

Table 3.3. Number of laboratories used for antibiotic resistance calculations during 2015-2021.

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

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 (April 2021). 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.

Overview of sampling and culture results including the effect of the COVID-19 pandemic

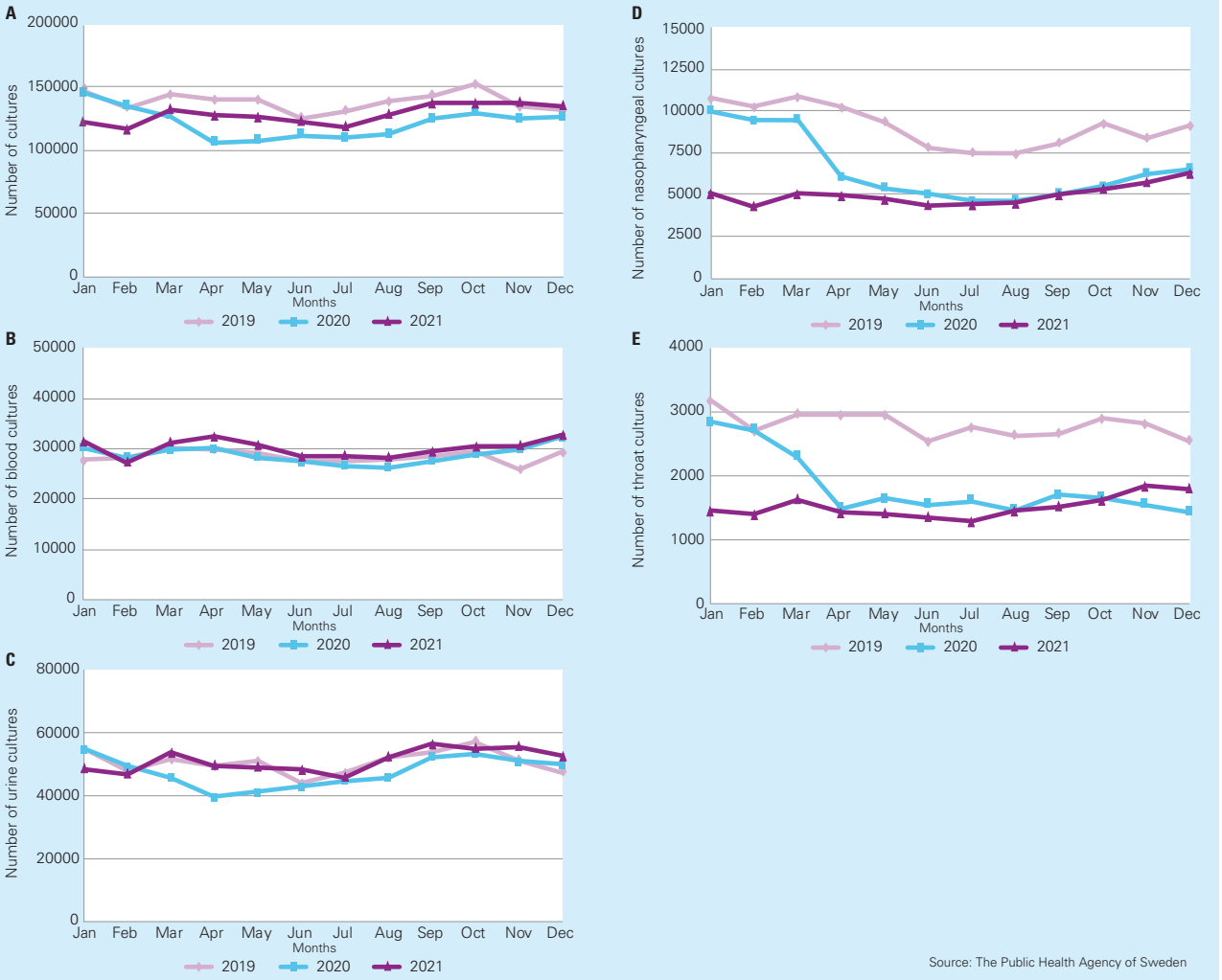
Since 2001 denominator data have been collected on a voluntary basis directly from the microbiological laboratories in Sweden and reported each year in Swedres-Svarm. From 2018 some of the data are derived from Svebar.

To evaluate the effect of the pandemic we used data from Svebar year 2019 to 2021. Twelve clinical laboratories covering around 60% of the population in Sweden were included. Complete data for 2021 from these twelve laboratories are given in Table 3.4. In Figure 3.2 the annual numbers of requested analyses are presented for: total number of cultures (A), blood cultures (B), urine cultures (C), nasopharyngeal cultures (D) and throat cultures (E). The respective numbers of isolated *S. aureus*, *E. coli*, *S. pneumoniae*, and *S. pyogenes* in all specimen types are presented in Table 3.4. The total number of cultures increased by 6% compared to 2020 but there is still a 7% decrease in total number of cultures compared to 2019. For blood cultures the increase was 4%, and for urine cultures 7%. A further decrese was seen for the number of nasopharyngeal cultures (23%) and for throat cultures (17%). The number of isolated *E. coli*, *S. aureus* and *S. pneumoniae*, regardless of specimen type, increased by 6%, 5% and 7% respectively. The number of isolated *S. pyogenes* decreased by 51%.

The extensive impact of the COVID-19 pandemic on society and health care has thus also affected the sampling for resistant bacteria, the number of hospital admissions, and the number of visits to health care facilities in general.

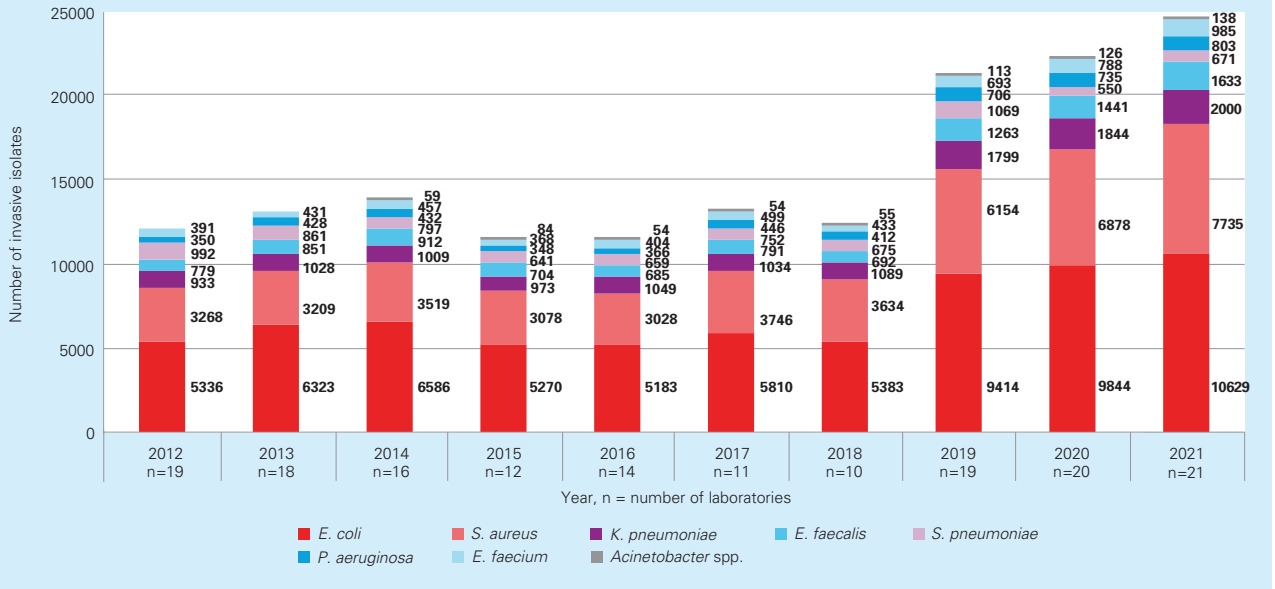
The number of bacteria reported to EARS-Net yearly is shown in Figure 3.3.

Figure 3.2 A to E. Number of requested analyses are presented for different and total number of cultures. Data from one laboratory is excluded in the calculation for blood analyses 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 2012-2021, reported to EARS-Net.



Source: The Public Health Agency of Sweden

Table 3.4. Denominator data from twelve laboratories, number of analysis, positive samples and number of cultures (*S. aureus, S. pneumoniae, S. pyogenes* and *E. coli*), year 2021. NP: Not Performed

Laboratory	Blood	Cerebro-spinal fluid (CFS)	Nasopharynx	Throat	Urine	Faeces SSYC	Blood (positive samples)	*Staphylococcus aureus*	*Streptococcus pneumoniae*	*Streptococcus pyogenes*	*Escherichia coli*
Stockholm, Karolinska Universitetsjukhuset	111 038	2 147	21 849	4 053	166 487	12 758	15 962	30 473	1 851	862	40 914
Kronoberg, Centrallasarettet Växjö	15 652	90	2 819	1 142	25 706	1 717	1 654	2 736	191	124	5 985
Region Skåne, Lund	148 938	1 020	12 901	5 579	155 041	577	14 545	19 498	957	670	34 694
Blekinge, Blekingesjukhuset Karlskrona	11 783	61	3 097	524	17 271	1 114	1 433	2 185	131	84	4 333
Kalmar, Länssjukhuset Kalmar	16 103	118	2 970	765	28 584	2 693	2 245	4 592	267	151	9 395
Västra Götalandsregionen, Norra Älvsborgs länssjukhus Trollhättan[a]	19 680	194	1 888	500	26 564	NP	2 335	3 375	103	95	6 843
Västra Götalandsregionen, Södra Älvsborgs sjukhus Borås[a]	22 392	187	2 492	680	22 606	NP	2 941	3 658	137	98	6 032
Östergötland, Universitetssjukhuset Linköping	65 181	1 183	6 497	1 700	55 925	541	4 974	8 881	370	197	13 617
Örebro, Universitetsjukhuset Örebro[a]	21 715	182	7 540	929	34 228	3 797	2 625	6 313	371	164	8 892
Värmland, Centralsjukhuset Karlstad	49 016	168	5 585	1 269	41 048	3 749	4 343	6 830	277	199	11 377
Gotland, Visby lasarett	2 941	36	1 461	179	7 871	700	544	1 411	81	20	2 251
Västerbotten, Norrlands Universitetsjukhus Umeå	37 857	521	4 160	939	32 024	2 109	3 481	5 588	308	161	10 495

[a]In 2021, data on blood are based on one culture per bottle, previous years per set of bottles. [b]Svebardata and data from local laboratory.

Escherichia coli, Klebsiella pneumoniae, and other Enterobacterales (previously Enterobacteriaceae) with ESBL and ESBL$_{CARBA}$

Mandatory reporting of ESBL-producing Enterobacterales (previously Enterobacteriaceae)

Results from 2021

- Number of reported cases: 7 860 (previous year 8 230), relative change -4%
- Number of bloodstream infections: 719 (previous year 727)

Trends

The ESBL incidence continued to decrease slightly in 2021, to 75 new cases per 100 000 inhabitants, see Figure 3.5. Since 2019, the incidence has decreased with 28%. The decrease was seen both 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 (previously Enterobacteriaceae) has increased steadily since it became notifiable but decreaed in 2020 and has then remained stable (Figure 3.4). *E. coli* was the most common cause of BSI, 79% followed by *K. pneumoniae* 13%.

All 21 regions in Sweden reported ESBL-cases and a more than twofold difference in incidence was noted, from 46 to 106 cases per 100 000 inhabitants. Different local practices in sampling could partly explaine the large variation.

The gender and age distribution has not changed significantly since the surveillance started and reflects the expected occurrence of urinary tract infections in the different groups (Table 3.2). Elderly, 85 years and older (n=777, incidence 289) followed by children under one year (n=275 incidence 240) 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 85% of all cases followed by *K. pneumoniae* with 9%. The remaining cases comprised of several other species of Enterobacterales (previously Enterobacteriaceae) (for detailed information see attached file Figure 3.5).

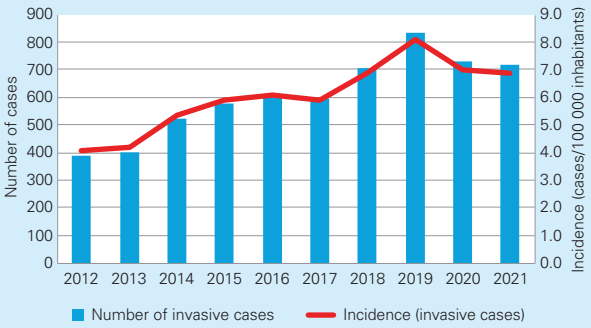
Outbreaks

In 2021, five clusters with ESBL were confirmed based on SNP-analysis (n=3-9 cases per cluster). One cluster started in 2020 with eight cases and only one additional case was reported in 2021. Four clusters were of ESBL-producing *E. coli* and one cluster were of ESBL-producing *K. pneumoniae*. All of these clusters were healthcare related. However, outbreaks with ESBL-producing Enterobacterales (previously Enterobacteriaceae) are not consistently reported.

Comments

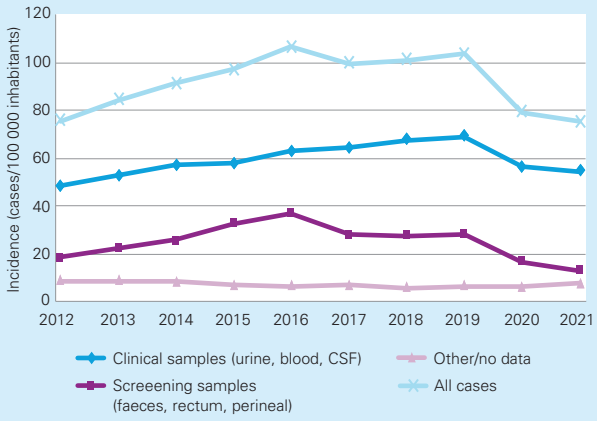
In 2021, the number of cases with ESBL-producing Enterobacterales (previously Enterobacteriaceae) continued to decrease. The decrease seen since 2019 is largely due to reduced international travel and screening for inpatient care due to the COVID-19 pandemic.

Figure 3.4. Number and incidence (cases/100 000 inhabitants) of invasive cases with ESBL-producing Enterobacterales (previously Enterobacteriaceae), reported during year 2012–2021.



Source: The Public Health Agency of Sweden

Figure 3.5. The incidence (cases/100 000 inhabitants) of cases with ESBL-producing Enterobacterales (previously Enterobacteriaceae) in relation to type of infection, year 2012–2021.



Source: The Public Health Agency of Sweden

Mandatory reporting of ESBL$_{CARBA}$-producing Enterobacterales (previously Enterobacteriaceae)

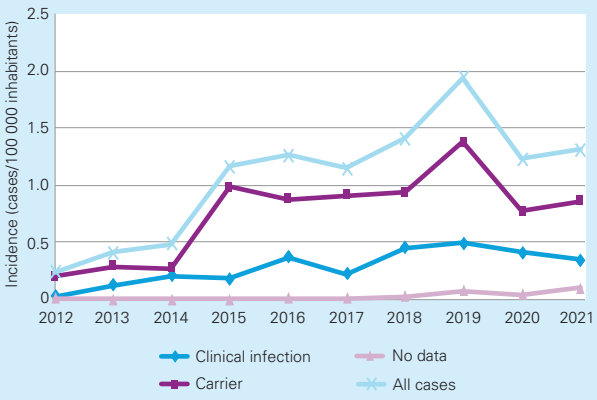
Results from 2021

- Number of reported cases: 137 (previous year 128), relative change 7%
- Number of bloodstream infections: 7 (previous year 11)

Trends

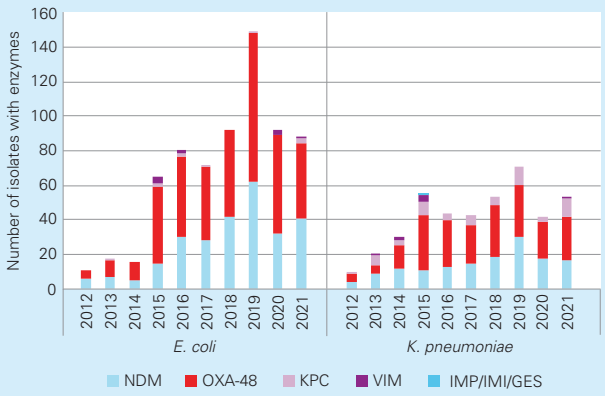
In 2021, the incidence for ESBL$_{CARBA}$ producing Enterobacterales (previously Enterobacteriaceae) was 1.3 cases per 100 000 inhabitants, a small increase with 7% (9 cases) compared to 2020. A majority, 66% of the cases, were carriers (Figure 3.6). Cases were reported from 19 of 21 regions in Sweden. The majority of cases were reported as acquired abroad (63%, n=86) and identified in targeted screening after hospitalisation abroad (n=45). Out of the 32 domestic cases, 19 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 (31%, n=10). For 15 domestic cases, information of acquisition was missing. ESBL$_{CARBA}$ cases were evenly distributed between women and men. The median age was 43 years for women and 59 years for men.

Figure 3.6. The incidence (cases/100 000 inhabitants) of cases with ESBL$_{CARBA}$ producing Enterobacterales (previously Enterobacteriaceae) in relation to type of infection, year 2012-2021.



Source: The Public Health Agency of Sweden

Figure 3.7. Number of isolates and enzyme types of ESBL$_{CARBA}$ in Enterobacterales (previously Enterobacteriaceae) in Sweden 2012-2021.



Source: The Public Health Agency of Sweden

Epidemiological typing of ESBL$_{CARBA}$

ESBL$_{CARBA}$ isolates from notified cases in 2021 have been characterised using whole genome sequencing (WGS). The most common carbapenemase-producing Enterobacterales (previously Enterobacteriaceae) was *E. coli*, accounting for 58% of all cases, followed by *K. pneumoniae* (31%). Genes encoding for carbapenem resistance have also been detected in several other species of Enterobacterales (previously Enterobacteriaceae). The dominating enzyme type in 2021 was OXA-48 and this enzyme was detected in *E. coli* and *K. pneumoniae* isolates, in most cases together with CTX-M (=ESBL$_A$) (Figure 3.7). The occurrence of ESBL$_{CARBA}$ with combinations of two carbapenemases (most commonly NDM + OXA-48) are still rare.

Table 3.5 A and B. Antibiotic resistance in $ESBL_{CARBA}$ producing *E. coli* and *K. pneumoniae*, year 2021. A, antibiotic resistance in the OXA-48-group and B, antibiotic resistance in NDM, NDM+OXA-48 group, VIM and KPC. Breakpoints for tigercycline and nitrofurantoin are only provided for *E. coli*.

A. OXA-48-group

Antibiotic	***E. coli*** (n=42)**, % S**	***E. coli*, % R**	***K. pneumoniae*** (n=21[b])**, % S**	***K. pneumoniae*, % R**
Amoxicillin-clavulanic acid[a]	-	100%	-	100%
Piperacillin-tazobactam	-	100%	-	100%
Cefotaxime	31%	67%	14%	81%
Ceftazidime	33%	57%	19%	81%
Ceftazidime-avibactam	98%	2%	100%	-
Ceftolozane-tazobactam	40%	60%	24%	76%
Tigecycline	100%	-	-	-
Colistin	100%	-	68%	32%
Nitrofurantoin	98%	2%	-	-
Trimethoprim-sulphamethoxazole	60%	38%	33%	52%
Amikacin	100%	-	62%	38%
Gentamicin	86%	12%	38%	62%
Tobramycin	81%	19%	24%	76%
Ciprofloxacin	48%	38%	14%	86%
Ertapenem	38%	62%	-	100%
Imipenem	95%	-	43%	33%
Meropenem	95%	-	48%	48%

[a]One isolate with OXA-181+NDM are excluded. [b]Six isolates with OXA-48/232+NDM are excluded.

B. NDM, NDM+OXA-48-group, VIM and KPC

Antibiotic	***E. coli*** (n=46)**, % S**	***E. coli*, % R**	***K. pneumoniae*** (n=36)**, % S**	***K. pneumoniae*, % R**
Amoxicillin-clavulanic acid[a]	-	100%	-	100%
Piperacillin-tazobactam	-	100%	-	100%
Cefotaxime	-	100%	-	100%
Ceftazidime	-	100%	-	100%
Ceftazidime-avibactam	9%	91%	31%	69%
Ceftolozane-tazobactam	-	100%	-	100%
Tigecycline	98%	2%	-	-
Colistin	100%	-	83%	11%
Nitrofurantoin	91%	9%	-	-
Trimethoprim-sulphamethoxazole	7%	93%	19%	81%
Amikacin	83%	15%	50%	50%
Gentamicin	65%	35%	56%	44%
Tobramycin	43%	57%	8%	92%
Ciprofloxacin	4%	96%	6%	94%
Ertapenem	-	100%	-	100%
Imipenem	-	89%	3%	92%
Meropenem	2%	98%	6%	83%

Apart from the genotypic analysis, isolates have been tested for antibiotic susceptibility using broth microdilution (BMD) (since June 2020) see Table 3.5. Of the 145 isolates of *E. coli* and *K. pneumoniae* tested for colistin, 10 isolates were resistant (10 *K. pneumoniae*).

Outbreaks/Clusters

In 2021, six smaller clusters of $ESBL_{CARBA}$ in Sweden were confirmed based on SNP analysis (n=2-6 cases per cluster). Five of those clusters were related to cases previous years. Four clusters were $ESBL_{CARBA}$-producing *E. coli* and two clusters were $ESBL_{CARBA}$-producing *K. pneumoniae* (see Table 3.6). A majority of the cases linked to the clusters were reported to be acquired in Sweden.

Table 3.6. Number of clusters with $ESBL_{CARBA}$ in Sweden identified by "single nucleotide polymorphism" SNPs based analysis, year 2021 (number of cases).

Resistance gene	Species	No of isolates	Year of isolation (number of cases)
NDM-5	*E. coli*	3	2021 (1), 2020 (1), 2019 (1)
NDM-5	*E. coli*	6	2021 (2), 2018 (3), 2017 (1)
OXA-244	*E. coli*	5	2021 (1), 2019 (4)
OXA-48	*E. coli*	3	2021 (1), 2020 (2)
NDM-1	*K. pneumoniae*	2	2021 (2)
KPC-2	*K. variicola*	3	2021 (2), 2020 (1)

Comments

The number of $ESBL_{CARBA}$ cases is still low in Sweden. The small increase during 2021 compared to 2020 is seen for cases infected abroad. The lack of information on the way of acquisition for nearly 50% of the domestic cases is worrisome but due to the national surveillance program, spreads can still be detected.

Escherichia coli, from blood and urine cultures

Results from 2021

- Number of reported cases with $ESBL_{CARBA}$-producing *E. coli*: 88
- Number of reported cases with bloodstream infections caused by $ESBL_{CARBA}$-producing *E. coli*: 2
- Number of reported cases with ESBL-producing *E. coli*: 6 839
- Number of reported cases with bloodstream infections caused by ESBL-producing *E. coli*: 575

Trends

The age and gender distributions (Figure 3.8 and 3.9) among patients with *E. coli* isolated from blood and urine reflects the expected occurrence of UTI and sepsis in the different groups. Resistance in *E. coli* causing urinary tract infections divided by age group and gender is shown in Figure 3.10. Ciprofloxacin resistance was higher among men compared to women, especially in ages over 20 years. No other large difference in resistance was seen in relation to increasing age.

Comments

The proportion of ESBL producing *E. coli* among invasive isolates has increased continually over the years to the current 7% (Figure 3.11). For ESBL in bloodstream infections, one of the indicators for AMR, the proportion of resistance is in general higher among men (Figure 3.12). 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 3.7). The increase in piperacillin-tazobactam resistance during 2021 is most likely due to revised breakpoints.

Resistance to commonly prescribed oral antibiotics for treatment of urinary tract infections (UTI) caused by *E. coli* remained stable (Figure 3.13). Cefadroxil resistance, which can be used as an indicator for production of ESBL, remained at 6%.

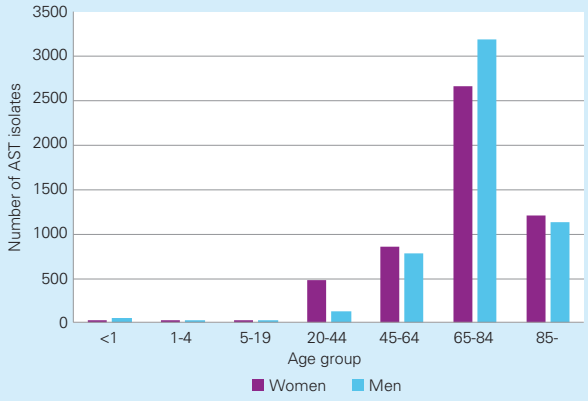
Resistance to ciprofloxacin is still high, and is now at approximately 14% and 10% for blood and urine isolates respectively (Table 3.7, Figure 3.11 and Figure 3.13). The increasing ciprofloxacin resistance seen during 2016-2017 can mostly be explained by a breakpoint change for ciprofloxacin. The high level of ciprofloxacin resistance must be considered when choosing empirical treatment for febrile UTI, especially among men in ages over 20 years (Figure 3.10 and 3.11).

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.

Table 3.7. Proportion (%) of antibiotic resistant *E. coli* from blood or urine 2021. (Revised breakpoints 2021 for piperacillin-tazobactam, EUCAST). NA: Not Applicable.

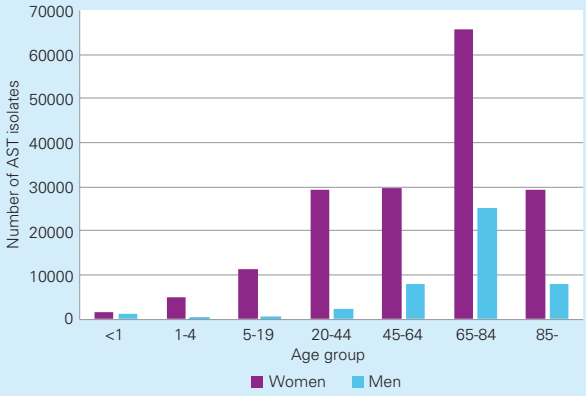
Antibiotic	Blood isolates, % R (n=10 629)	Urine isolates, % R (n=218 100)
Ampicillin	NA	28.9
Cefadroxil	NA	5.9
Cefotaxime	7.0	3.6
Ceftazidime	5.8	2.5
Ciprofloxacin	13.7	10.2
Gentamicin	5.9	NA
Tobramycin	5.6	NA
Mecillinam	NA	4.6
Meropenem	0.1	NA
Nitrofurantoin	NA	1.2
Piperacillin-tazobactam	4.7	NA
Trimethoprim	NA	18.4
Trimethoprim-sulphamethoxazole	18.5	NA
Combined resistance to Cefotaxime/ceftazidime + Gentamicin/tobramycin	2.2	NA
Combined resistance to both Piperacillin-tazobactam + Gentamicin/tobramycin	1.3	NA

Figure 3.8. Age and gender distribution among patients with *E. coli* isolated from blood. The number of isolates is based on cefotaxime AST.



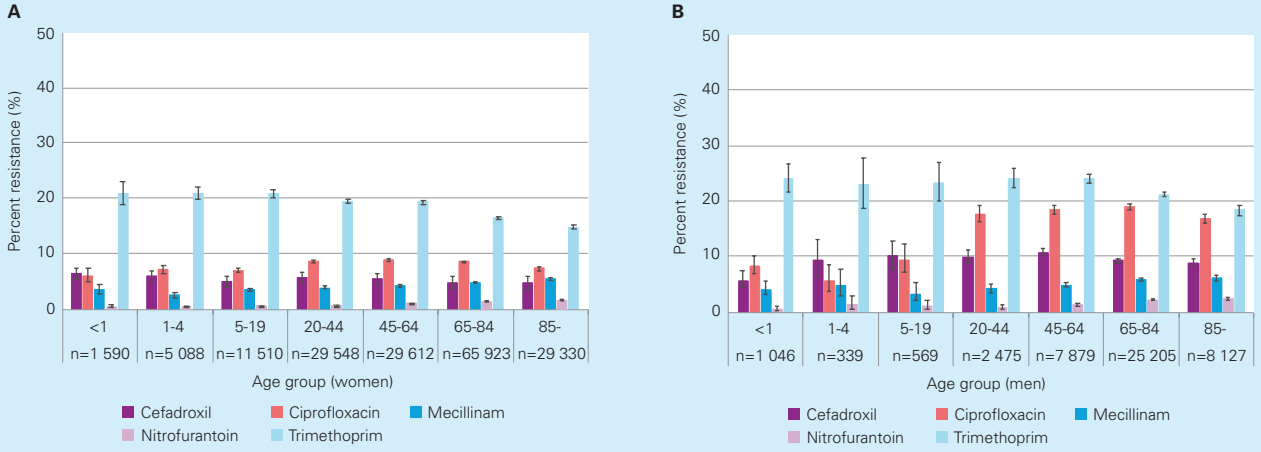
Source: The Public Health Agency of Sweden

Figure 3.9. Age and gender distribution among patients with *E. coli* isolated from urine. The number of isolates is based on ciprofloxacin AST.



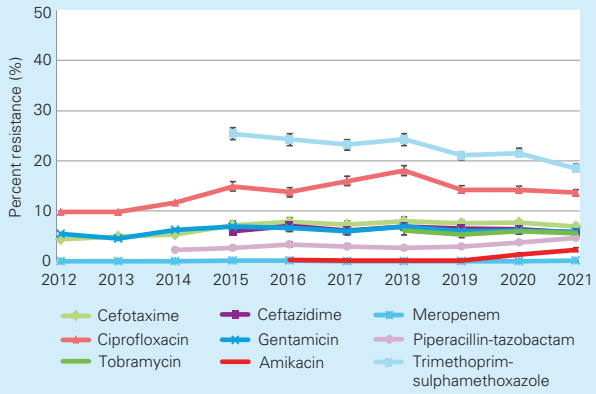
Source: The Public Health Agency of Sweden

Figure 3.10 A and B. Antibiotic resistance in *E. coli* from urine in women (A) and men (B) divided in age groups, year 2021.



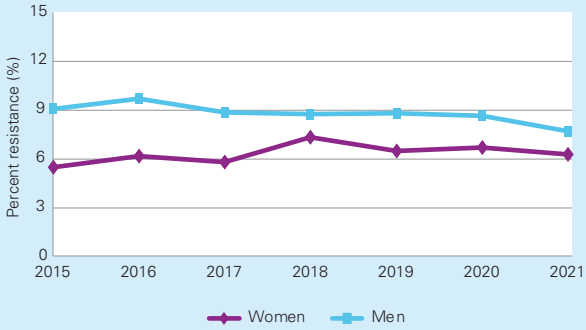
Source: The Public Health Agency of Sweden

Figure 3.11. Antibiotic resistance in *E. coli* isolated from blood during the years 2012-2021. The numbers of AST isolates for all years and antibiotics ranges from 3 983 to 10 629. The exact numbers are given in the attached file. (Revised breakpoints 2021 for piperacillin-tazobactam EUCAST version 11.0).



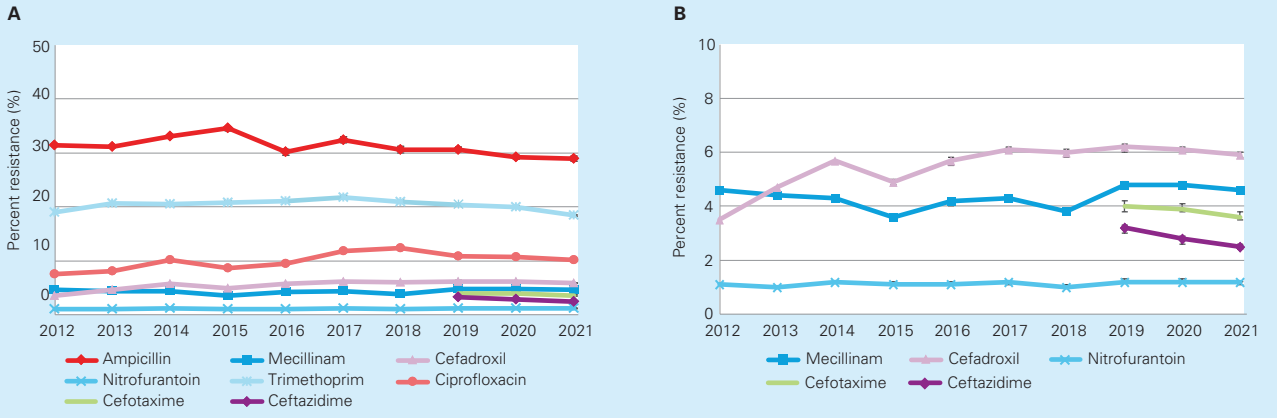
Source: The Public Health Agency of Sweden

Figure 3.12. Antibiotic resistance to cefotaxime in *E. coli* (ESBL) isolated from blood from women and men during 2015-2021.



Source: The Public Health Agency of Sweden

Figure 3.13 A and B. Antibiotic resistance in *E. coli* isolates from urine during the years 2012-2021. Figure A shows all tested antibiotics and Figure B shows more detailed data (below 10% resistance) for some antibiotics. The numbers of AST isolates for all years and antibiotics ranges from 6 417 to 218 100. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Klebsiella pneumoniae, from blood and urine cultures

Results from 2021

- Number of reported cases with $ESBL_{CARBA}$-producing *K. pneumoniae*: 47
- Number of reported cases with bloodstream infections caused by $ESBL_{CARBA}$-producing *K. pneumoniae*: 4
- Number of reported cases with ESBL-producing *K. pneumoniae*: 754
- Number of reported cases with bloodstream infections caused by ESBL-producing *K. pneumoniae*: 97

Table 3.8. Proportion (%) of antibiotic resistant *K. pneumoniae* from blood or urine 2021. Revised breakpoints for Piperacillin-tazobactam EUCAST 2021. NA: Not Applicable.

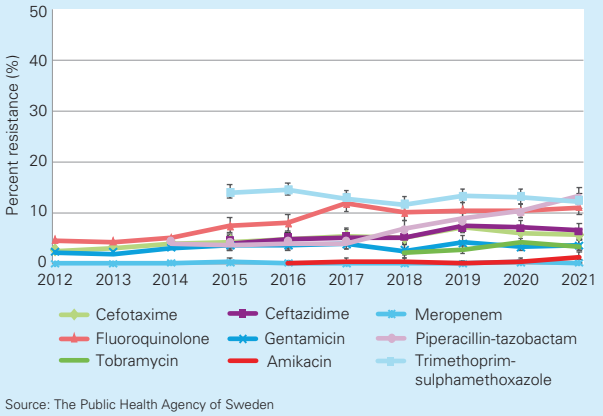
Antibiotic	Blood isolates, % R (n=2 000)	Urine isolates, % R (n=22 206)
Cefadroxil	NA	5.3
Cefotaxime	5.7	2.9
Ceftazidime	6.7	3.0
Ciprofloxacin	11.1	7.5
Gentamicin	3.7	NA
Tobramycin	3.5	NA
Mecillinam	NA	8.8
Meropenem	0.2	NA
Piperacillin-tazobactam	13.5	NA
Trimethoprim	NA	16.3
Trimethoprim-sulphamethoxazole	12.3	NA
Combined resistance to Cefotaxime/ceftazidime + Gentamicin/tobramycin	2.5	NA
Combined resistance to Piperacillin-tazobactam + Gentamicin/tobramycin	2.4	NA

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 sharp increase in piperacillin-tazobactam resistance during 2021, is most likely due to revised breakpoints. The resistance to cefotaxime was 5.7%. Combined resistance to cefotaxime/ceftazidime and gentamicin/tobramycin or the combination piperacillin-tazobactam and gentamicin/tobramycin was 2.5% and 2.4% respectively (Table 3.8 and Figure 3.14).

Resistance to commonly prescribed oral antibiotics for treatment of urinary tract infections caused by *K. pneumoniae* has remained relative stable and declined slightly during the last years (Figure 3.15). Cefadroxil resistance, which can be used as an indicator for production of ESBL, was 5.3%. 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

Figure 3.14. Antibiotic resistance in *K. pneumoniae* isolated from blood during the years 2012-2021. The numbers of AST isolates for all years and antibiotics ranges from 751 to 2 000. The exact numbers are given in the attached file. (Revised breakpoints 2021 for piperacillin-tazobactam, EUCAST).

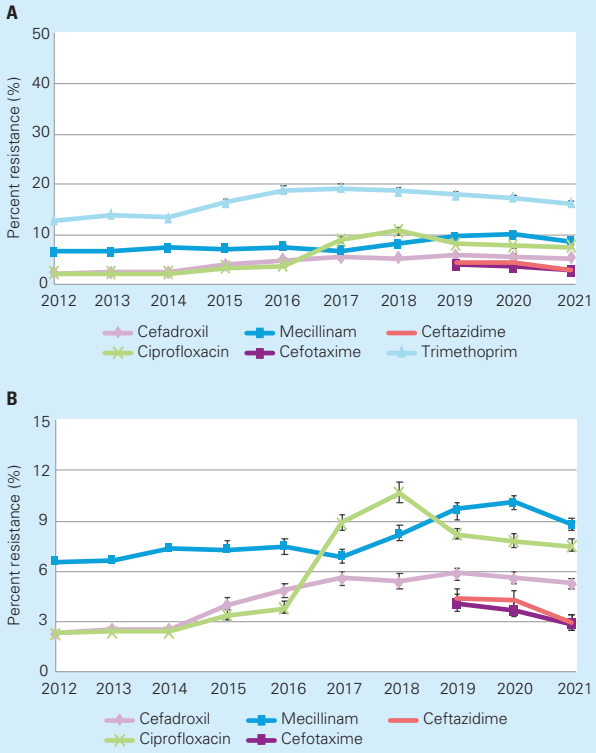


Source: The Public Health Agency of Sweden

to ciprofloxacin must be taken into account when choosing empiric treatment for febrile UTI (Figure 3.16).

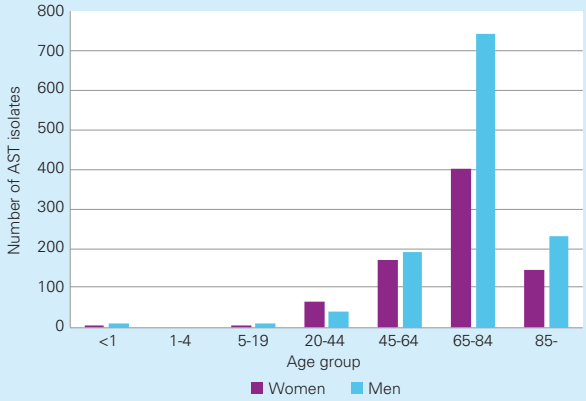
Colistin resistance is occasionally seen in *E. coli* as well as in *K. pneumoniae*, *P. aeruginosa* and *Acinetobacter*. This is mainly tested in multiresistant isolates most of which have a connection with healthcare abroad. It is important to determine colistin susceptibility with broth microdilution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

Figure 3.15 A and B. Antibiotic resistance in *K. pneumoniae* isolates from urine during the years 2012-2021. Figure A shows all tested antibiotics and figure B shows more detailed data (below 15% resistance) for some antibiotics. The numbers of AST isolates for all years and antibiotics ranges from 2 241 to 22 206. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Figure 3.16. Age and gender distribution among patients with *K. pneumoniae* isolated from blood. The number of isolates is based on cefotaxime AST.



Source: The Public Health Agency of Sweden

Staphylococcus aureus including MRSA

Mandatory reporting of methicillin-resistant *Staphylococcus aureus*

Results from 2021

- Number of reported cases: 2 895 (previous year 3 112), relative change -7%
- Number of bloodstream infections: 97 (previous year 98)

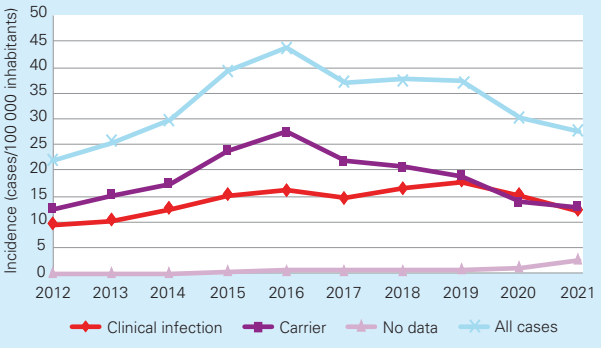
Trends

In 2021, the incidence of MRSA was 28 cases per 100 000 inhabitants compared to 30 cases per 100 000 inhabitants in 2020 (Figure 3.17). The number of cases reported with clinical infections were 1 265 (44%) while 1 347 cases (47%) were listed as carriers. MRSA-cases were reported from all 21 regions in Sweden with incidences varying from 14 to 41 cases per 100 000 inhabitants. Differences in screening and contact tracing practices between the regions could explain these variations in incidence.

There was almost equal distribution between women and men, 52% and 48%, with a median age of 32 and 36 years respectively. Among the domestic MRSA cases (n=1 713, 59%), the incidence was highest for children below one year of age (n=126, 110 cases/100 000 inhabitants) followed by the elderly, 85 years or older (n=134, 50 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.

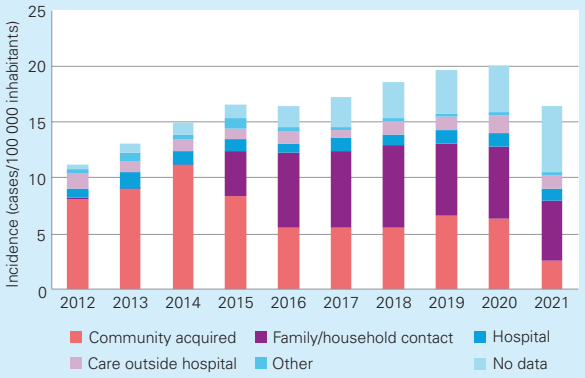
Community-acquired infections continue to be the most prominent route of acquiring MRSA (Figure 3.18). In 2015, community-acquired infections were divided into family/household-acquired or community-acquired. Among MRSA cases acquired in Sweden, 33% (n=565) were reported as acquired from family/household contacts and 16% as community-acquired (n=275). The proportion of domestic cases with MRSA acquired in hospital as well as healthcare/care outside hospital was 6% and 8% respectively (n=100 and n=130) which is the same as in year 2020. A third (n=616) of the domestic cases lacked information on acquisition.

Figure 3.17. The incidence (cases/100 000 inhabitants) of cases with MRSA in relation to type of infection, year 2012–2021.



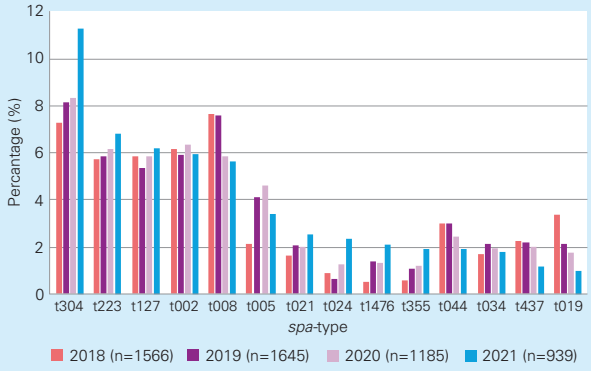
Source: The Public Health Agency of Sweden

Figure 3.18. Epidemiological classification of notified cases with MRSA acquired in Sweden, year 2012-2021. Presented as incidence (cases/100 000 inhabitants).



Source: The Public Health Agency of Sweden

Figure 3.19. The ten most common *spa*-types each year among MRSA cases with clinical infection, 2018-2021. The order of types is based on their proportions in 2021.



Source: The Public Health Agency of Sweden

Epidemiological typing of MRSA

Epidemiological typing of MRSA has since 2006 included *spa*-typing and analysis of PVL-status. PVL-status is used as an epidemiological marker that differentiates MRSA variants within *spa*-types. 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 939 (74%) of the clinical cases and for 606 isolates (45%) sampled from asymptomatic carriers. The ten most common *spa*-types were seen in 48% of the clinical cases (Figure 3.19). Among types that were previously in top ten, *spa*-type t019 has decreased over time, but also t008, t044, t034 and t437 (Figure 3.19). In 2021, *spa*-type t304 in particular increased, but also t024, t1476 and t355, all three are newly added among the ten most common types.

Outbreaks

Several minor healthcare associated transmissions of MRSA were reported from the regions during 2021 among others within neonatal ward and care homes for the elderly.

Comments

The number of reported cases continued to decrease between 2020 and 2021. Since 2019, cases with MRSA have declined with 25%. The decrease during 2020 and 2021 is largely due to reduced international travel and screening for inpatient care due to the COVID-19 pandemic. It is worrying that the proportion of domestic cases with missing information on where the infection was acquired has increased from 6% to 36% since 2012.

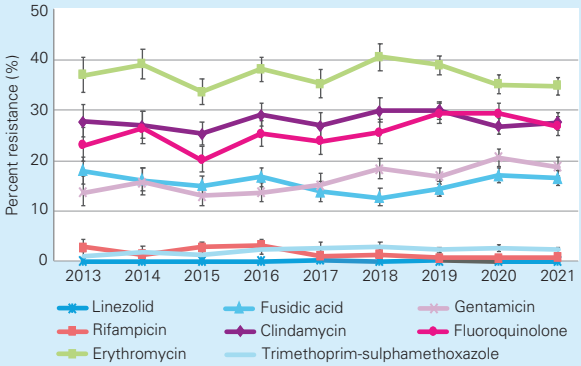
Antibiotic resistance in voluntary reported clinical isolates of MRSA

AST results for *S. aureus* from clinical isolates are presented in Table 3.9 and Figure 3.20. Here, isolates from screening and case finding have been excluded.

Comments

The proportion of MRSA has increased almost every year since 2013 (Table 3.9) with the exception of 2021. The proportion of MRSA among clinical *S. aureus* isolates were 2.1% in 2021. The resistance in MRSA to other antibiotics remained stable (Figure 3.20).

Figure 3.20. Antibiotic resistance in clinical MRSA isolates 2013-2021. The numbers of AST isolates for all years and antibiotics ranges from 576 to 2 702. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Table 3.9. Number of *S.aureus* and MRSA from clinical isolates and proportion of MRSA 2013-2021.

	2013	2014	2015	2016	2017	2018	2019	2020	2021
Number of *S.aureus*	72 560	95 444	100 543	105 990	83 362	75 034	135 924	120 204	131 035
Number of MRSA	827	1 099	1 423	1 708	1 355	1 368	2 710	2 875	2 776
Proportion of MRSA	1.1%	1.2%	1.4%	1.6%	1.6%	1.8%	2.0%	2.4%	2.1%

Staphylococcus aureus from blood and skin and soft tissue cultures

Results from 2021

- Number of cases with MRSA reported: 2 895
- Number of cases with bloodstream infections caused by MRSA: 97
- The proportion of MRSA among *S. aureus* isolated from blood has decreased to 2.0%, compared to 2.3% 2020.

Comments

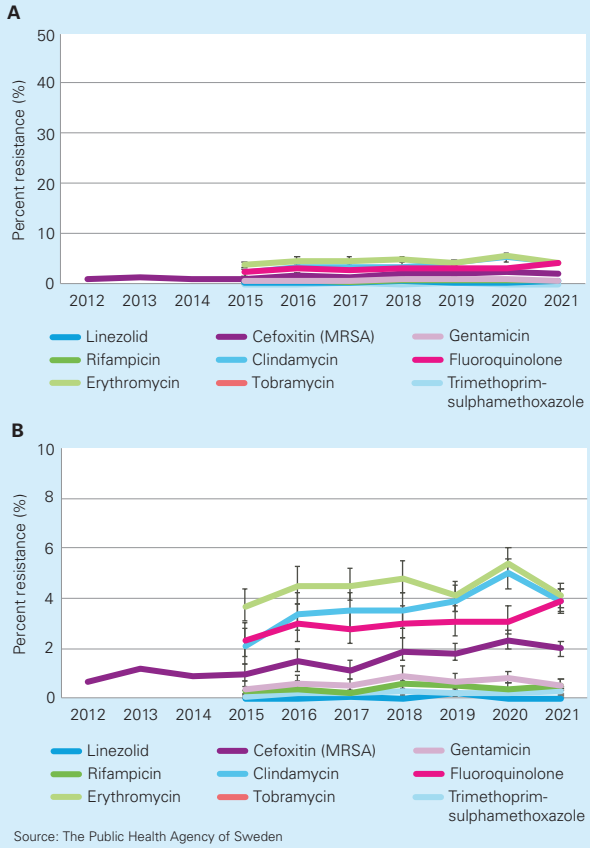
MRSA isolated from blood has slowly increased and is now 2.0% of isolated *S. aureus* (indicated by cefoxitin resistance) and the same proportion is seen for skin and soft tissue infections (Figure 3.21, Figure 3.22 and Table 3.10). For MRSA in bloodstream infections, one AMR indicator, the proportion of resistance (%) was 2.1% among men and 1.9% among women. Susceptibility testing to vancomycin is not routinely performed on cefoxitin-susceptible *S. aureus* and in 2021, 228 out of 7 735 (3%) isolates from blood were tested for vancomycin resistance with no resistance detected.

Table 3.10. Proportion (%) of antibiotic resistant isolates in *S. aureus* from blood and skin and soft tissue infections 2021. NA: Not Applicable.

Antibiotic	Blood isolates, % R (n=7 735)	Skin and soft tissue isolates, % R (n=79 811)
Cefoxitin	2.0	1.9
Clindamycin	3.9	5.5
Erythromycin	4.1	5.5
Gentamicin	0.5	NA
Tobramycin	0.7	NA
Fluoroquinolone[a]	3.9	3.9
Fusidic acid	NA	3.0
Linezolid	0.0	NA
Rifampicin	0.3	NA
Trimethoprim-sulphamethoxazole	0.3	NA

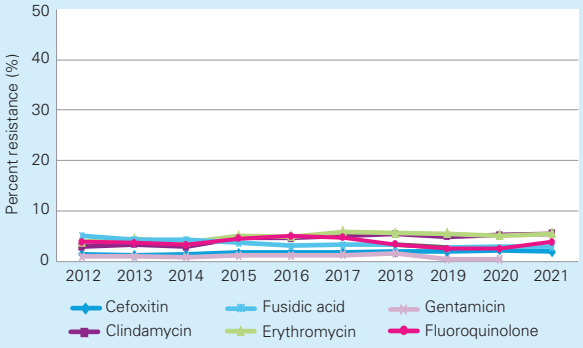
[a]Based on norfloxacin.

Figure 3.21 A and B. Antibiotic resistance in *S. aureus* from blood during the years 2012-2021. Figure A shows all tested antibiotics and Figure B shows more detailed data (below 10% resistance) for some antibiotics. The numbers of AST isolates for all years and antibiotics ranges from 3 028 to 7 735. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Figure 3.22. Antibiotic resistance for *S. aureus* from skin and soft tissue samples 2012-2021. The resistance for norfloxacin is based on results from less than five laboratories in 2018-2020 and for gentamicin in 2020. In 2021, data for aminoglycosides 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 2021

- Total number of reported cases: 209 (previous year: 79), relative change +64%.
- Number of reported cases of *E. faecium* with vancomycin resistance: 204 (previous year: 77), relative change +65%
- Number of reported cases of *E. faecalis* with vancomycin resistance: 1 (previous year: 4)
- There were three cases infected with both *E. faecium* and *E. faecalis*.
- Number of bloodstream infections: 2 (previous year: 4)

Trends

The national incidence increased from 0.8 to 2.0 cases per 100 000 inhabitants between 2020 and 2021. Nineteen out of twenty-one regions reported cases of VRE during 2021. Out of these cases, 163 (78%) were healthcare related. A majority of the isolates (n=161, 77%) were from faeces, and only 10% from urine, wound or other clinical samples (Figure 3.23). Two invasive VRE infections were reported in 2021.

In 2021, more than half of the cases were reported as acquired in Sweden (62%). Among the domestic cases 47% were found through contact tracing and 41% through screening. Cases acquired abroad were detected mostly through screening (93%).

The median age for VRE was 63.5 years and it is still most common among men, 57%. In 2021, 204 *E. faecium* cases and 1 *E. faecalis* cases were reported (not specified for 1 case). The *vanA* genotype was most commonly found (n=146) (Figure 3.24). In some cases, different genotypes of VRE were detected in the same patient and therefore a few more isolates than cases were epidemiologically typed.

Epidemiological typing

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 2021, five large hospital-related outbreaks with 11-36 cases each and six smaller clusters with 2-7 cases each were identified, all *E. faecium*. Two of the outbreaks, one reported in region Östergötland (SE-EfmA-2108) and one reported from region Gävleborg (SE-EfmA-2110), were identified during the last couple of months of 2021 and were still ongoing at the end of the year. The remaining three outbreaks were reported from region Stockholm (SE-EfmB-2005), region Västra Götaland (SE-EfmA-2102) and region Östergötland (SE-EfmA-2101).

The isolates from the invasive cases were two *E. faecium*, one carrying *vanA* and the other *vanB*, both isolates were determined as unique (Table 3.11). The isolate with *vanB* also harboured optrA, a gene connected to linezolid-resistance, and this was the only isolate identified with optrA among VRE epidemiologically typed in 2021.

Comments

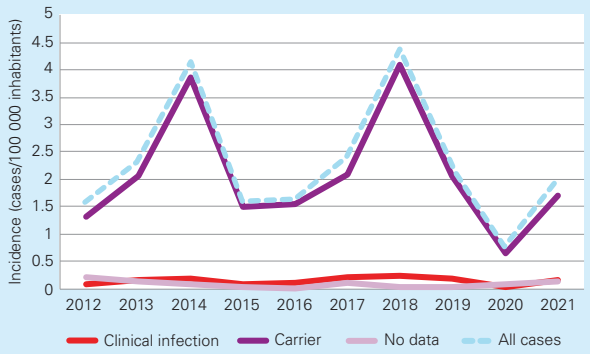
The number of VRE cases increased with over 60% during 2021. This increase was mainly due to several hospital related outbreaks. This stresses the importance of preventing spread of VRE in hospitals. The number of invasive cases decreased to 2 compared to 4 cases last year. None of the invasive cases 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.

Table 3.11. Epidemiological typing of VRE 2021.

Epidemiological typing *E. faecium*	Sequence type (ST)	Number of typed VRE
EfmA unique	15 different sequence types	63
EfmB unique	5 different sequence types	13
SE-EfmB-1707	80	1 (total 284 isolates)
SE-EfmB-2005	117	36 (total 38 isolates)
SE-EfmA-2101	203	12 (total 13 isolates)
SE-EfmA-2102	80	22
SE-EfmA-2103	203	1 (total 2 isolates)
SE-EfmA-2104	1839	7
SE-EfmA-2105	80	2
SE-EfmA-2106	80	3
SE-EfmB-2106	80	3
SE-EfmB-2107	80	3
SE-EfmA-2108	612	18
SE-EfmA-2109	375	3
SE-EfmA-2110	117	11
Total number of typed VRE	**17 different sequence types**	**198[a]**
Epidemiological typing *E. faecalis*	**Sequence type (ST)**	**Number of typed VRE**
EfsA unique	19, 6	3
EfsB unique	40	1
Total number of typed VRE	**3 different sequence types**	**4[a]**

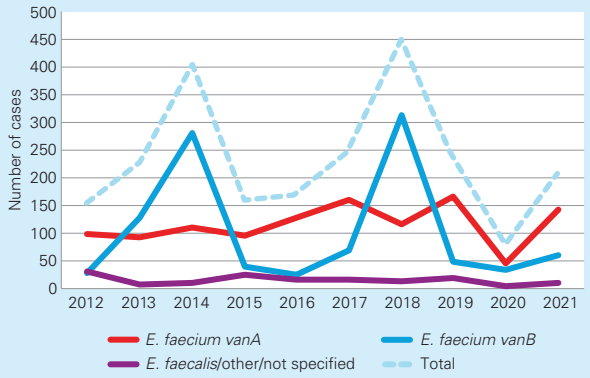
[a]The total number of isolates varies compared to the number of cases reported, since some patients have more than one isolate of *E. faecium/E. faecalis*, and not all isolates are sent to the Public Health Agency of Sweden for epidemiological typing.

Figure 3.23. The incidence (cases/100 000 inhabitants) of VRE in relation to type of infection, year 2012-2021.



Source: The Public Health Agency of Sweden

Figure 3.24. Number of VRE cases and their corresponding *van*-type.



Source: The Public Health Agency of Sweden

Enterococcus faecalis and *Enterococcus faecium*, from blood cultures

Results from 2021

- Total number of reported cases: 209 (previous year: 79), relative change +64%.
- Number of reported cases of *E. faecium* with vancomycin resistance: 204 (previous year: 77), relative change +65%
- Number of reported cases of *E. faecalis* with vancomycin resistance: 1 (previous year: 4)
- There were three cases infected with both *E. faecium* and *E. faecalis*.
- Number of bloodstream infections: 2 (previous year: 4)

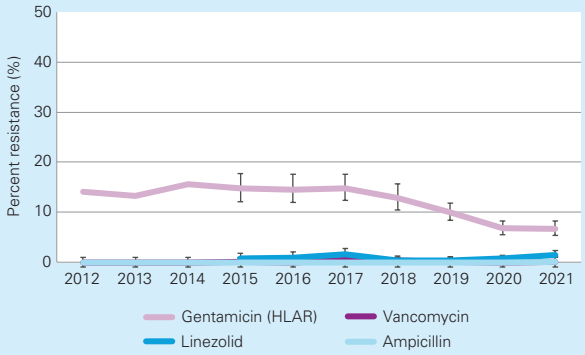
Comments

The vancomycin resistance among invasive isolates remains low and was 0.1% for *E. faecalis* and 0.3% for *E. faecium* in 2021. High-level aminoglycoside resistance (HLAR) has gradually decreased since 2017 (Table 3.12 and Figures 3.25 and 3.26).

Table 3.12. Proportion (%) of antibiotic resistant *E. faecalis* and *E. faecium* isolated from blood 2021.

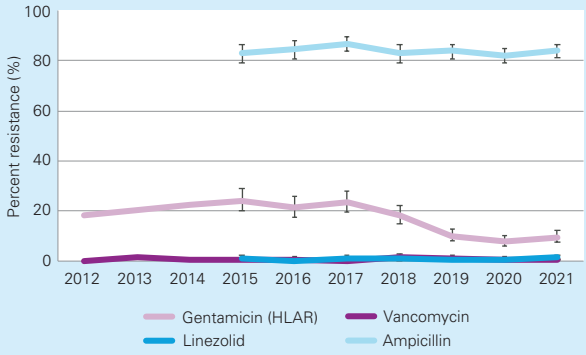
Antibiotic	Blood isolates *E. faecalis*, % R (n=1 633)	Blood isolates *E. faecium*, % R (n=985)
Ampicillin	0.1	83.8
Gentamicin (HLAR)	6.7	9.6
Linezolid	1.5	1.3
Piperacillin-tazo-bactam	0.2	84.6
Vancomycin	0.1	0.3

Figure 3.25. Antibiotic resistance in *E. faecalis* isolated from blood during the years 2012-2021. 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 3.26. Antibiotic resistance in *E. faecium* isolated from blood during the years 2012-2021. The numbers of AST isolates for all years and antibiotics ranges from 368 to 985. 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 2021

- Number of reported cases: 92 (previous year 112), relative change -17%
- Number of bloodstream infections: 3 (previous year 4)

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.

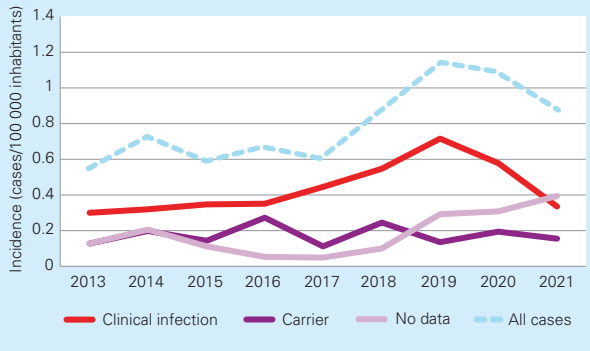
Trends

The national incidence of PNSP in 2021 was 0.9 cases per 100 000 inhabitants. The incidence for PNSP acquisition was highest among children under five years of age (3.2 cases per 100 000 inhabitants) representing 21% of all cases. Most cases were found in the age group 60-69 years (18%). Of all cases, 59% were men and 41% women.

PNSP was most often found in cultures from the nasopharynx (58%). Nineteen isolates were found in sputum/bronchoalveolar lavage (21%). Thirty-five cases were reported with clinical infections (38%, incidence 0.3) and 15% (n=16, incidence 0.2) as carriers (Figure 3.27).

A majority of the cases had been acquired in Sweden (47%, n=43) and four percent of the cases were acquired abroad. For the remaining cases, no country of acquisition was given (49%).

Figure 3.27. The incidence (cases/100 000 inhabitants) of cases with PNSP in relation to type of infection, year 2013-2021.



Source: The Public Health Agency of Sweden

Epidemiological typing

A total of 84 isolates with PcG MIC > 1 mg/L were sent to PHAS for serotyping during 2021 (91% of notified cases). Of these isolates, 52% (n=45) belonged to serotypes included in the conjugate vaccines (PCV10 and/or PCV13); Figure 3.28. The corresponding figures for 2020 and 2019 were 44% and 60% respectively. Two of the three isolates from invasive cases typed in 2021 were of vaccine type (6B och 19A) and the third case, were of 9N type (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 PNSP isolates with PcG MIC ≥ 0.5 mg/L for serotyping. In 2021, 206 isolates were collected (including the 86 isolates from cases of PNSP). The serotype distribution were, in decending order: 19A (13%), NT (12%), 35B (9%), 19F (8%), 23B (7%), 3 (7%), 6B (5%) and 23F (5%). Of the 206 isolates, 36% constituted of types included in the conjugate vaccines (PCV10 and/or PCV13).

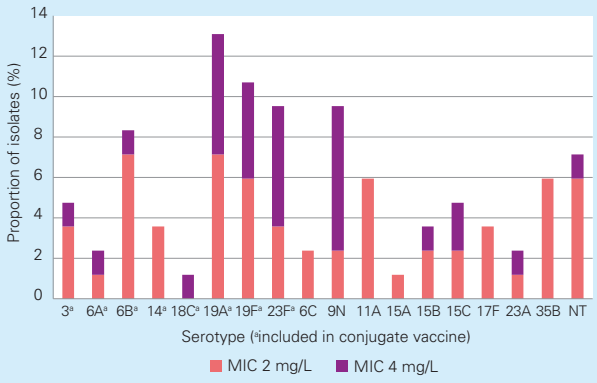
Outbreaks

No clusters were reported during 2021.

Comments

Overall, the incidence of PNSP has remained fairly stable up to 2017 after the case definition was changed in May 2012 (Figure 3.27). The increase from 2017 could partly be due to changes in diagnostics, as more laboratories have switched to reporting data based on broth microdilution.

Figure 3.28. Distribution of serotype MICs among PNSP with PcG MIC > 1 mg/L (n=84).



Source: The Public Health Agency of Sweden

Streptococcus pneumoniae, from blood

Results from 2021

- Number of reported cases of PNSP: 92 cases
- Cases with bloodstream infections caused by PNSP: 3
- Number of reported cases of invasive pneumococcal disease: 731

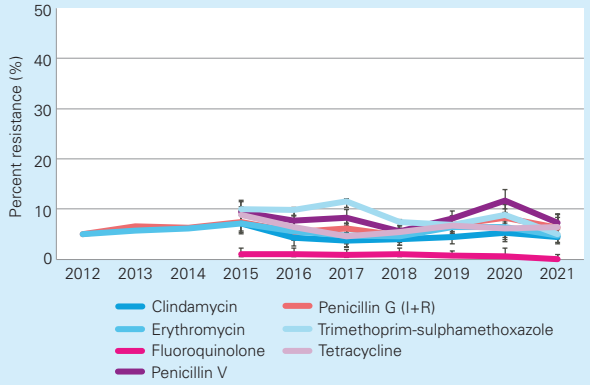
Table 3.13. Proportion (%) of antibiotic resistant *S. pneumoniae* isolated from blood 2021.

Antibiotic	Blood isolates, % R (n=671)
Clindamycin	4.5
Erythromycin	4.8
Fluoroquinolone	0.0
Penicillin G (I+R)	6.3
Penicillin V	7.3
Tetracycline	6.4
Trimethoprim-sulphamethoxazole	5.1

Comments

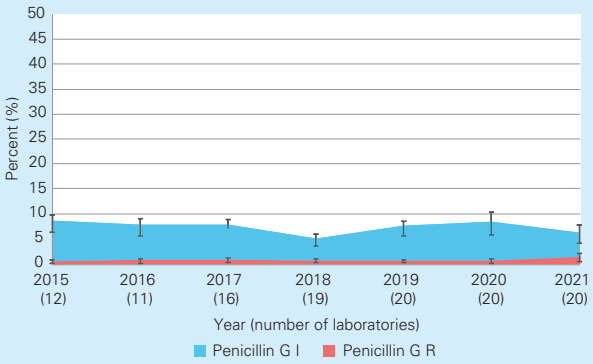
The methodological problem with underestimation of benzylpenicillin (PcG) MIC when using gradient tests does not influence the resistance proportions since I and R are reported together. Among invasive infections, the proportion of PcG non-susceptible isolates was 6.3% in 2021 (Table 3.13 and Figure 3.29).

Figure 3.29. Antibiotic resistance in *S. pneumoniae* isolated from blood during the years 2012-2021. Penicillin V resistance is based on susceptibility testing using oxacillin. The numbers of AST isolates for all years and antibiotics ranges from 550 to 1 069. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Figure 3.30. Penicillin resistance in *S. pneumoniae* from bloodstream infections (I+R) presented as proportion of susceptible, increased exposure (I) and resistant (R) to penicillin.



Source: The Public Health Agency of Sweden

Haemophilus influenzae, from blood and nasopharynx cultures

Results from 2021

- Number of reported cases of invasive *H. influenzae*: 78

Trends

During 2021, 18 isolates were received within the microbiological characterisation program for cephalosporin resistance in *H. influenzae* at PHAS. The majority of these (n=15) showed high-level resistance to extended-spectrum cephalosporins, caused by alterations in penicillin-binding protein 3 (PBP3). Four of these isolates also carried the betalactamase $bla_{\text{TEM-1}}$ gene which is the most prevalent gene of the acquired betalactamases. The remaining three isolates showed lower level resistance to cephalosporins. Four of the isolates also had genetic mutations in known genes that can give rise to fluoroquinolone resistance.

No clusters were detected during 2021, however one isolate was found to be part of the large cluster with high-level cephalosporin resistant *H. influenzae* from 2019 to 2020, now with 25 cases.

Table 3.14. Proportion (%) of antibiotic resistant *H. influenzae* from blood or nasopharynx 2021.

Antibiotic	Blood isolates, % R (n=72)	Nasopharynx isolates, % R (n=2 460)
Ampicillin/Amoxicillin	25.5	26.8
Amoxicillin-Clavulanic acid	NA	14.2
Cefotaxime	1.9	NA
Fluoroquinolone[a]	6.1	1.8
Penicillin G	26.9	33.6
Tetracycline	0.0	0.6
Trimethoprim-sulphamethoxazole	13.9	23.9

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

Table 3.15. Antibiotic resistance in *H. influenzae* isolated from blood during the years 2015-2021. The numbers of AST isolates for all years and antibiotics ranges from 70 to 209. The exact numbers are given in the attached file.

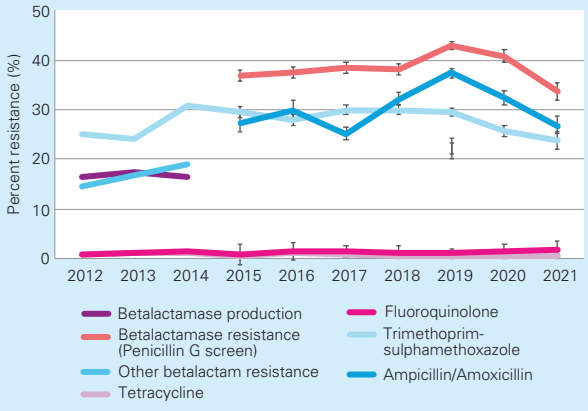
Antibiotic	2015			2016			2017			2018			2019			2020			2021		
	n tested	% R[a]	95% CI	n tested	% R[a]	95% CI	n tested	% R[a]	95% CI	n tested	% R[a]	95% CI	n tested	% R[a]	95% CI	n tested	% R[a]	95% CI	n tested	% R[a]	95% CI
Number of AST isolates	**109**			**78**			**122**			**111**			**209**			**74**			**73**		
Betalactamase resistance (Penicillin G screen)	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)
Trimethoprim-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)
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)
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)
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)
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)
Cefaclor													98	30.6	(22.4-40.3)	35	28.6	(16.3-45.1)	NA	NA	NA

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

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 3.14 and Table 3.15). Among respiratory isolates, the resistance levels were decreasing (Figure 3.31). Since there is a large decrease in the number of isolates, 2 460 in 2021 compared to 5 655 in 2020 and 13 332 in 2019, the results should be interpreted with caution.

Figure 3.31. Antibiotic resistance in *H. influenzae* isolated from nasopharynx during the years 2012-2021. The numbers of AST isolates for all years and antibiotics ranges from 2 149 to 13 332. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Pseudomonas aeruginosa, from blood and non-respiratory cultures

Results from 2021

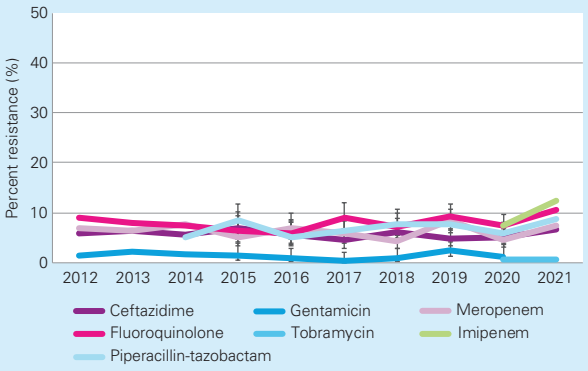
Table 3.16. Proportion (%) of antibiotic resistant *P. aeruginosa* isolated from blood and non-respiratory specimens 2021. NA: not applicable.

Antibiotic	Blood isolates % R (n=803)	Non-respiratory isolates % R (n=18 832)
Ceftazidime	6.6	4.6
Ciprofloxacin	10.7	9.6
Gentamicin	NA	NA
Tobramycin	0.7	0.8
Meropenem	7.5	5.0
Piperacillin-tazobactam	8.7	6.6

Comments

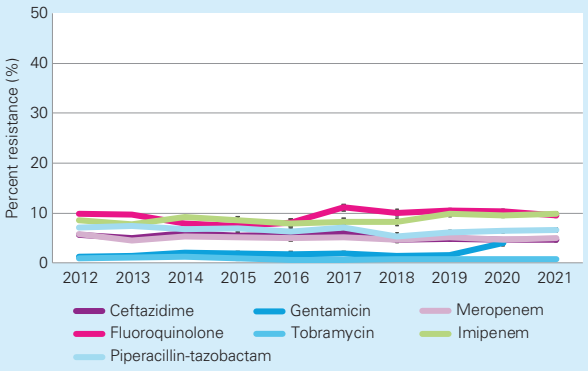
Resistance to ceftazidime is most often due to efflux pumps and porin loss, not ESBL production. The resistance for most antibiotics is stable for both blood isolates and non-respiratory isolates (Table 3.16, Figure 3.32 and 3.33). Tobramycin has replaced gentamicin as recommended aminoglycoside. Colistin 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.

Figure 3.32. Antibiotic resistance in *P. aeruginosa* isolated from blood during the years 2012-2021. The numbers of AST isolates for all years and antibiotics ranges from 348 to 803. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Figure 3.33. Antibiotic resistance in *P. aeruginosa* from non-respiratory isolates 2012-2021. 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

Acinetobacter spp., from blood cultures

Results from 2021

Table 3.17. Antibiotic resistance in *Acinetobacter* species isolated from blood.

Antibiotic	2014		2015		2016			2017			2018			2019			2020			2021		
	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
Number of AST isolates	**59**		**84**		**54**			**54**			**55**			**113**			**126**			**138**		
Meropenem		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)
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)
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)
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)
Tobramycin														67	0.0	(0.0-5.4)	65	12.3	(6.4-22.5)	75	2.7	(0.7-9.2)
Amikacin														65	7.7	(3.3-16.8)	61	11.5	(5.7-21.8)	66	1.5	(0.3-8.1)

Comments

During 2021, a total of 138 isolates of *Acinetobacter* spp. from blood was reported to Svebar. The carbapenem resistance was 0.8% (Table 3.17). 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 2021

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

Table 3.18. Antibiotic resistance in *S. pyogenes* isolated from blood 2015-2021.

Antibiotic	2015			2016			2017			2018			2019			2020			2021		
	n tested	% R	95% CI	n tested	% R	95% CI	n tested	% R	95% CI	n tested	% R	95% CI	n tested	% R	95% CI	n tested	% R	95% CI	n tested	% R	95% CI
Erythromycin	235	3.4	(1.7-6.6)	266	2.6	(1.3-5.3)	337	3.2	(1.8-5.7)	343	4.2	(0.0-1.1)	539	3.7	(2.4-5.7)	298	3.4	(1.8-6.1)	139	14.4	(9.5-21.2)
Clindamycin	233	3.0	(1.5-6.1)	270	3,0	(1.5-5.7)	336	1.5	(0.6-3.4)	344	3,2	(0.0-1.1)	536	3,0	(1.8-4.8)	298	3.4	(1.8-6.1)	139	14.4	(9.5-21.2)
Tetracycline	154	7.1	(4.0-12.3)	153	9.2	(5.5-14.8)	195	8.7	(5.5-13.5)	175	6.9	(4.0-11.6)	125	6.4	(3.3-12.1)	103	7.8	(4.0-14.6)	38	26.3	(15.0-42.0)
Trimethoprim-sulphamethoxazole	135	1.5	(0.4-5.2)	155	2.6	(1.0-6.4)	201	9.5	(6.1-14.3)	165	6.1	(3.3-10.8)	338	3.8	(2.3-6.5)	214	4.7	(2.6-8.4)	104	5.8	(2.7-12.0)
Penicillin G	170	0.0	(0.0-2.2)	183	0.0	(0.0-2.1)	232	0.0	(0.0-1.6)	347	0.0	(0.0-1.1)	539	0.0	(0.0-0.7)	298	0.0	(0.0-1.3)	138	0	(0.0-2.7)

Comments

Invasive cases of *S. pyogenes* are notifiable according to the Communicable Disease Act and in 2021, 157 cases were reported. This is a further decrease with 58% compared with previous year (n=376) and in line with most respiratory infections during the COVID-19 pandemic. The invasive cases have decreased with 80% since year 2019. AST results from 139 isolates were available from Svebar (Table 3.18). Some laboratories did not test susceptibility for trimethoprim-sulphamethoxazole and tetracycline. The variation in resistance should be interpreted with caution since there is a small number of tested isolates.

Streptococcus agalactiae, from blood cultures

Results from 2021

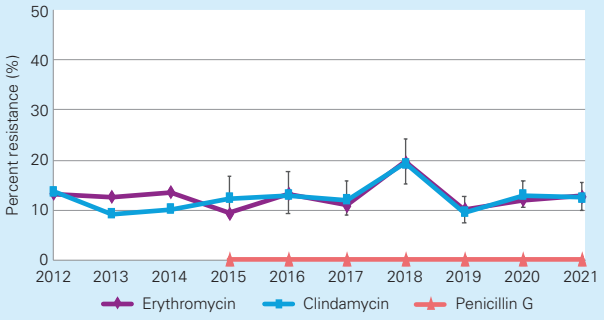
Table 3.19. Proportion of antibiotic resistant *S. agalactiae* isolated from blood 2021.

Antibiotic	Blood isolates, % R (n=607)
Penicillin G	0.0
Erythromycin	12.9
Clindamycin	12.5

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 approximately 13% (Table 3.19 and Figure 3.34).

Figure 3.34. Antibiotic resistance in *S. agalactiae* (GBS) from bloodstream isolates during the years 2012-2021. 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*

A total of 187 cases with shigellosis were notified in 2021, a slight increase of cases compared to 2020 (161 cases), but much fewer cases in comparison to the pre-pandemic year 2019 when 524 cases were reported. Primarily travel-related cases have decreased, because of the changing travel patterns during the pandemic.

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 half of all cases in 2021 the infection was acquired abroad and 43 percent were reported as acquired in Sweden. Species identification were available for 77 of the cases. Here,

Table 3.20. Antibiotic resistance in *Shigella* spp. from faecal samples 2017-2021. Data for azithromycin are not shown for 2021 due to the low number of tested samples. The numbers of AST isolates for all years and antibiotics ranges from 40 to 242.

***Shigella* spp.**	**2017**			**2018**			**2019**			**2020**			**2021**		
Sample: faeces	**n tested**	**% R**	**95% CI**	**n tested**	**% R**	**95% CI**	**n tested**	**% R**	**95% CI**	**n tested**	**% R**	**95% CI**	**n tested**	**% R**	**95% CI**
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)
Trimethoprim-sulphamethoxazole	111	76.6	(67.9-83.5)	179	80.4	(74.0-85.6)	240	71.7	(65.7-77.0)	63	73	(61.0-82.4)	65	69.2	(57.2-79.1)
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)
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)
Meropenem	93	0	(0.0-4.0)	145	0	(0.0-2.6)	204	0	(0.0-1.8)	55	0	(0.0-6.5)	51	0	(0.0-7.0)
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)			
Piperacillin-tazobactam	74	0	(0.0-4.9)	102	0	(0.0-3.6)	152	0	(0.0-2.5)	40	2.5	(0.4-12.9)	44	0	(0.0-8.0)

S. sonnei were identified in 51 of the isolates, *S. flexneri* in 21 isolates and five were *S. boydii*.

In 2021, 17 cases with Shigella were also mandatory notified as ESBL-producing Enterobacterales (previously Enterobacteriaceae). Of the six cases with known ESBL-type, five had $ESBL_A$ and one $ESBL_M$. No cases with Shigella carrying $ESBL_{CARBA}$ have been reported during 2021.

Shigella spp., from faecal samples

In 2021, 81 isolates of Shigella were reported in Svebar and AST results were available for 65 isolates. The majority of isolates with AST were *S. sonnei* and *S. flexneri*, with 51% and 28% 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 3.20).

Comments

In 2021, few isolates with an AST were available for analysis. 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

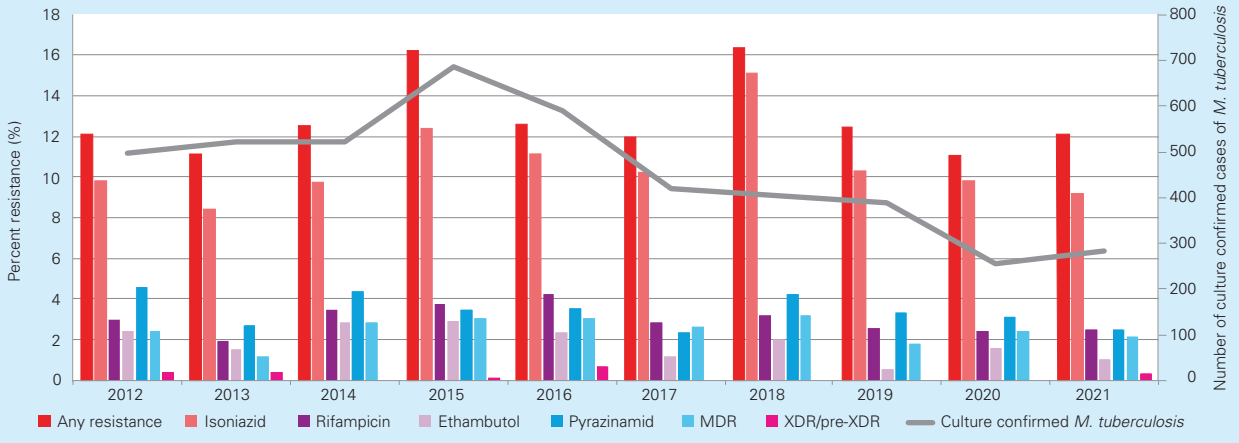
During 2021 a total of 365 cases of tuberculosis (TB) were reported compared to 335 cases during 2020 which is an increase of 9%. Out of the 365 cases six were already on TB treatment when arriving in Sweden.

The number and proportion of culture confirmed cases were 286 (79%) compared to 264 (79%) in 2020. *Mycobacterium bovis* was identified in four cases and *Mycobacterium tuberculosis* in 282 cases. The proportions of cases diagnosed with MDR-TB was 2.1% (6/282) compared to 2.4% (6/255) in 2020. One of the MDR-cases was classified as pre-XDR-TB (additional resistance to fluoroquinolones).

Isolates of *M. tuberculosis* resistant to at least one of the four first line drugs (isoniazid, rifampicin, ethambutol or pyrazinamid) were identified in 30 patients corresponding to 11% of the 282 cases with culture confirmed *M. tuberculosis*, see Figure 3.35. As always the most common resistance found was against isoniazid.

Of 40 cases born in Sweden none of 28 with culture confirmed diagnosis had resistant TB. Of all the TB cases reported in Sweden 2021, 90% were born in another country. In total, 254 in this group had a culture confirmed infection with *M. tuberculosis* and 29 (11%) had some kind of resistance out of which six had MDR-TB.

Figure 3.35. Drug resistance and number of culture confirmed *M. tuberculosis* in Sweden 2012-2021.



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, 11% (41/365) were considered as infected in Sweden and of 279 (including *M. bovis*) cases analysed with whole genome sequencing 84% were unique isolates not belonging to any cluster.

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

Overall the number of cases reported and the proportion of patients with *M. tuberculosis* resistant against any antibiotics including the proportion of MDR-TB has been decreasing for some years now.

Neisseria gonorrhoeae, mandatory reporting

Gonorrhoea is a notifiable infection and in 2021, 2 700 cases (26 cases per 100 000 inhabitants) of gonococcal infections were reported to the Public Health Agency of Sweden. This is the same level as in 2020 (2 692 cases, incidence of 26 cases per 100 000 inhabitants). Notably, the decreased gonorrhoea incidences in 2020 and 2021 compared to in 2019 (3 245 cases, incidence of 31 cases per 100 000 inhabitants) were most likely largely caused by the COVID-19 pandemic and its associated restrictions, e.g. the impact of social and physical distancing, travel restrictions, and decreased diagnostic testing. From 2009 to 2019, the gonorrhoea incidence increased by a mean of 15% each year. As in earlier years, most of the gonorrhoea cases in 2021 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 Swedish 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; Department of Clinical Bacteriology, The Sahlgrenska Academy at University of Gothenburg, Göteborg, and Department of Clinical Microbiology, Karolinska University Hospital, Stockholm. In 2021, 1 583 clinical *N. gonorrhoeae* isolates (multiple isolates from some patients) were characterised in regard to antimicrobial susceptibility.

Antimicrobial susceptibility testing was performed according to standardised and quality assured methodology using Etest for MIC determination of ceftriaxone, cefixime, azithromycin, 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 3.21, the antimicrobial resistance in clinical gonococcal isolates cultured in 2021 are compared with those from 2011 to 2020. Briefly, the level of resistance to ciprofloxacin, which previously was used as first-line treatment for gonorrhoea, remains very high and increased to 69% in 2021. The proportion of isolates above the azithromycin ECOFF was 25%, which represents a substantial increase since 2020 (19%). Notably, 92% of the isolates with an azithromycin MIC above the azithromycin ECOFF had an MIC of 2 mg/L, i.e. only one 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 decreased from 2% in 2020 to <1% (0.5%) in 2021, which is a similar level of resistance as documented in 2016-2019. As in 2015-2020, no resistance to ceftriaxone was identified in 2021. This is exceedingly promising because ceftriaxone is the last remaining option for empirical antimicrobial monotherapy of gonorrhoea. Similar decreases in the resistance to the extended-spectrum cephalosporins (ceftriaxone and cefixime) have been reported in several additional European countries. The reasons for this decline are likely complex, however, most likely the European recommendations to use ceftriaxone (500-1000 mg) plus azithromycin (2 g) OR ceftriaxone 1000 mg monotherapy in the empiric first-line treatment of gonorrhoea have been effective to eradicate cefixime- and ceftriaxone-resistant gonococcal strains that have been spreading internationally. 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.

Table 3.21. Antibiotic resistance rates (%) of Swedish clinical *Neisseria gonorrhoeae* isolates 2012-2021.

	2012 (n=877)	2013 (n=967)	2014 (n=384)	2015 (n=462)	2016 (n=601)	2017 (n=528)	2018 (n=580)	2019 (n=1 035)	2020 (n=1 713)	2021 (n=1 583)
Cefixime	10	4	2	2	1	<1 (0.6)	1 (1.2)	<1 (0.8)	2	<1 (0.5)[b]
Ceftriaxone	1	<1 (0.3)	<1 (0.3)	0	0	0	0	0	0	0
Azithromycin	10	13	9	10	3	5	5[a]	12[a]	19[a]	25[a]
Ciprofloxacin	62	53	60	53	53	47	57	60	58	69
Spectinomycin	0	0	0	0	0	0	0	0	0	0[b]

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

Neisseria meningitidis, mandatory reporting

Invasive meningococcal disease is a notifiable disease and in 2021, only 10 cases (0.1 cases per 100 000 inhabitants) of the disease were reported. This represents a continuous decrease with 64% compared to 2020 (28 cases), which in turn represented a decrease with 58% from the 66 reported cases in 2019. Eight of the 10 clinical invasive isolates from blood and/or cerebrospinal fluid (one isolate per patient) in 2021 were analysed at the Swedish 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. The pronounced decrease in incidence of invasive meningococcal disease 2021 as well as 2020 is most likely associated with the COVID-19 pandemic restrictions, e.g. social and physical distancing, and travel restrictions.

Antimicrobial susceptibility testing was performed according to standardised 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 discs.

One isolate had an intermediate susceptibility to penicillin G (MIC=0.25 mg/L). All isolates (100%) were susceptible to cefotaxime (MIC values of 0.002-0.008 mg/L), meropenem (MICs: 0.004-0.032 mg/L), chloramphenicol (MICs: 0.25-2 mg/L), ciprofloxacin (0.002-0.008 mg/L), and rifampicin (MICs: 0.002-0.125 mg/L). None of the isolates obtained in 2021 produced β-lactamase, and in fact no β-lactamase-producing meningococcal isolate has ever been identified in Sweden.

Clostridioides difficile

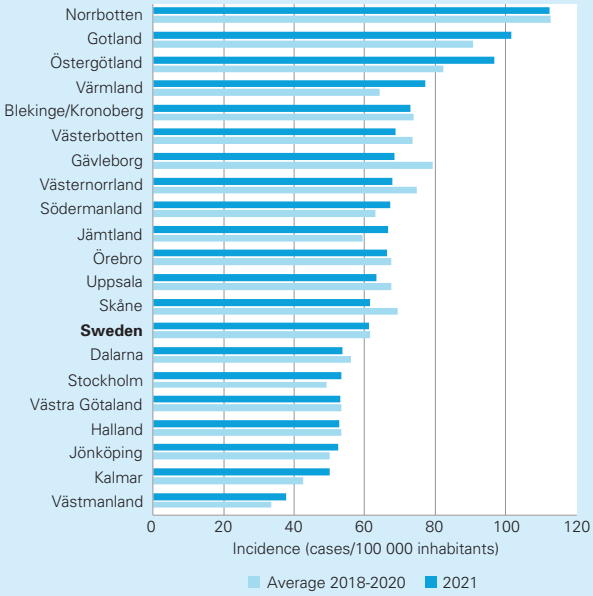
Incidence of CDI

In 2021, 6 417 new CDI cases were reported corresponding to an incidence of 61 cases per 100 000 inhabitants (data corrected for reccurent CDI for two laboratories reporting all cases). As in previous years, there are major differences between regions (spread 38-113 cases per 100 000 inhabitants; Figure 3.36). The incidence has remained stable the last years.

In the national surveillance program, isolates collected during weeks 39-40 (n=276/290 from 24 out of 26 laboratories) were typed and 61 ribotypes were identified. The 20 most common types accounted for about 80% of all isolates compared to 78% in 2020. Type 014 was again the most common type, followed by 002 and 005. The diversity of types varied between regions and the national average (0.76) was at the same level compared to previous years.

Since the resistance situation has been stable in recent years, no testing of isolates for antibiotic susceptibility was done in 2021.

Figure 3.36. The incidence of new cases with *C. difficile* (cases/100 000 inhabitants) by region in 2021 and average for the years 2018-2020. The regions are ranked from highest to lowest incidence in 2021. 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* and *Salmonella*

Mandatory reporting of *Campylobacter*

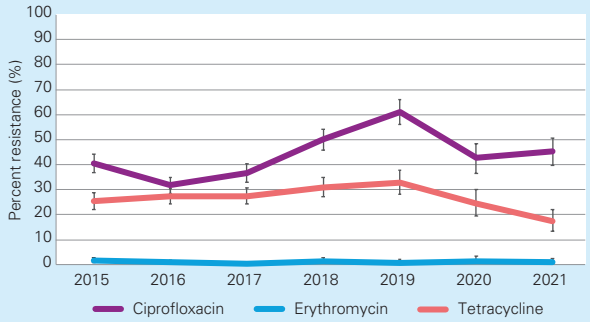
A total of 4 059 cases were reported in 2021. This is an increase in cases with 20% compared with 2020, but still approximately 40% less than in 2019. The decrease is a result of the COVID-19 pandemic and, most likely, a result of decrease in international travel. Almost three quarters of cases were considered to be acquired in Sweden during 2021. In 2019, 55% of cases were acquired abroad.

In the national surveillance program, isolates from domestic cases were collected during four weeks in 2021 (week 34-37). The focus of the epidemiological typing using whole-genome sequencing is species identification and cluster analysis to identify common sources.

Campylobacter jejuni, from faecal samples

A total of 2 565 *Campylobacter* species were found in faecal sampling. More than half of the isolates were reported as *C. jejuni* (59%), 30% as *C. jejuni/C. coli* and 11% were other species. The presence of AST data, and in a sufficient number of isolates, were highest for *C. jejuni* (23% of all *C. jejuni* isolates).

Figure 3.37. Antibiotic resistance in *Campylobacter jejuni* from faecal samples 2015-2021. 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

Comments

For *C. jejuni* the resistance to ciprofloxacin was 45% and 17% for tetracycline in 2021. Just below one percent were resistant to erythromycin (Figure 3.37). The proportion of isolates fully susceptible to erythromycin, ciprofloxacin and tetracycline were 53% and fully resistant were 0.3% (Table 3.22). It should be noted that the number of isolates with combined AST are low and only one fully resistant isolate was reported.

During the pandemic years, 2020-2021, the total number of notified cases have decreased and the proportion of cases infected in Sweden have increased. During 2018-2019, the majority of notifiable Campylobacter infections were acquired abroad. 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 3.37) and a higher percentage of isolates were fully susceptible as well (Table 3.22).

Table 3.22. Combined susceptibility and resistance to erythromycin, ciprofloxacin and tetracycline in *Campylobacter jejuni* from faecal samples 2015-2021.

	2015	2016	2017	2018	2019	2020	2021
Number of isolates with combined AST for erythromycin, ciprofloxacin and tetracycline	659	793	697	544	352	253	304
Proportion fully susceptible to erythromycin, ciprofloxacin and tetracycline, %	54	61	60	47	38	56	53
Proportion fully resistant to erythromycin, ciprofloxacin and tetracycline, %	1.4	0.8	0.4	0.9	0.6	1.2	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 (previously Enterobacteriaceae).

In 2021, a total of 946 cases were notified with *Salmonella* infections (*S.* Typhi and *S.* Paratyphi excluded), 11 cases with typhoid fever and 8 cases with paratyphoid fever. For *Salmonella* infections, the number of notified cases increased with 15% in 2021 compared with 2020. The reason was a larger number of cases acquired in Sweden reported during 2021 as the limited international travel throughout 2020 gave a record low number of people whom acquired the infection abroad. Of the *Salmonella* infections, 20% of the cases were reported as acquired abroad, 76% were acquired in Sweden and information about country of acquisition was lacking for 4% of the cases. In 2020 this proportion were 46%, 51% and 3%, respectively. As comparison, in 2019 before the pandemic, 61% were acquired abroad and 38% acquired in Sweden.

The national surveillance program, using whole-genome sequencing, focus on epidemiological typing of domestic isolates in order to identify potential outbreaks.

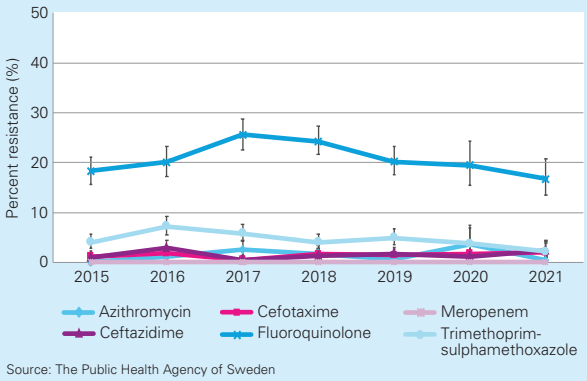
A total of 8 cases in 2021 were reported having *Salmonella* with ESBL, four cases had $ESBL_A$ and one $ESBL_M$. No cases with *Salmonella* species have been reported with $ESBL_{CARBA}$.

Invasive infections were reported for 86 cases in the mandatory reporting, 69 cases with *Salmonella* infection (*S.* Typhi and *S.* Paratyphi excluded), in 10 with typhoid fever and 7 of the cases with parathyphoid fever.

Salmonella spp., from faecal and urine samples

A total of 1 083 *Salmonella enterica* isolates were reported in Svebar, 77%were from faecal samples, 13% from blood and 7% from urine. In approximately half of the faecal and urine isolates an AST were reported.

Figure 3.38. Antibiotic resistance in *Salmonella enterica* from faecal and urine samples 2015-2021. 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 3.23. Antibiotic resistance in *Salmonella enterica* (*S.* Typhi and *S.* Paratyphi excluded) isolated from blood or from faeces and urine samples in 2021. NA: not applicable.

Antibiotic	Blood, % R (n = 76)	Faeces/urine, % R (n= 401)
Azithromycin	NA	0.4
Cefotaxime	7.9	2.0
Ceftazidime	7.9	2.3
Fluoroquinolone	25.7	16.7
Meropenem	0.0	0
Piperacillin-tazobactam	0.0	1.0
Trimethoprim-sulphamethoxazole	1.3	2.2

Table 3.24. Combined susceptibility and resistance to azithromycin, cefotaxime and ciprofloxacin in *Salmonella enterica* from faecal and urine samples 2015-2021. Results from *S.* Typhi and *S.* Paratyphi have been excluded.

	2015	2016	2017	2018	2019	2020	2021
Number of isolates with combined AST for azithromycin, cefotaxime and ciprofloxacin	424	328	426	454	404	183	238
Proportion fully susceptible to azithromycin, cefotaxime and ciprofloxacin, %	80	75	74	76	79	77	75
Proportion fully resistant to azithromycin, cefotaxime and ciprofloxacin, %	0.0	0.6	0.0	0.2	0.3	0	0

Comments

Both the number of reported cases and the number of AST isolates were halved during 2020 and 2021. No significant changes in antibiotic resistance is seen between 2015 and 2021 (Figure 3.38). During this period no carbapenem-resistent *Salmonella* have been reported. The highest resistance was against fluoroquinolones in isolates from faeces and urine, 17% in 2021 (Table 3.23). Three quarters of the *Salmonella* from faecal and urine samples are fully susceptible to azithromycin, cefotaxime and ciprofloxacin (Table 3.24).

Salmonella from blood

Comments

In 2021, there were 76 isolates of *Salmonella* reported in blood with an AST (Table 3.25). Previous years the number of isolates, with an AST, have ranged between 47-125 per year and antibiotic. The data may contain duplicates and there is a risk of overestimation of the resistance. Hence, results should be interpreted with caution. No carbapenem resistance were detected.

Table 3.25. Antibiotic resistance in *Salmonella enterica* from blood samples 2015-2021. Results for *S.* typhi and *S.* paratyphi are excluded. Data for azithromycin are not shown for 2021 due to the low number of tested samples. The numbers of AST isolates for all years and antibiotics ranges from 32 to 125.

***Salmonella* spp., *S.*typhi and *S.*paratyphi excluded**	2015			2016			2017			2018			2019			2020			2021		
Sample: Blood	**n tested**	**% R**	**95% CI**	**n tested**	**% R**	**95% CI**	**n tested**	**% R**	**95% CI**	**n tested**	**% R**	**95% CI**	**n tested**	**% R**	**95% CI**	**n tested**	**% R**	**95% CI**	**n tested**	**% R**	**95% CI**
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)			
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)
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)
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)
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)
Piperacillin-tazobactam	75	0	(0.0-4.9)	71	0	(0.0-5.1)	100	2	(0.6-7.0)	89	0	(0.0-4.1)	123	0	(0.0-3.0)	56	3.6	(1.0-12.1)	73	0.0	(0.0-5.0)
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)

Antibiotic resistance in animals

Notifiable diseases

In Sweden, findings of $ESBL_{CARBA}$-producing Enterobacterales (previously Enterobacteriaceae) 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 (previously Enterobacteriaceae) 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 (previously Enterobacteriaceae)

Healthy farm animals

Escherichia coli

In Sweden, carbapenemase-producing Enterobacterales (previously Enterobacteriaceae) ($ESBL_{CARBA}$) in animals are notifiable but not classical ESBLs ($ESBL_A$) or plasmid-mediated AmpC ($ESBL_M$). Active screening for *Escherichia 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 shown in Table 4.1. During 2021, various samples from healthy farm aninmals 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). The samples of intestinal contents were collected at slaughter and were from healthy fattening pigs (n=300) and broilers (n=101) as well as from healthy cattle under one year of age (n=57). The samples from cattle were collected from September 2020 to august 2021.

Fattening pigs

Eschericia coli with ESC-resistance was isolated from 25 (8%) of 300 samples and a transferable gene coding for ESC resistance was detected in 3 isolates, i.e., 1% of the samples. All of these were $ESBL_A$ and carried $bla_{CTX\text{-}M\text{-}1}$ (n=1) or $bla_{CTX\text{-}M\text{-}15}$ (n=2). The remaining 22 isolates with ESC-resistance 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, in all of these.

Carbapenem resistant *E. coli* was not isolated from any sample.

The most common traits of additional resistance, apart from resistance against beta-lactams, were resistance to tetracycline (28%), sulphonamides (24%), trimethoprim (24%), and chloramphenicol (20%). Ten (40%) of the tested isolates were resistant to at least two other antibiotics apart from resistance against beta-lactams, including ESCs, i.e. they were multiresistant.

Cattle under one year

Eschericia coli with ESC-resistance was isolated from 8 (14%) of 57 samples and a transferable gene coding for ESC resistance was detected in 7 isolates, i.e., 12% of the samples. All of these were $ESBL_A$ and carried $bla_{CTX\text{-}M\text{-}15}$ (n=6) or $bla_{CTX\text{-}M\text{-}55}$ (n=1). The remaining isolate with ESC-resistance 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.

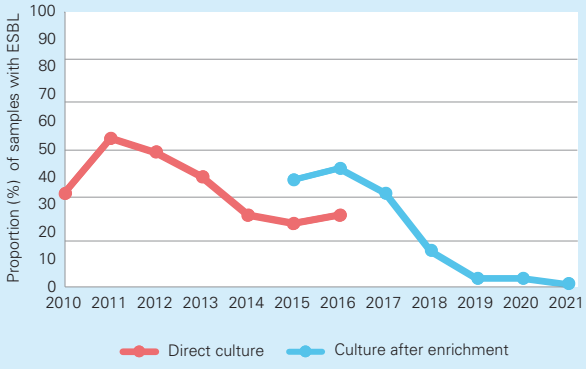
Five of the isolates were from animals slaughtered at the same slaughterhouse during one day in September and one day in November 2020 and four of these isolates were closely related. They were all of ST616, carried $bla_{CTX\text{-}M\text{-}15}$, and had only three single nucleotide polymorphisms (SNP) among them. Apart from resistance against beta-lactams, they were resistant to ciprofloxacin but not nalidixic acid and carried the *qnrS1* gene.

Carbapenem resistant *E. coli* was not isolated from any sample.

Broilers

Eschericia coli with ESC-resistance was isolated from 5 (5%) of 101 samples and a transferable gene coding for ESC resistance was detected in 1 isolate, i.e., 1% of the samples. The isolate had an $ESBL_A$ phenotype and carried $bla_{CTX\text{-}M\text{-}1}$. The remaining isolates with ESC-resistance had an AmpC phenotype and genome sequencing revealed a mutation causing hyper-production of AmpC beta-lactamases, i.e., a shift

Figure 4.1. Proportion (%) of samples from broilers positive for *Escherichia coli* with $ESBL_A$ or $ESBL_M$ from 2010 to 2021. The number of samples each year varies (n=100-302, 2021 n=101).



from C to T at position 42, in three of these. The remaining isolate is still pending genome sequencing but no transferrable genes conferring ESC-resistance were detected by PCR.

Carbapenem resistant *E. coli* was not isolated from any sample.

The isolate with transferable ESC-resistance was also resistant to sulphonamides and tetracycline. This was also 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 were cultured in duplicate with both relevant methods (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).

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. The proportions of samples positive for *E. coli* with $ESBL_A$ or $ESBL_M$ in screenings of meat of Swedish origin are shown in Table 4.1. During 2021, various 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). The samples of meat were collected at retail (305 samples of pig meat and 303 samples of bovine meat) as well as at border control posts (3 samples of pig meat and 18 samples of bovine meat).

Pig meat

The 305 samples of pig meat collected at retail comprised of fresh meat originating both from Sweden (n=258) and other EU countries (n=45) as well as two samples where the origin could not be determined. *Escherichia coli* with ESC-resistance was not isolated from any of these samples (Table 4.1).

The three samples of pig meat collected at border control posts comprised of fresh meat originating from one shipment. *Escherichia coli* with ESC-resistance was not isolated from any of these samples.

Carbapenem resistant *E. coli* was not isolated from any samples of pig meat.

Bovine meat

The 303 samples of bovine meat collected at retail comprised of fresh meat originating both from Sweden (n=267), other EU countries (n=27), countries outside EU (n=4) as well as five samples where the origin could not be determined. In total, *E. coli* with ESC-resistance was isolated from 1 (<1%) of the samples. The sample from which *E. coli* with ESC-resistance was isolated originated from Sweden (Table 4.1). This isolate had an $ESBL_A$ phenotype and carried $bla_{CTX\text{-}M\text{-}3}$. The isolate was not resistant to any other substances besides beta-lactams.

The 18 samples of bovine meat collected at border control posts comprised of fresh meat originating from 6 different shipments. *Escherichia coli* with ESC-resistance was not isolated from any of these samples.

Carbapenem resistant *E. coli* was not isolated from any samples of bovine meat.

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, the results of the screenings for ESC resistant *E. coli* that have been performed are shown in Table 4.1.

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. During 2021, 40 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=6), dogs (n=10) and horses (n=24).

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 two thirds of the investigated isolates were also resistant to at least two other antibiotics, i.e. multiresistant. The most common resistances were against trimethoprim-sulphonamides (64%) and gentamicin (61%). Resistance to quinolones and tetracycline were also common traits. The occurrence of resistance to trimethoprim-sulphonamides and tetracycline was slightly higher among isolates from companion animals than among isolates from horses.

Table 4.1. Results of the screening studies for *Escherichia coli* with $ESBL_A$ or $ESBL_M$ in healthy individuals of different animal species and meat of Swedish origin.

Animal species	Matrix	Year	No. of samples	No. of samples with ESC resistance	No. of samples with $ESBL_A$ or $ESBL_M$	% samples with $ESBL_A$ or $ESBL_M$	Beta-lactamase (No. of isolates)								
							CTX-M-1	CTX-M-3	CTX-M-14	CTX-M-15	CTX-M-27	CTX-M-55	TEM-52	SHV	CMY-2
Broilers	Intestine	2021	101	5	1	1	1								
Broilers	Intestine	2020	300	34	10	3	10								
Broilers	Meat	2020	284	22	7	2	6								1
Broilers	Intestine	2019	101	8	3	3	3								
Broilers	Intestine	2018	300	42	38	13	13							1	24
Broilers	Meat	2018	242	35	28	12	8								20
Broilers	Intestine	2017	100	40	34	34	14								20
Broilers	Intestine	2016	302	130	127	42	93[a]								34[b]
Broilers	Meat	2016	243	109	107	44	66[a]			1					40[b]
Broilers	Intestine	2015	100	40	39[c]	39[c]	18[c]								22[c]
Broilers	Intestine	2014	200	72	71	36	1								70[d]
Broilers	Intestine	2013	100	45	40	40							2		38[d]
Broilers	Meat	2013	59	31	30	51									30[d]
Broilers	Intestine	2012	200	102	97	49									97[d]
Broilers	Meat	2012	97	41	40	41									40[d]
Broilers	Intestine	2011	100	57	54	54	3								51
Broilers	Intestine	2010	200	77	68	34	12								56
Broilers	Meat	2010	100	49	44	44	4								40
Cattle	Meat	2021	267	1	1	<1		1							
Cattle[e]	Intestine	2020-21	57	8	7	12				6		1			
Cattle	Meat	2019	264	1	0	0									
Cattle[e]	Intestine	2017-18	67	3	2	3	1			1					
Cattle	Meat	2017	249	3	2	<1				1	1				
Cattle	Intestine	2015	103	5	0	0									
Cattle	Meat	2015	289	0	0	0									
Cattle[e]	Intestine	2013	202	3	1	<1				1					
Cattle[e]	Intestine	2012	742	81	9	1	1			4					4
Cattle[e]	Intestine	2009	256	11	0	0									
Pigs	Intestine	2021	300	25	3	1	1			2		1			
Pigs	Meat	2021	258	0	0	0									
Pigs	Intestine	2019	300	39	8	3			4	3		1			
Pigs	Meat	2019	254	1	1	<1							1	1	
Pigs	Intestine	2017	241	29	9	4			6	2		2			
Pigs	Meat	2017	228	0	0	0									
Pigs	Intestine	2015	303	35	4	1				1					1
Pigs	Meat	2015	286	1	1	<1						1			
Pigs	Intestine	2011	184	9	3	2		1		1					
Pigs	Meat	2011	100	0	0	0									
Pigs	Intestine	2008	452	9	0	0									
Pigs	Meat	2008	50	0	0	0									
Turkeys	Intestine	2020	45	0	0	0									
Turkeys	Intestine	2018	72	0	0	0									
Turkeys	Intestine	2016	86	1	1	1	1								
Turkeys	Intestine	2014	60	12	0	0									
Turkeys	Intestine	2013	55	16	0	0									
Sheep	Meat	2018	95	0	0	0									
Laying hens	Intestine	2012	69	11	9	13	3								6
Dogs	Rectal swab	2017-18	325		3	<1	1				1	1			
Dogs	Faeces	2012	84	6	1	1									1[d]
Horses	Faeces	2010	431	9	6	1								6	

[a]CTX-M-1-group, ten caecal and four meat isolates were sequenced and possessed the gene blaCTX-M-1. [b]CIT-group, five caecal and three meat isolates were sequenced and possessed the gene blaCMY-2. [c]One isolate carried both an ESBLA and an ESBLM gene. [d]CIT-group, all isolates from broilers or broiler meat with a CIT-group enzyme in other years possessed the gene blaCMY-2. [e]Cattle under 1 year, in 2012 calves 1-4 weeks of age.

Table 4.2. Clinical isolates of different bacterial species of Enterobacterales (previously Enterobacteriaceae), producing $ESBL_A$ or $ESBL_M$, from companion animals and horses, 2008-2021.

Animal species	Beta-lactamase group	Beta-lactamase gene	Bacterial species	08	09	10	11	12	13	14	15	16	17	18	19	20	21
CATS	**All**	**All**	**Enterobacterales**		**1**	**3**	**3**			**1**	**2**	**2**	**5**	**3**	**4**	**8**	**6**
	ACT/MIR	ACT-9	*Enterobacter cloacae* group													1	
		MIR-5	*Enterobacter cloacae* group													1	
	CIT	CMY-2	*Escherichia coli*		1	1						1			1	1	
		CMY-2 + CTX-M-65	*Escherichia coli*										1	1			
		CMY-2 + SHV-28	*Klebsiella pneumoniae*													1	1
		CMY-16	*Escherichia coli*							1							
	CTX-M-1	CTX-M-3	*Escherichia coli*										1				
		CTX-M-15	*Enterobacter cloacae* group								1						
			Escherichia coli			1						1	2	1	2	4	2
			Klebsiella pneumoniae			1	1										
	CTX-M-9	CTX-M-14	*Escherichia coli*											1	1		1
			Kluyvera sp.				1										
		CTX-M-27	*Escherichia coli*														1
	DHA	DHA-1	*Escherichia coli*														1
	SHV	SHV-12	*Escherichia coli*										1				
	TEM	TEM-52	*Escherichia coli*								1						
	unknown	unknown	*Escherichia coli*				1										
DOGS	**All**	**All**	**Enterobacterales**	**1**	**3**	**5**	**18**	**12**	**14**	**22**	**24**	**31**	**17**	**22**	**17**	**24**	**10**
	CIT	CMY-2	*Escherichia coli*			1	9	4	5	5	6	5	4	9	6	5	1
			Klebsiella pneumoniae								1						
			Proteus mirabillis				1				2	2					1
		CMY-2 + CTX-M-15	*Escherichia coli*														1
		CMY-2 + CTX-M-15 + SHV-67	*Klebsiella pneumoniae*													1	
		CMY-2 + CTX-M-27	*Escherichia coli*										1				
		CMY-4	*Escherichia coli*												2	1	
	CTX-M-1	CTX-M-1	*Enterobacter cloacae* group							4							
			Escherichia coli			1		1	1	3			3	2	2	1	
		CTX-M-3	*Enterobacter* spp.						1								
			Escherichia coli						2		1	2					
		CTX-M-15	*Enterobacter cloacae* group								2	2	1	1		1	
			Enterobacter spp.		1	2	1	2	1	6							
			Escherichia coli	1			2	3	2		2	7	1	6	2	7	4
			Klebsiella pneumoniae		1						1	2			1	1	
			Morganella morganii									1					
		CTX-M-55	*Escherichia coli*								1	1					
		CTX-M-57	*Escherichia coli*								1						
	CTX-M-2	CTX-M-2	*Escherichia coli*				1										1
	CTX-M-9	CTX-M-9	*Escherichia coli*				1	2	1	1							
		CTX-M-14	*Escherichia coli*								5	5	2	1	1		
			Klebsiella pneumoniae								1			1			
		CTX-M-27	*Escherichia coli*				3		1	1	1	1	3		2	4	1
		CTX-M-65	*Escherichia coli*													1	
			Proteus mirabillis													1	
	DHA	DHA-1	*Escherichia coli*											1		1	1
	SHV	SHV-12	*Escherichia coli*							2		3	2				
			Klebsiella oxytoca												1		
	TEM	TEM-52-like	*Escherichia coli*											1			
	unknown	unknown	*Escherichia coli*		1	1											
HORSES	**All**	**All**	**Enterobacterales**	**2**	**5**	**24**	**16**	**6**	**9**	**8**	**14**	**18**	**32**	**22**	**14**	**25**	**24**
	ACT/MIR	ACT-15	*Enterobacter cloacae* group													1	
	CIT	CMY-2	*Escherichia coli*												1	1	
	CTX-M-1	CTX-M-1	*Enterobacter cloacae* group								1		2				1
			Enterobacter spp.						1								
			Escherichia coli		2	9	8	3	3	2	3	5	13	6	1	3	4
			Klebsiella oxytoca							1							
			Serratia odorifera			1											
		CTX-M-15	*Escherichia coli*		1	1						1			4		
			Klebsiella pneumoniae		1						3			1			
	CTX-M-9	CTX-M-14	*Escherichia coli*				1				1						
		CTX-M-9	*Escherichia coli*							1							
	SHV	SHV-12	*Citrobacter braakii*			1											
			Citrobacter spp.											1			
			Enterobacter aerogenes									1					
			Enterobacter amnigenus							1							
			Enterobacter cloacae group							1	2	5	8	8	3	18	19
			Enterobacter spp.		1	3	5	3	3								
			Escherichia coli	2		2	2					3	6	6	1	1	
			Escherichia hermanii			1											
			Escherichia species												1		
			Klebsiella oxytoca						2		1	1	3		1	1	
			Klebsiella pneumoniae							1					1		
			Leclercia adecarboxylata									1					
			Pantoea agglomerans									1					
		SHV-12 like	*Klebsiella pneumoniae*												1		
	unknown	unknown	*Enterobacter cloacae* group							1	3						
			Escherichia coli			1											
			Klebsiella pneumoniae			5											

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 in 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). Results, including index cases of clinical isolates and isolates from screenings, are presented in Table 4.3 (farm animals), Table 4.4 (horses), Table 4.5 (dogs) and Table 4.6 (cats and rabbits).

Farm animals

Screening studies in pigs have been performed five times since 2006, with only two positive samples from pigs at slaughter in 2010. 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 1350 isolates have been tested up to and including 2021. The monitoring is performed on isolates with anonymised origin. Since 2010 five PVL-negative isolates with *mecC*, two PVL-negative isolates with *mecA* and one PVL-positive isolate with *mecA* have been detected. In 2021 no MRSA was detected of the 33 isolates screened for occurrence of *mecA* and *mecC*. In 2012, PVL-positive MRSA with *mecA* was isolated from several animals in a dairy herd (Unnerstad et al., 2013).

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 sampled 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. In total 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 2021, a total of 197 cases of MRSA in companion animals and horses have been confirmed. These include 62 dogs, 35 cats, 2 rabbits and 98 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 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 2021, MRSA was detected in clinical samples, from wound infections, urine and one otitis, from three dogs and nine cats. Isolates from all three dogs and six cats were of different *spa*-types, excluding a common source of infection. During the years the identified *spa*-types have varied, and most have previously been detected in humans (Table 4.5 and 4.6).

In 2021, MRSA was isolated from 23 horses which is comparable to the figures from 2020, but an increase compared to previous years (2007-2019) when between one and nine cases were notified per year (Table 4.4). The relatively high figure could partly be explained by an outbreak of, the in horses in Sweden not earlier detected *spa*-type t034, including eight horses. Historically, MRSA *spa*-type t011, CC398, has been dominating among horses in Sweden. However, in 2020 and 2021 new *spa*-types were introduced, although *spa*-type t011 were still notified. During the two years, 2020-21, the two most common *spa*-types were t1971 and t011 with 18 of 48 isolates respectively. The third most common *spa*-type was t034 with eight isolates (notified only in 2021). The remaining isolates were sporadic findings, two isolates of t223 (two horses, one owner) and one each of t1257 and t373 (the latter a *mecC* variant). All the mentioned *spa*-types have also been detected more or less frequently in samples from humans.

Wild animals

High occurrence of *mecC*-MRSA has been described in hedgehogs in Sweden, 64%, Denmark, 61% (Bengtsson et al., 2017 and Rasmussen et al., 2019) and other countries. 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).

Table 4.3. Farm animals. Isolates of methicillin-resistant *Staphylococcus aureus* (MRSA) in Swedish pigs, cows, goats, and sheep up to and including 2021. All isolates were positive for the *nuc* gene and *mecA* or *mecC* genes, *mec*-gene showed in bold indicates PVL-positivity. Shaded areas indicate MIC above EUCAST ECOFF.

			Antibiotic, MIC (mg/L)											
Animal species	**Year**	**No. of isolates**	**Beta-lactams**	**Cli>0.5**	**Ery>1**	**Tet>1**	**Fus>0.5**	**Gen>2**	**Cip>1**	**Tmp >2**	**Chl >16**	**Lin >4**	***spa*-type**	***mec*-gene**
Pig	2010	1	R	0.5	1	64	0.5	>64	0.25	>32	16		t011	*A*
Pig	2010	1	R	≤0.25	≤0.25	≤0.5	≤0.25	0.5	0.5	0.5	4	2	t373	*C*
Cow	2010	2	R	≤0.25	≤0.25-0.5	≤0.5	0.25-0.5	≤0.5	0.25-0.5	1-2	4-8		t524	*C*
Cow	2010	1	R	≤0.25	0.5	≤0.5	0.25	≤0.5	0.5	2	8		t524	*C*
Cow	2011	1	R	≤0.25	0.5	≤0.5	0.12	≤0.5	0.25	1	8		t9111	*C*
Cow	2012	2	R	≤0.25	0.5-1	≤0.5	0.25-0.5	≤0.5-1	0.25-0.5	2	8		t002	***A***
Cow	2013	1	R	≤0.25	1	≤0.5	0.5	≤0.5	0.5	2	8		t843	*C*
Cow	2014	1	R	≤0.25	>32	16	0.25	≤0.5	0.25	2	8		t127	*A*
Cow	2015	1	R	≤0.25	≤0.25	≤0.5	0.12	≤0.5	0.25	1	8		t843	*C*
Cow	2017	1	R	≤0.25	≤0.25	≤0.5	4	0.25	0.25	0.5	4		t008	*A*
Goat	2016	1[a]	R	≤0.25	≤0.25	≤0.5	0.12	≤0.5	1	≤0.5	8		t9268	*C*
Goat	2017	1	R	≤0.25	≤0.25	≤0.5	≤0.25	0.5	0.25	0.5	8	2	t9268	*C*
Goat	2017	9	R	≤0.25	≤0.25	≤0.5	≤0.25	0.25-0.5	0.25	0.5	4-8	≤1-2	t373	*C*
Goat	2019	1	R	0.25	0.5	≤0.5	≤0.25	≤0.5	0.5	≤2	8	≤1-2	t373	*C*
Sheep	2016	3[b]	R	≤0.25	≤0.25	≤0.5	≤0.25	≤0.5	0.25	0.5-1	8		t9268	*C*

[a]Two isolates were tested from an outbreak including 20 goats at a zoo; [b]Three isolates were tested from an outbreak including six sheep at a zoo.

Table 4.4. Isolates of methicillin-resistant *Staphylococcus aureus* (MRSA) in Swedish horses up to and including 2021. 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	**Year**	**No. of isolates**	**Beta-lactams**	**Cli>0.5**	**Ery>1**	**Tet>1**	**Fus>0.5**	**Gen>2**	**Cip>1**	**Tmp >2**	**Chl >16**	**Lin >4**	***spa*-type**	***mec*-gene**
Horse	2007-2014	21	R	≤0.25	≤0.25-1	16-64	≤0.06-0.5	4->64	0.12-1	>8->32	4-8		t011	*A*
Horse	2008-2013	3	R	≤0.25	1	32-64	1	>64	1	>32	8-16		t011	*A*
Horse	2010	1	R	0.5	2	64	1	>64	1	>32	16		t011	*A*
Horse	2010	2	R	≤0.25	1	32	0.5	16->64	0.25-0.5	>32	8		t064	*A*
Horse	2011	1	R	≤0.25	≤0.25	64	0.5	≤0.5	0.25	1	8		t011	*A*
Horse	2012	1	R	1	1	64	0.25	>64	0.5	>32	8		t011	*A*
Horse	2014	2	R	≤0.25	≤0.25	32	≤0.06-0.12	64	>4	>32	8		t011	*A*
Horse	2015	1	R	≤0.25	≤0.25	32	0.25	32	0.25	>32	8		t1451	*A*
Horse	2017	2	R	≤0.25	≤0.25	32	≤0.25	16->16	0.5	>8	8	2	t011	*A*
Horse	2017	1	R	≤0.25	≤0.25	32	≤0.25	>16	>4	>8	4	≤1	t011	*A*
Horse	2017	2	R	>32	>32	64	≤0.25	>16	>4	>8	8-16	≤1	t011	*A*
Horse	2017-2020	4	R	≤0.25	>8->32	>16	≤0.5	>16	>4->8	>8->32	8-16	<1-4	t1257	*A*
Horse	2018-2021	25	R	≤0.25	<0.25-0.5	>16	≤0.5	>16	≤0.25-0.5	>32	8-16	≤1-2	t011	*A*
Horse	2019-2020	2	R	≤0.25	>8	>16	≤0.5	>16	>8	>32	8	≤1-2	t1971	*A*
Horse	2020-2021	16	R	<0.25	0.5-1	>16	<0.5	>16	>8	>32	<4-16	<1-4	t1971	*A*
Horse	2020	1	R	<0.12	0.5	8	<0.5	<1	<0.25	<2	8	4	t088	*A*
Horse	2020	1	R	0.25	0.5	<0.5	<0.5	<1	<0.25	<2	8	2	t843	*C*
Horse	2021	1	R	<0.12	0.5	>16	1	>16	>8	>32	8	2	t1971	*A*
Horse	2021	6	R	4->4	0.5-1	>16	<0.5	<1	<0.25-0.5	>32	8-16	2-4	t034	*A*
Horse	2021	2	R	>4	0.5-1	>16	<0.5	>16	<0.25	>32	8-16	2	t034	*A*
Horse	2021	2	R	<0.12	0.5	<0.5	<0.5	<1	<0.25	>32	8	2	t223	*A*
Horse	2021	1	R	0.25	0.5	<0.5	<0.5	<1	0.5	>2	8	2	t373	*C*

Table 4.5. Isolates of methicillin-resistant *Staphylococcus aureus* (MRSA) in Swedish dogs up to and including 2021. All isolates were positive for the *nuc* gene and *mecA* or *mecC* genes, *mec*-gene showed in bold indicates PVL-positivity. Shaded areas indicate MIC above EUCAST ECOFF.

				Antibiotic, MIC (mg/L)										
Animal species	Year	No. of isolates	Beta-lactams	Cli	Ery	Tet	Fus	Gen	Cip	Tmp	Chl	Lin	*spa*-type	*mec*-gene
Dog	2006-14	13	R	≤0.25	≤0.25-1	≤0.5	≤0.06-0.5	≤0.5-1	>4	1-2	8		t032	*A*
Dog	2007	1	R	0.5	0.5	2	-	1	>4	2	4		t032	*A*
Dog	2008	1	R	0.5	>32	≤0.5	0.5	32	>4	>32	16		t127	*A*
Dog	2009	1	R	0.5	1	1	0.5	1	>4	4	16		t032	*A*
Dog	2010	1	R	>32	>32	≤0.5	0.5	1	>4	2	16		t002	*A*
Dog	2010	1	R	≤0.25	≤0.25	≤0.5	8	1	0.5	2	8		t002	*A*
Dog	2010	1	R	≤0.25	>32	≤0.5	0.5	≤0.5	>4	8	4		t020	*A*
Dog	2013	1	R	0.5	1	1	1	1	>4	4	8		t032	*A*
Dog	2013	1	R	≤0.25	1	≤0.5	0.25	≤0.5	0.5	2	8		t127	*A*
Dog	2013	1	R	≤0.25	>32	16	0.25	2	0.25	2	8		t127	*A*
Dog	2013	1	R	≤0.25	0.5	≤0.5	0.5	≤0.5	0.5	>32	8		t223	*A*
Dog	2013	1	R	≤0.25	1	≤0.5	0.5	≤0.5	0.5	4	8		t304	*A*
Dog	2014	1	R	≤0.25	>32	≤0.5	≤0.06	≤0.5	0.25	1	8		t002	***A***
Dog	2014	1	R	≤0.25	1	16	0.5	1	0.5	4	8		t325	*A*
Dog	2015	1	R	≤0.25	>32	16	0.12	≤0.5	0.25	1	4		t177	*A*
Dog	2015	1	R	0.5	≤0.25	≤0.5	0.5	≤0.5	0.25	≤0.5	8		t373	*C*
Dog	2015	1	R	≤0.25	≤0.25	≤0.5	0.12	≤0.5	0.25	1	8		t843	*C*
Dog	2015	1	R	≤0.25	>32	16	0.25	≤0.5	0.5	2	8		t948	*A*
Dog	2015-2019	6	R	≤0.12-0.25	>8 - >32	>16 - 32	≤0.06-0.5	≤0.5 - ≤1	0.12-0.5	1-2	≤4-8		t127	*A*
Dog	2016	1	R	16	≤0.25	32	0.5	16	>4	>32	64		t034	*A*
Dog	2016	1	R	≤0.25	>32	8	4	≤0.5	0.5	4	8		t044	***A***
Dog	2017	1	R	≤0.25	2	≤0.5	≤0.25	0.25	>4	0.5	4	≤1	t008	*A*
Dog	2017	1	R	≤0.25	≤0.25	≤0.5	≤0.25	0.25	>4	0.5	4	2	t022	*A*
Dog	2017	1	R	≤0.25	≤0.25	≤0.5	>4	0.25	>4	0.5	8	2	t032	*A*
Dog	2017	1	R	8	≤0.25	64	≤0.25	0.5	>4	>8	4	≤1	t034	*A*
Dog	2017	1	R	>32	>32	≤0.5	≤0.25	0.5	1	2	8	≤1	t127	*A*
Dog	2017	1	R	≤0.25	≤0.25	≤0.5	≤0.25	0.25	0.5	1	4	2	t2734	*A*
Dog	2017	1	R	≤0.25	≤0.25	≤0.5	≤0.25	0.5	0.25	>8	8	2	t5634	*A*
Dog	2017	1	R	≤0.25	≤0.25	≤0.5	≤0.25	8	>4	>8	8	2	t891	***A***
Dog	2018	1	R	0.25	0.5	≤0.5	≤0.5	≤1	≤0.25	>32	8	2	t223	*A*
Dog	2019	1	R	>4	>8	>16	≤0.5	≤1	≤0.25	>32	8	2	t034	*A*
Dog	2019	1	R	≤0.12	≤0.5	≤0.5	≤0.5	≤1	≤0.25	≤2	8	4	t10893	*C*
Dog	2019	1	R	≤0.12	≤0.25	≤0.5	≤0.5	≤1	0.5	≤2	8	≤1	t1339	*A*
Dog	2019	1	R	≤0.12	0.5	≤0.5	≤0.5	≤1	≤0.25	≤2	8	2	t18886	*C*
Dog	2019	1	R	≤0.12	≤0.25	≤0.5	≤0.5	≤1	≤0.25	>32	8	2	t790	*A*
Dog	2019	1	R	0.25	0.5	≤0.5	≤0.5	≤1	≤0.25	≤2	8	2	t843	*C*
Dog	2019-2020	2	R	>4	>8	≤0.5	≤0.5	≤2	>8	≤2	8-16	2	t003	*A*
Dog	2020	1	R	0.25	1	≤0.5	≤0.5	≤1	>8	≤2	16	8	t032	*A*
Dog	2020	2	R	>4	>8	16->16	≤0.5	≤1	≤0.25-0.5	≤2	16	≤1	t034	***A***
Dog	2020	1	R	≤0.12	0.5	≤0.5	≤0.5	≤1	≤0.25	>32	8	≤1	t309	*A*
Dog	2021	1	R	>4	>8	≤0.5	≤0.5	≤1	>8	≤2	16	2	t003	*A*
Dog	2021	1	R	0.25	1	1	>4	≤1	0.5	≤2	8	2	t1171	*A*
Dog	2021	1	R	≤0.12	>8	16	≤0.5	≤1	0.5	≤2	8	≤1	t127	*A*

Table 4.6. Cats and rabbits. Isolates of methicillin-resistant *Staphylococcus aureus* (MRSA) in Swedish cats and rabbits up to and including 2021. All isolates were positive for the *nuc* gene and *mecA* or *mecC* genes, *mec*-gene showed in bold indicates PVL-positivity. Shaded areas indicate MIC above EUCAST ECOFF. One isolate from a cat from 2013 was not available for further testing and is not included in the table.

				Antibiotic, MIC (mg/L)										
Animal species	**Year**	**No. of isolates**	**Beta-lactams**	**Cli**	**Ery**	**Tet**	**Fus**	**Gen**	**Cip**	**Tmp**	**Chl**	**Lin**	***spa*-type**	***mec*-gene**
Cat	2009	1	R	≤0.25	0.5	≤0.5	0.25	≤0.5	>4	4	4		t032	*A*
Cat	2009-2012	3	R	≤0.25	≤0.25-0.5	≤0.5	0.25-0.5	≤0.5-1	>4	1-2	8		t032	*A*
Cat	2010	1	R	≤0.25	0.5	≤0.5	1	≤0.5	>4	1	8		t032	*A*
Cat	2011	1	R	≤0.25	≤0.25	≤0.5	0.25	≤0.5	>4	1	8		t022	*A*
Cat	2012	1	R	0.5	1	1	1	1	>4	2	16		t032	*A*
Cat	2014	2	R	≤0.25	≤0.25	≤0.5	≤0.06-0.25	≤0.5	0.25	0.5	8		t978	*C*
Cat	2015	1	R	≤0.25	≤0.25	≤0.5	≤0.06	≤0.5	0.25	1	8		t843	*C*
Cat	2015	1	R	≤0.25	0.5	≤0.5	0.12	≤0.5	0.25	1	8		t933	*A*
Cat	2016	1	R	≤0.25	>32	≤0.5	0.5	≤0.5	2	2	8		t008	***A***
Cat	2016	1	R	≤0.25	≤0.25	≤0.5	≤0.06	≤0.5	0.12	≤0.5	4		t304	*A*
Cat	2017	1	R	≤0.25	≤0.25	≤0.5	≤0.25	0.5	0.25	>8	4	≤1	t786	*A*
Cat	2018	2	R	0.25	0.5	≤0.5	≤0.5	≤1	>8	≤2	8	2	t032	*A*
Cat	2018	1	R	≤0.12	0.5	≤0.5	≤0.5	≤1	≤0.25	≤2	8	2	t12236	***A***
Cat	2018	2	R	0.25	0.5	≤0.5	>4	≤1	≤0.25	≤2	8	2	t132	*A*
Cat	2019	1	R	≤0.12	0.5	≤0.5	≤0.5	≤1	0.5	≤2	8	8	t002	*A*
Cat	2019	1	R	>4	0.5	>16	≤0.5	≤1	≤0.25	>32	8	4	t034	*A*
Cat	2019	1	R	≤0.12	0.5	≤0.5	≤0.5	≤1	0.5	≤2	8	2	t373	*C*
Cat	2020	1	R	≤0.12	0.5	≤0.5	≤0.5	≤1	≤0.25	≤2	8	4	t304	*A*
Cat	2020	1	R	≤0.12	0.5	≤0.5	≤0.5	≤1	0.5	≤2	8	2	t359	*A*
Cat	2020	2	R	≤0.12 - 0.25	0.5	≤0.5	≤0.5	≤1	≤0.25 - 0.5	≤2	8-16	2	t843	*C*
Cat	2021	2	R	≤0.12 - 0.25	0.5	≤0.5 - 1	≤0.6	≤2	>8	≤2	8-16	2-4	t032	*A*
Cat	2021	1	R	2	0.5	>16	≤0.5	≤1	≤0.25	>32	8	2	t034	*A*
Cat	2021	1	R	≤0.12	0.5	≤0.5	1	≤1	≤0.25	≤2	8	4	t304	*A*
Cat	2021	1	R	≤0.12	>8	≤0.5	≤0.5	≤1	8	≤2	8	2	t304	*A*
Cat	2021	1	R	0.25	1	1	≤0.5	≤1	≤0.25	≤2	8	4	t304	*A*
Cat	2021	1	R	≤0.12	0.5	≤0.5	≤0.5	≤1	0.5	≤2	8	2	t359	*A*
Cat	2021	1	R	>4	>8	≤0.5	≤0.5	≤1	1	≤2	>64	2	t437	***A***
Cat	2021	1	R	≤0.12	0.5	≤0.5	≤0.5	>16	>8	>32	8	2	t442	*A*
Rabbit	2017	1	R	≤0.25	≤0.25	≤0.5	4	0.5	0.25	0.5	4	≤1	t132	*A*
Rabbit	2019	1	R	≤0.12	≤0.25	≤0.5	>4	≤1	≤0.25	≤2	8	2	t132	*A*

Methicillin-resistant *Staphylococcus pseudintermedius* (MRSP)

In 2021, there were 43 MRSP cases from 41 dogs, one cat, and one horse reported to the Swedish Board of Agriculture (Figure 4.2). This number is around the same level as in previous years. All isolates were available for further susceptibility testing and genome sequencing. Information on the sampling site was available for 40 cases; skin 10 cases, external ear canal 7 cases, wounds (mostly postoperative surgical wounds) 12 cases and the remaining 11 were isolated from urine, eye, abscesses, and various other sites. Thirty-eight isolates were defined as multiresistant. For resistance phenotypes, see Table 4.7.

The results of the genome sequencing of, to date, 41 isolates, divided the isolates into 25 different multi-locus sequence types, of which ST551 was the most common type with 14 isolates. The ST551 was first detected in 2016 and was also the most common ST in 2020 with 18 out of 49 and in 2019 with 13 out of 42 genome sequenced isolates. In earlier years, ST71, a sequence type spread in Europe and described by Perreten et al. (2010), was dominating among Swedish isolates. In 2021 there was one isolates of this type. The other sequence types occurring in 2021: ST258 (3 isolates), ST1095 (2 isolates) and single isolates of ST25, ST71, ST157, ST181, ST496, ST642, ST672, ST690, ST1179, ST1296, ST1383, ST1691, ST2269-2273, ST2342, ST2352, ST2353, ST2355 and ST2358.

Figure 4.2. Number of cases of methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) in Sweden 2006-2021. 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.

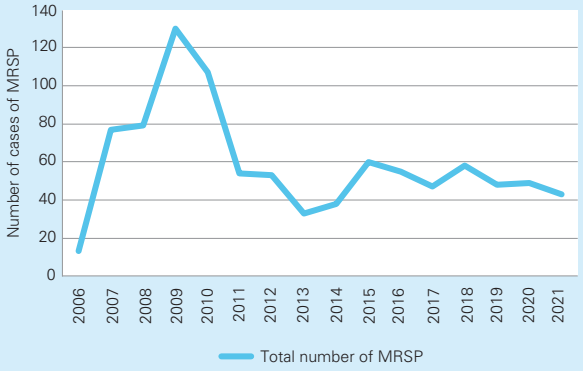


Table 4.7. Resistance phenotypes (beta-lactams excluded) of isolates of methicillin resistant *Staphylococcus pseudintermedius* (MRSP) in 2021. All isolates were positive for the *mecA* gene. Shaded areas indicate resistance.

	Antibiotic MIC (mg/L)								
Beta-lactams	Tet	Tsu	Ery	Cli	Gen	Enr	Fus	Nit	Number of isolates
R	>4	>4	>2	>2	>4	>1	1	≤16	1
R	>4	>4	>2	>2	>4	>1	≤0.5	32	1
R	>4	>4	>2	>2	>4	>1	≤0.5	≤16	15
R	>4	>4	>2	>2	>4	1	≤0.5	≤16	2
R	>4	>4	>2	>2	4	>1	2	≤16	1
R	>4	>4	>2	>2	4	>1	≤0.5	≤16	5
R	>4	>4	>2	>2	4	>1	≤0.5	≤16	1
R	>4	>4	>2	>2	2	>1	≤0.5	≤16	1
R	>4	>4	>2	>2	≤1	≤0.25	>2	≤16	1
R	>4	>4	≤0.5	≤0.5	>4	>1	≤0.5	≤16	1
R	>4	>4	≤0.5	≤0.5	≤1	≤0.25	≤0.5	≤16	1
R	>4	4	>2	>2	≤1	≤0.25	≤0.5	≤16	1
R	>4	0.5	≤0.5	≤0.5	>4	>1	≤0.5	≤16	1
R	>4	0.5	≤0.5	≤0.5	≤1	0.5	≤0.5	≤16	2
R	>4	≤0.25	>2	>2	>4	0.5	≤0.5	≤16	1
R	≤0.25	>4	>2	>2	>4	0.5	≤0.5	≤16	1
R	≤0.25	>4	>2	>2	4	>1	≤0.5	≤16	1
R	≤0.25	>4	1	≤0.5	≤1	≤0.25	≤0.5	≤16	1
R	≤0.25	>4	≤0.5	≤0.5	4	>1	≤0.5	≤16	1
R	≤0.25	0.5	>2	>2	≤1	≤0.25	≤0.5	≤16	1
R	≤0.25	≤0.25	≤0.5	≤0.5	≤1	≤0.25	1	≤16	1
R	≤0.25	≤0.25	≤0.5	≤0.5	≤1	≤0.25	≤0.5	≤16	2
								Sum	43

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

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. From incidents in companion animals and wild animals a selection of isolates is tested. 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. However, the number of cases vary between years and in 2021 the number of isolates from both birds and cats were low. For details on methodology, see Materials and methods, resistance in bacteria from animals.

All animals 2021

A total of 130 *Salmonella* isolates were tested in 2021, all belonging to the species *S. enterica* and with two subspecies represented, subsp. *enterica* (102 isolates) and subsp. *diarizonae* (28 isolates) (Table 4.8). The isolates were shared into 29 different serological entities with *S.* Typhimurium as the most dominant serovar with 39 isolates, including one isolate belonging to the monophasic *S.* Typhimurium variant type 4,[5],12:i:- (Table 4.8). Some isolates belonged to exotic serovars, which are rarely observed in Sweden, such as *S.* Fulica and *S.* Mapo.

The highest number of isolates was from cattle, 29 isolates, belonging to 10 different serovars dominated by *S.* Typhimurium and *S.* Dublin. *Salmonella* Dublin is a host adapted serovar, which is rarely found in other animal species than cattle, whereas *S.* Typhimurium can infect a large range of animal species. Other serovars from cattle were represented by only one or two isolates.

In pigs, five different serovars were found, also dominated by *S.* Typhimuium. Three isolates belonged to *S.* Derby, which is a serovar that is well known as a dominant serovar in pig production in many other countries.

Table 4.8. Serovar distribution and number of *Salmonella* isolates (n=130) tested for antimicrobial susceptibility, 2021.

Serovar	Cattle	Pig	Poultry	Sheep	Goat	Horse	Cat	Dog	Wild birds	Wild mammals	Total
S. Agona								1			**1**
S. Choleraesuis		3								6	**9**
S. Coeln								1			**1**
S. Derby	1	3						1			**5**
S. Dublin	7										**7**
S. Duesseldorf	2						1			1	**4**
S. enterica subsp. *diarizonae* 38:r:-										1	**1**
S. enterica subsp. *diarizonae* 38:r:z										3	**3**
S. enterica subsp. *diarizonae* 38:-:z							1				**1**
S. enterica subsp. *diarizonae* 42:r:z										1	**1**
S. enterica subsp. *diarizonae* 61:-:-				1							**1**
S. enterica subsp. *diarizonae* 61:-:1,5				20							**20**
S. enterica subsp. *diarizonae* 65:i:-										1	**1**
S. enterica subsp. *enterica* 68:-:e,n,x										1	**1**
S. enterica subsp. *enterica* 68:-.1,2										1	**1**
S. enterica subsp. *enterica* 4,5:-:1,5	1										**1**
S. enterica subsp. *enterica* 6,7:-:1,5	2	1								4	**7**
S. enterica subsp. *enterica* 6,7:-:5		1									**1**
S. enterica subsp. *enterica* 6,7:c:-										1	**1**
S. Enteritidis			10							2	**12**
S. Fulica									1	1	**2**
S. Hassarek									2		**2**
S. Infantis								2			**2**
S. Mapo	1										**1**
S. Newport	1										**1**
S. Reading	2										**2**
S. Tennessee			2								**2**
S. Typhimurium	11	9	3			2	8	1	2	2	**38**
S. Typhimurium, monophasic variant	1										**1**
Total	**29**	**17**	**15**	**21**		**2**	**10**	**6**	**5**	**25**	**130**
% of total	**22**	**13**	**12**	**16**		**2**	**8**	**5**	**4**	**19**	**100**

Again in 2021 a number of *S.* Choleraesuis were found. This serovar, which is host adapted to pigs and may cause severe disease outbreaks in infected farms, was not found in Swedish pig production for many years but reappeared in 2020. Isolates of this serovar were found in both domestic pigs and wild boars (Table 4.6). It is a general assumption that the wild boar population constitutes a reservoir for *S.* Choleraesuis which may spill over to domestic pigs via routes that do not include direct contact, although this has not been epidemiologically proven. It emphasizes wildlife as a potential reservoir of zoonotic pathogens. Nine isolates, two from cattle, two from pigs and five from wild boars had the antigenic formulae 6,7:-:1,5, 6,7:-:5, or 6.7:c:- and it is possible that these isolates or most of them were in fact monophasic derivatives of *S.* Choleraesuis, which has the antigenic formula 6,7:c:1,5. The true number of *S.* Choleraesuis cases may therefore be higher than nine.

Isolates from poultry were dominated by *S.* Enteritidis, which is a well known serovar in poultry worldwide, and a major source of human salmonellosis. Other serovars found in poultry were *S.* Tennessee and *S.* Typhimurium. One of the *S.* Typhimurium isolates was from geese, and the other two from chickens.

The subspecies *diarizonae* is usually associated with reptiles, but none of the subspecies *diarizonae* isolates in 2021 were recovered from reptiles. The serovar *S. enterica* subsp. *diarizonae* 61:-:1,5 is present in sheep in both Sweden and several other countries, such as Norway, Iceland, Switzerland, UK, Spain, Germany, and the USA. It is considered a serovar host adapted to sheep where it may cause both intestinal and extraintestinal infections, but in most cases the animals are healthy carriers of the bacterium in the intestine, vagina, tonsils, or nose. Although it is still notifiable in Sweden, it has for this particular serovar been decided not to follow up with backtracing and eradication. Twenty isolates from sheep belonged to this serovar. One isolate from a sheep had the antigenic formula 61:-:-, which may be an aphasic variant of 61:-:1,5 although this was not further investigated. The other subsp. *diarizonae* isolates were from a cat and from five wild boars.

Salmonella isolates from dogs and cats belonged to a variety of serovars, although isolates from cats were dominated by *S.* Typhimurium.

Five isolates from wild birds – two jackdaws, a bullfinch, a gull, and a greater woodpecker – were subjected to serotyping and susceptibility testing. Two of the isolates, both from jackdaws, were *S.* Hessarek, a serovar, which is generally considered host specific to birds, and it has also previously been found in Swedish wild birds. *Salmonella* Fulica, on the other hand, which is antigenically related to *S.* Hessarek, is very unusual, and has previously been described from harbour porpoises in Scotland.

Twenty-five isolates were from wild mammals. The two *S.* Enteritidis isolates were from hedgehogs, while the remaining 23 belonging to 12 different serovars all were from wild boars. This again underlines the potential of wild boars to carry zoonotic agents.

Distributions of MICs and resistance for all isolates are presented in Table 4.9 and for the subset *S.* Typhimurium in Table 4.10. 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*. Seven isolates had an MIC of 4 mg/L for colistin (Table 4.9). 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 seven isolates belonged to serovars Dublin (6 isolates) and Enteritidis (1 isolate); both are serovars that often display slightly higher MIC values to colistin than most other serovars.

Table 4.9. Distribution of MICs and resistance (%) in *Salmonella enterica* (n=130) from all animals, 2021.

Antibiotic	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	0									100								
Ampicillin	3							85.4	10.8	0.8				3.0				
Azithromycin	0								16.9	75.4	7.7							
Cefotaxime	0					100												
Ceftazidime	0					90.0	10.0											
Chloramphenicol	2										97.7	0.8			1.5			
Ciprofloxacin	9	66.9	24.6		7.7	0.8												
Colistin[a]	NA							83.8	10.8	5.4								
Gentamicin	0						90.8	9.2										
Meropenem	0		96.2	3.8														
Nalidixic acid	8									88.5	3.1				8.4			
Sulphamethoxazole	5										6.9	40.8	44.6	3.1				4.6
Tetracycline	5								94.6	0.8			0.8	3.8				
Tigecycline	0					95.4	4.6											
Trimethoprim	2					74.6	20.0	3.1					2.3					

[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 4.10. Distribution of MICs and resistance (%) in *Salmonella* Typhimurium, including monophasic variants (n=39) from all animals, 2021.

Antibiotic	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	0									100								
Ampicillin	8							76.9	12.8	2.6				7.7				
Azithromycin	0								38.5	53.8	7.7							
Cefotaxime	0					100												
Ceftazidime	0					84.6	15.4											
Chloramphenicol	5										92.3	2.6			5.1			
Ciprofloxacin	0	84.6	15.4															
Colistin	NA							76.9	23.1									
Gentamicin	0						71.8	28.2										
Meropenem	0		89.7	10.3														
Nalidixic acid	0									97.4	2.6							
Sulphamethoxazole	10										7.7	38.9	46.2					10.3
Tetracycline	8								92.3				2.6	5.1				
Tigecycline	0					92.3	7.7											
Trimethoprim	3					59.0	35.9	2.6					2.6					

NA: Not applicable.

The majority of the isolates (113 of 130; 87%) were susceptible to all antibiotics tested, only 17 isolates being resistant to one or more compounds. Interestingly, 10 *S.* Enteritidis isolates, all from poultry, were quinolone resistant, both to nalidixic acid and ciprofloxacin, but susceptible to all other antibiotics. In 2020, an isolate, also from poultry, with the same resistance profile was found. It must be assumed that these isolates are epidemiologically related, although no further investigations on this have been made. Two other *S.* Enteritidis that were recovered from hedgehogs were fully susceptible. Only one other isolate, a *S.* Infantis from a dog, was resistant to quinolones. One *S.* Typhimurium isolate was resistant only to sulphonamides, which is unusual, while two other *S.* Typhimurium were resistant to ampicillin, sulphonamides, tetracyclines, and chloramphenicol. The single monophasic isolate had the resistance profile, which is typical for monophasic *S.* Typhimurium, i.e., resistance to ampicillin, sulphonamides and tetracyclines.

Table 4.11. MICs (mg/L) in the 17 isolates of *Salmonella enterica* resistant to one or more antibiotics, 2021. Shaded fields indicate resistance.

Source	Serovar	Amp	Ctx	Caz	Mero	Gen	Amk	Sul	Tmp	Chl	Tet	Nal	Cip	Col	Azt	Tgz
Pig	Derby	>32	≤0.25	0.5	≤ 0.03	≤0.5	≤ 4	>512	>16	≤8	>32	≤4	≤0.015	≤1	4	0.5
Wild boar	6,8:-:e,n,x	≤1	≤0.25	≤0.25	≤ 0.03	≤0.5	≤ 4	32	≤0.25	≤8	>32	≤4	≤0.015	≤1	4	≤0.25
Poultry	Enteritidis	2	≤0.25	≤0.25	≤ 0.03	≤0.5	≤ 4	32	≤0.25	≤8	≤2	>64	0.12	≤1	4	≤0.25
Poultry	Enteritidis	≤1	≤0.25	≤0.25	≤ 0.03	≤0.5	≤ 4	16	≤0.25	≤8	≤2	>64	0.12	2	4	≤0.25
Poultry	Enteritidis	≤1	≤0.25	≤0.25	≤ 0.03	≤0.5	≤ 4	16	≤0.25	≤8	≤2	>64	0.12	2	4	≤0.25
Poultry	Enteritidis	≤1	≤0.25	≤0.25	≤ 0.03	≤0.5	≤ 4	32	0.5	≤8	≤2	>64	0.25	4	4	≤0.25
Poultry	Enteritidis	≤1	≤0.25	≤0.25	≤ 0.03	≤0.5	≤ 4	16	≤0.25	≤8	≤2	>64	0.12	≤1	4	≤0.25
Poultry	Enteritidis	≤1	≤0.25	≤0.25	≤ 0.03	≤0.5	≤ 4	16	≤0.25	≤8	≤2	>64	0.12	≤1	4	≤0.25
Poultry	Enteritidis	≤1	≤0.25	≤0.25	≤ 0.03	≤0.5	≤ 4	16	≤0.25	≤8	≤2	>64	0.12	≤1	4	≤0.25
Poultry	Enteritidis	≤1	≤0.25	≤0.25	≤ 0.03	≤0.5	≤ 4	32	≤0.25	≤8	≤2	>64	0.12	≤1	4	≤0.25
Poultry	Enteritidis	≤1	≤0.25	≤0.25	≤ 0.03	≤0.5	≤ 4	32	≤0.25	≤8	≤2	>64	0.12	≤1	4	≤0.25
Poultry	Enteritidis	≤1	≤0.25	≤0.25	≤ 0.03	≤0.5	≤ 4	32	≤0.25	≤8	≤2	>64	0.12	≤1	4	≤0.25
Dog	Infantis	2	≤0.25	0.5	≤ 0.03	≤0.5	≤ 4	>512	>16	≤8	>32	>64	0.12	≤1	4	0.5
Pig	Typhimurium	≤1	≤0.25	0.5	≤ 0.03	≤0.5	≤ 4	>512	0.5	≤8	≤2	≤4	0.03	≤1	8	≤0.25
Pig	Typhimurium	>32	≤0.25	0.5	≤ 0.03	≤0.5	≤ 4	>512	0.5	>64	>32	≤4	0.03	≤1	4	0.5
Pig	Typhimurium	>32	≤0.25	≤0.25	≤ 0.03	≤0.5	≤ 4	>512	0.5	>64	32	≤4	≤0.015	≤1	8	≤0.25
Cattle	Typhimurium[a]	>32	≤0.25	≤0.25	≤ 0.03	≤0.5	≤ 4	>512	>16	≤8	>32	≤4	≤0.015	≤1	4	0.5

[a]Monophasic variant.

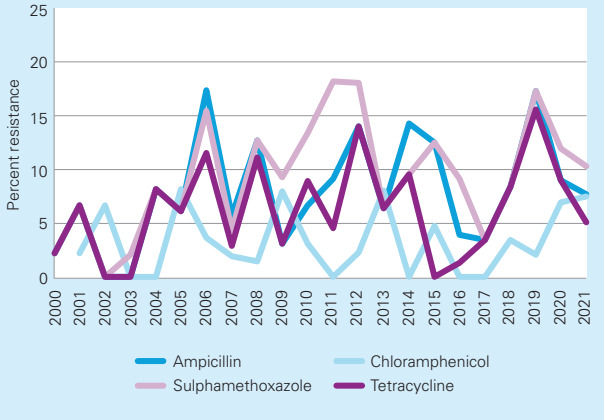
A single isolate from a wild boar was resistant to tetracycline, whereas all other isolates from wildlife were fully susceptible. This isolate had the antigenic formula 6,8:-:e,n,x, which is not included in the approved list of antigenic formulae of *Salmonella*. It may therefore represent a new serovar or alternatively be a monophasic variant of a known serovar. The absence of antibiotic resistance in isolates from wildlife suggests that although wildlife may constitute a reservoir for zoonotic pathogens, it is not a major reservoir for antibiotic resistant zoonotic pathogens.

All in all, only five isolates (4%) were multidrug resistant.

In 2021, amikacin was for the first time included in the test panel. No isolates were found resistant to amikacin. Likewise, no isolate was resistant to cefotaxime and ceftazidime (cephalosporins) or to meropenem (carbapenems) indicating that no isolates were ESBL or $ESBL_{CARBA}$.

In the subset of *S.* Typhimurium, resistance has varied over the years (Figure 4.3). The variation is largely due to differences in occurrence of multiresistant strains between the years (Table 4.10 and 4.11). Less resistance to ampicillin, sulphamethoxazole, and tetracycline seemed to occur in 2021 compared to 2019 and 2020, but care should be taken when drawing any conclusions on this since the numbers are low.

Figure 4.3. Resistance to ampicillin, chloramphenicol, sulphamethoxazole, and tetracycline in *Salmonella* Typhimurium in all animals, 2000-2021.



Farm animals 2000–2021

From a public health perspective, resistance in *Salmonella* from farm animals is of greater concern than resistance in isolates from wild animals or pets. This is because bacteria from animals raised for food production can contaminate carcasses at slaughter and be transmitted to humans through the food chain.

In the period 2000-2021, isolates from the vast majority of notified incidents in major farm animals were tested in Svarm, in total 928 isolates. About half of the isolates, 437 (47%), were *S.* Typhimurium and of these 166 (38%) were from pigs, 147 (34%) from cattle, 119 (27%) from poultry and 5 (1%) from sheep.

In 2021, 24 *S.* Typhimurium were isolated from farm animals. Of these only four were resistant to one or more compounds (Table 4.9), and three of these were multiresistant.

Two isolates from 2021, both from pigs, were resistant to ampicillin, sulphonamides, tetracycline, and chloramphenicol. This was the typical profile of the *S.* Typhimurium DT104 clone, which was widespread in many countries during the 1990'ies but now is less prevalent. However, since most countries have stopped using phage typing, it is difficult to know how prevalent this clone is now. The present isolates were not investigated further to determine whether they were indeed DT104. Isolates with this resistance combination are often also resistant to streptomycin and florfenicol, but this was not investigated. This resistance phenotype has also been found in previous years.

In 2021, a single isolate from farm animals was a monophasic *S.* Typhimurium, and it was from cattle. Since this variant was first found in 2006, only 18 incidents of monophasic *S.* Typhimurium had been confirmed in farm animals in Sweden up till 2021. Eleven of those involved only cattle, four only pigs, one only ducks and one incident involved both cattle and poultry. The majority of these monophasic isolates are multiresistant, which was also the case for the isolate found in 2021. Monophasic *S.* Typhimurium has spread over the last couple of decades in many European countries where it has become one of the most prevalent strains and it has been found in many different animal species. Most of these isolates display resistance to ampicillin, sulphonamides, and tetracycline which was also the case for the isolate from 2021 (Table 4.9).

Campylobacter

Campylobacter coli was isolated from samples of colon content from slaughter pigs collected at abattoirs for isolation of indicator bacteria. Isolates were species identified by MALDI-TOF MS. For details on methodology see Materials and methods, resistance in bacteria from animals.

Of the 174 isolates, 118 (68%) were susceptible to the six tested antibiotics. There was no resistance recorded against chloramphenicol, ertapenem, erythromycin, gentamicin, and tetracycline (Table 4.12). The level of quinolone resistance was comparable to previous years (Figure 4.4).

Figure 4.4. Ciprofloxacin resistance (%) in *Campylobacter coli* from pigs 1999-2021. In years 1999-2005 enrofloxacin was tested instead of ciprofloxacin. The number of isolates per year has varied (n=83-174, 2021 n=174).

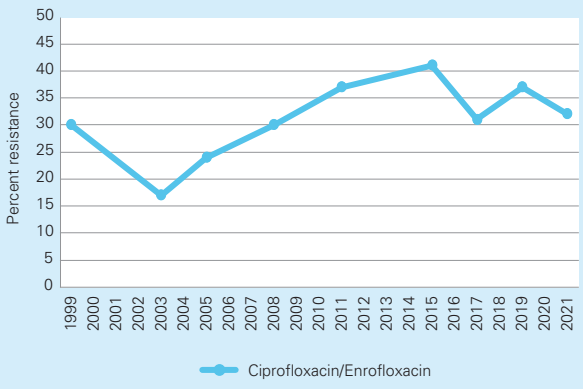


Table 4.12. Distribution of MICs and resistance (%) for *Campylobacter coli* from slaughter pigs, 2021.

Antibiotic	Resistance (%) n=174	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	>512
Chloramphenicol	0					68.4	31.0	0.6							
Ciprofloxacin	32	59.2	8.6				0.6	17.8	10.3	3.4					
Ertapenem	0	98.9	1.1												
Erythromycin	0				86.8	12.6	0.6								
Gentamicin	0			38.5	61.5										
Tetracycline	0			100											

Neither quinolones nor fluoroquinolones are authorised or used for treatment of groups of pigs via feed or water in Sweden. Additionally, a regulation (SJVFS 2013:42) has been restricting prescription of fluoroquinolones to animals in Sweden since 2013. It is mostly piglets that are treated individually with fluoroquinolons and to a lesser extent other age categories (Sjölund et al., 2015). Any selection for quinolone resistance in *Campylobacter* therefore probably mainly occurs in sows and suckling piglets.

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.

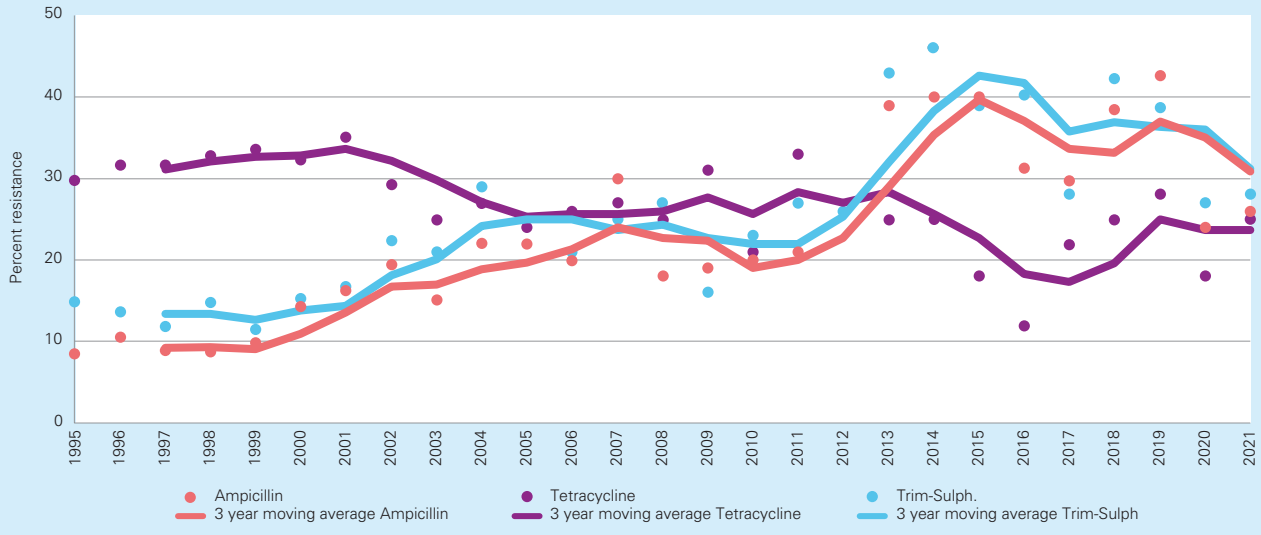
Pigs

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 4.13.

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 over the years with a peak in 2015-2016 but from 2019 there is a downward trend (Figure 4.5).

Figure 4.5. Resistance (%) in *Escherichia coli* from pigs 1995-2021 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, 2021 n=57). From 2020 only results from isolates with virulence factors are shown.



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 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 received by SVA as material from clinical submissions.

Multiresistance occurred in 16% (9/57) of the isolates in 2021 and has varied over the years (11% in 2020, 33% in 2019, 31% in 2018, 20% in 2017, 25% in 2016 and 2015). Fifty-six percent of the isolates were susceptible to all tested antibiotics. Four isolates were resistant to both first and second choice antibiotic (trimethoprim-sulphamethoxazole and neomycin) recommended in Sweden for treatment of diarrhea caused by ETEC (Medical Products Agency, 2022) and one isolate was also resistant to the last choice enrofloxacin. For comparison of resistance in *E. coli* from other animal species see Comparison of antibiotic resistance in *E. coli* and *Staphylococcus* spp., Table 4.37.

Brachyspira hyodysenteriae

Isolates of *Brachyspira hyodysenteriae* are from clinical submissions of faecal samples. Only the first isolate from each herd each year is tested for antibiotic susceptibility. 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 4.14 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 2017-2021.

Table 4.13. Distribution of MICs and resistance (%) in enterotoxigenic *Escherichia coli* from pigs 2021.

Antibiotic	Resistance (%)	Distribution (%) of MICs (mg/L)										
	2021 n=57	≤0.06	0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	26						59.7	14.0			26.3	
Cefotaxime	0			100								
Colistin[a]	2					96.5	1.8	1.8				
Enrofloxacin	2		98.2		1.8							
Gentamicin	2						98.2				1.8	
Meropenem	0	100.0										
Neomycin	7							93.0				7.0
Tetracycline	25						75.4				24.6	
Trim-Sulph.[b]	28				70.2	1.8			28.1			

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

Table 4.14. Resistance (%) in *Brachyspira hyodysenteriae* from pigs 2005–2021 and distribution of MICs for isolates from 2017-2021. Clinical isolates from faecal samples. The number of isolates each year varies (n=5-29, 2021 n=8).

Antibiotic	Resistance (%)					Distribution (%) of MICs (mg/L)												
	2005-06 n=54	2007-08 n=38	2009-11 n=40	2012-16 n=40	2017-21 n=47	≤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			19.2	63.8	17.0									
Tiamulin	7	18	8	10[a]	19[a]		34.0	6.4	40.4	8.5	6.4		2.1		2.1				
Tylosin	81	76	60	45	57							10.6	14.9	14.9	2.1				57.5
Tylvalosin		93	55	48	68					2.1	10.6	19.2	10.6	4.3	21.3	23.4		8.5	
Valnemulin	0	18	3	13	23	40.4	34.0	2.1	4.3	6.4	6.4	2.1	2.1	2.1					

[a]All isolates with MICs above 2 mg/L are from a defined outbreak in 2016-2017.

Brachyspira pilosicoli

Isolates of *Brachyspira pilosicoli* are from clinical submissions of faecal samples. ECOFFs for *B. pilosicoli* are not defined for the antibiotics tested. As guide for the choice of antibiotic for treatment of spirochaetal diarrhoea, clinical breakpoints for *Brachyspira hyodysenteriae* are used for tiamulin and tylosin at SVA but the assessed percentage of resistance using the same wild type cut-off value as for *B. hyodysenteriae* is also shown (Table 4.15).

Actinobacillus pleuropneumoniae

Isolates of *Actinobacillus pleuropneumoniae* are from post-mortem investigations of lungs. For 2021 the number of isolates were too few to present in a MIC distribution table. Data back to 2005 show that the resistance situation is favourable and almost no resistance has been detected to tested antibiotics including penicillin. 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.

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 2013-2017 (n=36) and 2018-2021 (n=52). Resistance to penicillin was detected from 2019 and onwards. (Table 4.16).

Table 4.15. Distribution of MICs for *Brachyspira pilosicoli* from pigs 2010-2021, n=204. Clinical isolates from faecal samples. The number of isolates each year varies (n=7-27, 2021 n=17).

Antibiotic	Resistance (%)		Distribution (%) of MICs (mg/L)													
	Clinical breakpoints[a]	Wild type cut-offs[b]	≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	>128
Doxycycline		5			37.3	52.9	4.9	2.9	1.5	0.5						
Tiamulin	9	23		54.4	13.2	9.8	9.8	2.5	1.5	1.5	2.5	4.9				
Tylosin	42	42							11.8	18.6	23.0	4.4	5.9	4.4	7.8	24.0
Tylvalosin		51				4.9	15.2	28.4	21.6	6.9	4.4	3.4	6.4	8.8		
Valnemulin		25	59.8	9.3	5.4	11.3	8.8	2.9	1.0		1.5					

[a]Resistance assessed by clinical breakpoints used for *B. hyodysenteriae*. [b]Resistance assessed by wild type cut-offs used for *B. hyodysenteriae*.

Table 4.16. Resistance (%) in *Streptococcus suis* from pigs 2013-2021. Distribution of MICs from 2018-2021. Clinical isolates from various organs of pigs. The number of isolates each year varies (2013-2017 n=36, 2018-2021 n=52, 2021=25).

Antibiotic	Resistance (%)		Distribution (%) of MICs (mg/L)								
	2013-2017	2018-2021	≤0.03	0.06	0.12	0.25	0.5	1	2	4	>4
Cephalothin	3	12						80.8	7.7	5.8	5.8
Enrofloxacin	NR[b]	NR[b]				42.3	53.8	3.8			
Erythromycin	8	8					92.3	1.9	1.9	3.8	
Gentamicin	NR[b]	NR[b]						3.8	34.6	42.3	19.2
Clindamycin	11	23					76.9		1.9	21.2	
Penicillin	0	14	76.9	5.8		3.8	7.7	3.8	1.9		
Tetracycline	67	65				28.8	5.8	3.8	34.6	9.6	17.3
Trim-Sulph.[a]	11	15				80.8	3.8	9.6	1.9	1.9	1.9

[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 4.17 and Figure 4.6). Multiresistance occurred in 23% (15/65) of the isolates from 2019-2021, compared to 47% in 2017-2018, 32% in 2016 and 56% in 2015. For resistance phenotypes in isolates in 2019-2021, see Table 4.18. For comparison of resistance in *E. coli* from other animal species see Comparison of antibiotic resistance in *E. coli* and *Staphylococcus* spp., Table 4.37.

Figure 4.6. Resistance (%) in *Escherichia coli* from calves 2007-2021. 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, 2019-2021=65).

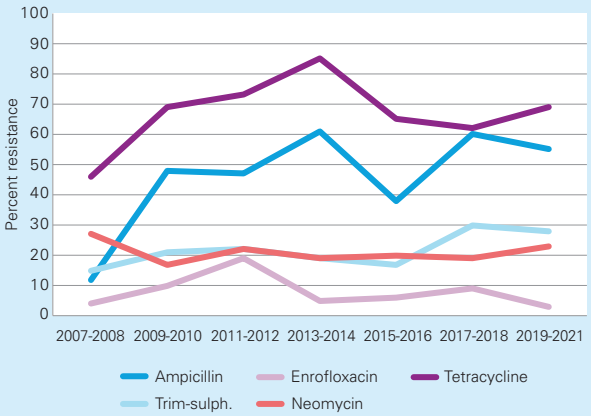


Table 4.17. Distributions of MICs and resistance (%) in *Escherichia coli* from calves 2019-21. Clinical isolates from faecal samples or from samples taken post-mortem from the gastro-intestinal tract.

Antibiotic	Resistance (%) 2019-2021 n=65	Distribution (%) of MICs (mg/L) ≤0.06	0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	55						43.1	1.5			55.4	
Cefotaxime[a]	2			98.5	1.5							
Colistin[b]	2					96.9	1.5			1.5		
Enrofloxacin	3		96.9	3.1								
Gentamicin	3						96.9	3.1				
Meropenem	0	100.0										
Neomycin	23							76.9		1.5	9.2	12.3
Tetracycline	69						29.2	1.5			69.2	
Trim-Sulph.[c]	28				72.3				27.7			

[a]45 isolates tested. The isolate with MIC 0.5 mg/L was further tested and $ESBL_A$ was detected. [b]The isolate with MIC 16 mg/L was tested with PCR for the *mcr-1* to *mcr-9* genes and found negative. [c]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphamethoxazole).

Table 4.18. Resistance phenotypes of isolates of *Escherichia coli* from calves 2019-21. Shaded areas with "R" indicate resistance.

Resistance phenotypes Tet	Amp	Tsu	Neo	Enr	Gen	Ctx	Col	Nit	Number of isolates
R	R	R		R					1
R	R	R							7
R	R			R					1
R	R					R			1
R	R								14
R		R	R						2
R			R		R				1
R			R						12
R									6
	R	R			R				1
	R	R					R		1
	R	R							6
	R								4
									8
								Sum	65

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 (78%, n=43) were susceptible to all antibiotics tested. Resistance to ampicillin (18%), tetracycline (9%), and trimethoprim-sulphamethoxazole (20%) were the most common traits (Table 4.19). Five isolates (9%) were multiresistant, i.e. resistant to three or more antibiotics.

Klebsiella pneumoniae from milk samples

Isolates of *Klebsiella pneumoniae* are from clinical submissions of milk samples from dairy cows (Table 4.20). All tested isolates (n=55) were susceptible to all tested antibiotics, excluding ampicillin to which there is an inherent low susceptibility

Staphylococcus aureus from milk samples

Isolates of *Staphylococcus aureus* are from clinical submissions of milk samples from dairy cows with clinical mastitis. In 2021, 605 isolates of *Staphylococcus aureus* were analysed for penicillinase production of which 1.2% (n=7) were positive.

Table 4.19. Resistance (%) in *Escherichia coli* from dairy cows 2017-2021. Distribution of MICs from 2021. Clinical isolates from milk.

Antibiotic	Resistance (%) 2017 n=79	2018 n=100	2019 n=74	2020 n=60	2021 n=55	Distribution (%) of MICs (mg/L) ≤0.06	0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	15	24	24	15	18						60	20.0	1.8		18.2	
Cefotaxime	0	0	0	0	0			100								
Colistin[a]	4[b]	0	0	0	0					100						
Enrofloxacin	3	1	3	2	0		100									
Gentamicin	0	1	3	2	0						100					
Meropenem				0[c]	0	100										
Neomycin	4	5	1	2	4							92.7	3.6		1.8	1.8
Tetracycline	9	8	18	7	9						89.1	1.8			9.1	
Trim-Sulph.[b]	9	14	11	5	20				78.2	1.8	1.8		18.2			

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphamethoxazole); [b]Three isolates with MIC 4 mg/L were negative for *mcr-1, mcr-2, mcr-3, mcr-4* and *mcr-5* genes with PCR; [c]Number of tested isolates n=55.

Table 4.20. Resistance (%) in *Klebsiella pneumoniae* from dairy cows 2017-2021. Distributions of MICs from 2021. Clinical isolates from milk.

Antibiotic	Resistance (%) 2017 n=34	2018 n=52	2019 n=34	2020 n=45	2021 n=39	Distribution (%) of MICs (mg/L) ≤0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	NR[b]	NR	NR	NR	NR								5.1	35.9	59.0		
Cefotaxime	0	0	0	0	0			100									
Colistin	9[c]	0	0	4[d]	0					100							
Enrofloxacin	3	8	6	4	0		100										
Gentamicin	0	0	0	2	0						100						
Meropenem				0[e]	0	100											
Neomycin	4	5	1	0	0							100					
Tetracycline	9	8	18	11	0						100						
Trim-Sulph.[a]	9	14	11	13	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; [d]Two isolates with MIC >8 mg/L were negative for *mcr-1* to *mcr-9* genes with PCR; [e]number of isolates tested n=44.

Microbiological diagnoses and antibiotic resistance for bovine mastitis pathogens

Mastitis is one of the most important infectious diseases in dairy cows and one of the diseases which causes most of the consumption of antibiotics for dairy cows. In Swedish dairy herds, mastitis accounts for about 60% of all antibiotics prescribed for parenteral treatment of dairy cows and benzylpenicillin administered systemically is used in over 80% of treatments for mastitis.

Since 2013, a continuous monitoring of the aetiology and antibiotic resistance in acute clinical mastitis in Swedish dairy cows has been in place under the SvarmPat programme. This monitoring is performed as a collaboration between the National Veterinary Institute, Farm and Animal Health AB, and veterinary practices under the District Veterinary Organization. District veterinarians collect samples from the first cases of clinical mastitis they observe every month and submit to SVA for laboratory examination. This procedure was chosen to avoid any sampling bias. At the same time certain information about the cow and the herd is collected. Here we report the results of the monitoring programme for the years 2013 – 2018.

A total of 823 bacterial diagnoses was obtained from 755 udder quarters in 734 cows. One or more microbial species assumed to be causal organism were isolated from 675 (89%) of the quarter samples. From 611 (90.5%) of them, only one species was isolated, from 61 (8.9%) samples two species were isolated, and from 4 (0.6%) samples three species (*Staphylococcus aureus*, *Streptococcus dysgalactiae* and *Trueperella pyogenes*) were isolated. Forty samples yielded no growth while another 40 samples were contaminated. *Staphylococcus aureus* (27.8%), *S. dysgalactiae* (15.8%), *Escherichia coli* (15.1%), and *Streptococcus uberis* (11.4%) were the most commonly detected species, while *Trueperella pyogenes*, non-*aureus* staphylococci

Table 1. Number of isolates (No), resistance (%), and MIC distribution (%) for *Staphylococcus aureus* (n=227) and non-*aureus* staphylococci (NAS) (n=21) from clinical mastitis in dairy cows, 2013-2018.

Antibiotic	Species	No	Resistance (%)	Distribution (%) of MICs (mg/L)												
				≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Cefoxitin	*S. aureus*	97	0						1.0	49.5	49.5					
	NAS	10	0				10.0			80.0	10.0					
Cephalothin	*S. aureus*	227	0			51.5	44.5	3.5	0.4							
	NAS	21	-			47.6	38.1	4.8	9.5							
Chloramphenicol	*S. aureus*	227	0								19.8	77.1	3.1			
	NAS	21	0							4.8	71.4	19.1	4.8			
Ciprofloxacin	*S. aureus*	227	0			21.6	55.1	22.5	0.9							
	NAS	21	0			57.1	38.1	4.8								
Clindamycin	*S. aureus*	227	<1				99.1	0.9								
	NAS	21	14				85.7	4.8	4.8	4.8						
Enrofloxacin	*S. aureus*	97	-			46.4	49.5	4.1								
	NAS	10	-			70.0	30.0									
Erythromycin	*S. aureus*	227	0				56.0	34.8	9.2							
	NAS	21	10				71.4	19.1				4.8		4.8		
Gentamicin	*S. aureus*	227	0					89.4	9.3	1.3						
	NAS	21	0					100.0								
Linezolid	*S. aureus*	62	0						14.5	82.3	3.2					
	NAS	5	0						60.0	40.0						
Oxacillin	*S. aureus*	165	<1				45.5	23.6	25.5	4.9	0.6[a]					
	NAS	16	6				50.0	25.0	18.8		6.2[a]					
Penicillin[b]	*S. aureus*	227	3	60.4	32.2	4.0	0.4	0.4	0.4	0.9	0.9	0.4				
	NAS	23	30	33.3	28.6		9.5	9.5	9.5		9.5					
Tetracycline	*S. aureus*	227	<1					96.5	2.6	0.9						
	NAS	21	0					95.2	4.8							
Trimethoprim	*S. aureus*	227	9					20.7	41.0	29.5	7.5	1.3				
	NAS	21	-					28.6	14.3	19.1	19.1	9.5	9.5			
Trimethoprim-Sulphonamide[c]	*S. aureus*	97	0			97.9	2.1									
	NAS	10	-			60.0	20.0	10.0	10.0							

[a]1 *S. aureus* and 1 NAS tested negative for the *mecA* and *mecC* gene.[b]No cut-off value given, classification according to beta-lactamase production.[c]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphonamide).

(NAS), *Klebsiella* spp., *Enterococcus* spp., and *Streptococcus agalactiae* were found less often. Other bacteria were only found in a few cases each and together accounted for 2.6% of the diagnoses. These belonged to several genera. The NAS comprised *S. chromogenes*, *S. epidermidis*, *S. haemolyticus*, *S. simulans*, *S. cochnii*, and *S. hyicus*. Other Enterobacterales found included species of *Enterobacter*, *Citrobacter*, *Serratia*, *Proteus*, and *Yersinia*. Yeast were found in six cases. Distributions of MICs are shown in Table 1 (*S. aureus* and NAS), Table 2 (*S. dysgalactiae*, *S. uberis* and *S. agalactiae*) and Table 3 (*E. coli* and *Klebsiella* spp.). For combinations where EUCAST ECOFF values were available, interpretation as resistant or sensitive was done.

Resistance among *S. aureus* was low, only 16 (7.0%) of the 227 isolates tested were resistant to one or more antibiotics. Penicillin resistance in *S. aureus*, i.e. beta-lactamase production, occurred in six isolates (2.6%). Furthermore, five isolates (2.2%) were resistant to more than one antibiotic. A higher fraction of the NAS isolates were resistant, i.e. 11 (52.3%) of the 21 NAS isolates were resistant to one or more antibiotic. Seven (30.4 %) of 23 tested isolates were resistant to penicillin through beta-lactamase production, while two isolates (9.5%) were resistant to more than one antibiotic. No *S. aureus* or NAS isolate carried a *mecA* or a *mecC* gene, i.e. no MRSA was observed.

Due to the lack of EUCAST cut-off values for streptococci for most antibiotics, the results are difficult to evaluate, but MICs were low for most antibiotics. While the penicillin MICs were low for most streptococci , some isolates had elevated values in particular among *S. uberis*, indicating penicillin resistance. For a few *S. uberis* isolates MICs of clindamycin and erythromycin were very high, indicating resistance to these compounds.

Table 2. Number of tested isolates (No), resistance (%), and MIC distribution (%) for *Streptococcus agalactiae, Streptococcus dysgalactiae* and *Streptococcus uberis* from clinical mastitis in dairy cows, 2013-2018.

Antibiotic	Species	No	Resistance (%)	Distribution (%) of MICs (mg/L)												
				≤0.03	≤0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Cephalothin	*S. agal.*	9	-			100.0										
	S. dysg.	120	-			96.7	1.7	0.8	0.8							
	S. uberis	89	-			74.2	12.4	11.2	2.3							
Chloramphenicol	*S. agal.*	9	-							100.0						
	S. dysg.	120	-					1.7	25.0	65.0	7.5	0.8				
	S. uberis	89	-						4.5	32.6	61.8	1.1				
Ciprofloxacin	*S. agal.*	9	0					77.8	22.2							
	S. dysg.	120	-				17.5	72.5	9.2	0.8						
	S. uberis	89	-			1.1	20.2	52.8	25.8							
Clindamycin	*S. agal.*	9	0				100.0									
	S. dysg.	120	0				100.0									
	S. uberis	89	-				96.6	1.1	1.1						1.1	
Enrofloxacin	*S. agal.*	2	-					50.0	50.0							
	S. dysg.	41	-			2.4	9.8	85.4	2.4							
	S. uberis	38	-				15.8	68.4	15.8							
Erythromycin	*S. agal.*	9	0				100.0									
	S. dysg.	120	-				99.2			0.8						
	S. uberis	89	-				96.7	1.1				1.1		1.1		
Gentamicin	*S. agal.*	9	-							44.4	44.4	11.1				
	S. dysg.	120	-					43.4	40.0	11.7	2.5	0.8	0.8	0.8		
	S. uberis	89	-					21.4	6.7	19.1	27.0	15.7	9.0	1.1		
Penicillin	*S. agal.*	9	0	44.4	44.4	11.1										
	S. dysg.	120	-	97.5	1.7		0.9									
	S. uberis	89	-	75.3	5.6	16.9	1.1				1.1					
Tetracycline	*S. agal.*	9	22					77.8				11.1			11.1	
	S. dysg.	120	-					8.4	10.0	49.2	27.5	2.5	0.8	0.8		0.8
	S. uberis	89	-					95.5	2.3			1.1			1.1	
Trimethoprim	*S. agal.*	9	-							33.3	55.6	11.1				
	S. dysg.	120	-					24.2	48.3	22.5	4.2		0.8			
	S. uberis	89	-					10.1	61.8	23.6	4.5					
Trimethoprim-Sulphonamide[a]	*S. agal.*	2	-			50.0	50.0									
	S. dysg.	41	-			85.4	14.6									
	S. uberis	38	-			78.9	21.1									

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

Also among the *E. coli* isolates, resistance was low, only 17 isolates (14.7%) were resistant to one or more antibiotics, most often to ampicillin (8.6%), streptomycin (7.8%), and/or sulphonamides (6.9%). Six isolates (5.2%) were resistant to all these antibiotics. No ESBL-producing isolates were found. Two isolates were resistant to ciprofloxacin. *Klebsiella* is considered intrinsically resistant to ampicillin, but apart from that, most isolates were susceptible to most antibiotics (Table 3).

Table 3. Number of tested isolates (No), resistance (%), and MIC distribution (%) for *Escherichia coli* and *Klebsiella* spp. isolated from cases of clinical mastitis in dairy cows, 2013-2018.

Antibiotic	Species	No	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	1024	>1024
Ampicillin	*E. coli*	116	9							17.2	58.6	14.7	0.9		0.9		0.9	6.9			
	Klebsiella	22	95										4.6	18.1	45.4	22.7	4.6	4.6			
Ceftazidime	*E. coli*	116	4					80.2	15.5	3.5	0.9										
	Klebsiella	22	0					81.8	18.2												
Cefotaxime	*E. coli*	116	0			57.8	39.7	2.6													
	Klebsiella	22	0			81.8	13.6	4.6													
Chloramphenicol	*E. coli*	116	0								7.8	57.8	34.5								
	Klebsiella	22	-								27.2	63.6	4.6		4.6						
Ciprofloxacin	*E. coli*	116	2	10.3	69.8	18.1			0.9	0.9											
	Klebsiella	22	5	4.6	31.8	36.3	22.7		4.6												
Colistin	*E. coli*	116	6						25.0	42.2	26.7	6.0									
	Klebsiella	22	5						9.1	63.6	22.7	4.6									
Enrofloxacin	*E. coli*	28	0			100.0															
	Klebsiella	6	-			100.0															
Florfenicol	*E. coli*	116	0									41.4	53.5	5.2							
	Klebsiella	22	-									68.2	27.3		4.5						
Kanamycin	*E. coli*	88	2										97.7		2.3						
	Klebsiella	16	-										100.0								
Gentamicin	*E. coli*	116	<1						79.3	18.1	1.7			0.9							
	Klebsiella	22	0						100.0												
Nalidixic acid	*E. coli*	116	<1								47.4	47.4	4.3					0.9			
	Klebsiella	22	-								45.4	40.9	4.6	9.1							
Streptomycin	*E. coli*	116	8									50.9	37.9	3.5	0.9	2.6	4.3				
	Klebsiella	22	-									72.7	4.6	13.6	4.6	4.5					
Sulpha-methoxazole	*E. coli*	116	7										19.0	50.9	23.3						6.9
	Klebsiella	22	-										9.1	22.7	45.4	18.2					4.6
Tetracycline	*E. coli*	116	4							64.7	31.0					2.6	0.9	0.9			
	Klebsiella	22	9							63.6	22.7	4.6		4.6	4.5						
Trimethoprim	*E. coli*	116	3				12.1	39.7	39.7	5.2					3.5						
	Klebsiella	22	-					31.8	50.0	13.6		4.6									
Trimethoprim-Sulphonamide[a]	*E. coli*	28	7						92.9				7.1								
	Klebsiella	6	0						100.0												

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

The probability of isolating *S. aureus* was higher if the cow was housed in tie stalls rather than loose housing, and if the cow was in early compared to mid lactation. *S. aureus* was also more common in quarters with two or more udder pathogens isolated compared to only one, and in mastitis cases occurring during the late housing season (January to April) compared to the early housing season (September to December). The probability of isolating NAS was higher during the late housing and pasture (May to August) seasons than during early housing season.

Streptococcus dysgalactiae was more common in quarters with two or more udder pathogens and from cases in early and peak than in mid lactation. The probability of isolating *S. uberis* was higher in cases during the early rather than the late housing season.

The risk of isolating *E. coli* was higher in peak and mid lactation compared to early lactation but was less common in quarters with two or more udder pathogens. *Klebsiella* spp. was 3.6 times more common in cows that had have a previous case of clinical mastitis in the current lactation, but more rarely isolated in the early housing season than during the pasture season.

Trueperella pyogenes was found much more often together with one or two other udder pathogens than in isolation and was also more common in cows in early lactation than in later lactation stages. It was also more common if the cow was in loose housing than in tie stalls and if the cow had a previous case of clinical mastitis in the current lactation.

Thus, season, housing conditions, stage of lactation, and history of previous intramammary infection all affected the likelyhood of infection with a given bacterial species.

In Sweden, benzylpenicillin is the drug of choice for treatment of mastitis caused by Gram positive bacteria, while mastitis caused by Gram negative bacteria are in general not treated with antibiotics. Fortunately, resistance to penicillin was low among staphylococci, streptococci and *Trueperella*, which indicates that Sweden is in a fortunate situation concerning the possibility to treat bovine mastitis.

This In focus is a summary of Duse et al. (2021). Further description of the study and a list of references can be found in the paper.

References

Duse A, Persson Waller K, et al. 2021, Microbial aetiology, antibiotic susceptibility and pathogen-specific risk factors for udder pathogens from clinical mastitis in dairy cows. *Animals*, 11:2113.

Pasteurella spp.

Most isolates of *Pasteurella* spp. are from nasal swabs from calves with respiratory disease or from post-mortem investigations of lungs. Isolates from 2013-2021 were identified to species level by MALDI-TOF MS and are *Pasteurella multocida*. Isolates from earlier years were identified with biochemical methods. Most of these isolates are also *P. multocida*, but species identification of some isolates is uncertain. Cut-off values for *P. multocida* (Table 6.11) are used for all isolates in Table 4.21.

Antibiotic resistance was generally rare among isolates of *Pasteurella* spp. (Table 4.21), but beta-lactamase producing *P. multocida* have been isolated every year since 2016. 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.

Mycoplasma bovis

Isolates of *Mycoplasma bovis* are from clinical submissions of nasal swabs or post-mortem investigations of lungs from calves with respiratory disease (Table 4.22). Published data regarding antibiotic susceptibility of *M. bovis* are scarce and no established breakpoints for either microbiological or clinical resistance are available. Mycoplasmas are intrinsically resistant to β-lactams due to their lack of a cell wall. For tetracycline and gamithromycin, the MICs were high for 34 (89%) and 36 (95%) of the isolates, respectively. For the majority of the isolates the florfenicol MICs were higher than the VetCast clinical breakpoints for *Pasteurella multocida* (R > 1 mg/L) and *Mannheimia haemolytica* (R > 2 mg/L) (VetCAST, 2019). Enrofloxacin MICs were low for all the tested isolates.

Sheep

Mannheimia haemolytica and *Bibersteinia trehalosi*

Isolates of *Mannheimia haemolytica* and *Bibersteinia trehalosi* are from post-mortem investigation of lungs from 2013-2014 (n=44) and 2019-2021 (n=34) (Table 4.23). ECOFFs for *Mannheimia haemolytica* have been used when available. Resistance to penicillin was more common in 2019-2021. Two of four isolates above the breakpoint were tested for penicillinase production and were negative.

Table 4.21. Resistance (%) in *Pasteurella* spp. from calves 2005-2021. Distribution of MICs from 2020-21. Clinical isolates from the respiratory tract, isolated from nasal swabs or from post-mortem investigations of lungs.

Antibiotic	Resistance (%)						Distribution (%) of MICs (mg/L)									
	2005-2015 n=239	2016 n=104	2017 n=86	2018 n=79	2019 n=63	2020-2021 n=89	≤0.06	0.12	0.25	0.5	1	2	4	8	16	>16
Ampicillin	0	13	2	5	3	3			93.3	3.4						3.4
Enrofloxacin	0[a]	0	0	0	0	0		100								
Florfenicol						0			31.5	68.5						
Penicillin	0	13	2	5	8	4		88.8	6.7			1.1			3.4	
Tetracycline	0	0	0	0	0	0				97.8	2.2					

[a]314 isolates tested.

Table 4.22. Distribution of MIC values in *Mycoplasma bovis* from calves 2018-2021 (n=38). Clinical isolates from the respiratory tract, isolated from nasal swabs or from post-mortem investigations of lungs.

Antibiotic	Distribution (%) of MICs (mg/L)												
	≤0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	>32
Enrofloxacin				2.6	89.5	7.9							
Florfenicol									13.2	76.3	10.5		
Gamithromycin									2.6	2.6		94.7	
Penicillin								100					
Tetracycline							10.5		10.5	78.9			

Table 4.23. Resistance (%) in *Mannheimia haemolytica* and *Bibersteinia trehalosi* from sheep 2013-2014 and 2019-2021. Distribution of MICs from 2019-2021. Clinical isolates from the respiratory tract.

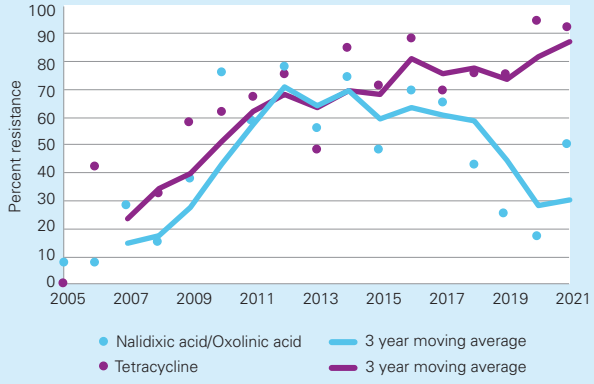
Antibiotic	Resistance (%)		Distribution (%) of MICs (mg/L)										
	2013-2014 (n=44)	2019-2021 (n=34)	≤0.12	0.25	0.5	1	2	4	8	16	32	64	128
Ampicillin	0	0		88.2	8.8	2.9							
Enrofloxacin	21	6	94.1			2.9		2.9					
Florfenicol	0	3		5.9	82.4	8.8				2.9			
Oxitetracycline	0	0			64.7	29.4	5.9						
Penicillin	5	12	26.5	38.2	23.5	5.9	5.9						
Tulathromycin		35				2.9	2.9	8.8	17.6	32.4	23.5	5.9	5.9

Farmed fish

Flavobacterium psycrophilum

Isolates of *Flavobacterium psycrophilum* are from clinical submissions of farmed fish. Data from 2016-2021 are compiled and presented as distributions of MICs in Table 4.24. Most isolates are from rainbow trout. Epidemiological cut-offs issued by CLSI are being used (CLSI, 2020c). Resistance to oxolinic acid and oxytetracycline was high in this material whereas no resistance to florfenicol was detected.

Figure 4.7. Resistance (%) in *Flavobacterium psycrophilum* from farmed fish 2005-2021 with a three-year moving average. The number of isolates each year varies (n=8-31, 2021 n=12).



In Figure 4.7 resistance to tetracycline and quinolones (nalidixic acid or oxolinic acid) in *F. psycrophilum* 2005-2021 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). However, for nalidixic acid/oxolinic acid a downward trend is seen the last five 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).

Flavobacterium columnare

Isolates of *Flavobacterium columnare* are from clinical submissions of farmed fish. Data from 2016-2021 are compiled and presented as distributions of MICs in Table 4.25. Most isolates of *F. columnare* are from rainbow trout and brown trout. Epidemiological cut-offs issued by CLSI are being used (CLSI, 2020c).

Table 4.24. Distributions of MICs and resistance (%) in *Flavobacterium psycrophilum* from farmed fish 2016-2021. The number of isolates each year varies (n=8-31, 2021 n=12).

Antibiotic	Resistance (%) 2016-2021 n=105	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					5.7	21.9	49.5	20.0	2.9			
Oxolinic acid	50	1.0			3.8	29.5	16.2	1.0	4.8	43.8			
Oxytetracycline	82			1.0	15.2	1.9	1.0	1.9	8.6	23.8	39.0	7.6	

Table 4.25. Distributions of MICs and resistance (%) in *Flavobacterium columnare* (n=42) from farmed fish 2016-2021.

Antibiotic	Resistance (%) 2016-2021 n=42	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					2.4	16.7	45.2	35.7				
Oxolinic acid	0		4.8	19.0	35.7	38.1	2.4						
Oxytetracycline	7			50.0	38.1	2.4	2.4	4.8	2.4				

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, by activities that increase knowledge of antibiotic resistance and prudent use of antibiotics, and by communication of knowledge to practitioners and farmers.

Selected studies within SvarmPat

Some of the resistance results 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 and 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* (27.8%), *Streptococcus dysgalactiae* (15.8%), *Escherichia coli* (15.1%), *Streptococcus uberis* (11.4%) and *Trueperella pyogenes* (7.7%). Most pathogens were susceptible to antibiotics used in Sweden. Resistance to penicillin was low in *S. aureus* (2.6%), 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. See also In focus Microbiological diagnoses and antibiotic resistance for bovine mastitis pathogens.

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 2021 about 1350 isolates of anonymous origin have been tested. Between 2010 and 2017 MRSA was confirmed in ten isolates.

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.

Lung ultrasound as a tool to assess pneumonia in calves

The aim of a project was to evaluate the criteria for initiating antibiotic therapy and its effect in calves with respiratory symptoms (Sandelius, 2022). All recently introduced calves in one fattening herd were examined daily by lung ultrasound. In the study group antibiotic treatment was given to calves when consolidated areas in the lungs >2 cm was detected, whereas in the control group, treatment was given to calves with clinical signs according to general veterinary guidelines. The results indicate that ultrasound detects pneumonia at a much earlier phase and that criteria for antibiotic treatment of calves with respiratory signs might need to be modified. The project continues and will be further evaluated in 2022.

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.

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. Multiresistance has varied between 11 and 42% without a clear trend. This emphasizes the importance of susceptibility testing in herds with neonatal and post-weaning diarrhoea.

In 50 herds *Escherichia coli* was isolated from neonates and weaned piglets with diarrhoea, and antibiotic use in the herd was investigated by a questionnaire (Backhans et al., 2022a). Resistance to ampicillin and trimethoprim-

sulphamethoxazole was more common in isolates from neonates, but tetracycline resistance was more common in weaned pig isolates. Antibiotic treatments were most common in neonates and sows. The results indicate that resistance in *E. coli* correlates with the level of antibiotic use in each age group.

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 less severe but more common than swine dysentery. Cases with treatment failure have been reported, but breakpoints for antibiotic resistance specific for *B. pilosicoli* are lacking. In a project, tiamulin MICs and tylosin MICs for isolates from herds with a history of swine dysentery the past 10 years were compared to isolates from herds free of swine dysentery. In dysentery herds, 34% of isolates were resistant to tiamulin, compared to 22% in dysentery free herds. For tylosin, 44% were resistant in dysentery herds and 39% in dysentery herds. About 30 isolates with different MICs for tiamulin and tylosin were analysed by whole genome sequencing, with the aim to search for resistance mechanisms by looking for genetic changes previously associated with reduced susceptibility to pleuromutilins and macrolides. The results were inconsistent in that some changes were found in isolates with reduced susceptibility but not all, and also in susceptible isolates. Probably other yet unknown mechanisms are involved.

Bacteria in milk from sows

Mastitis in lactating sows is common and sometimes treated with antibiotics. The knowledge of the pathogens that cause mastitis in sows is deficient, partly due to the difficulties in obtaining good samples. In a project since 2016, milk samples from 30 sows with clinical mastitis were cultured and isolates susceptibility tested. One specific bacterial species was isolated from 21 samples whereas 13 resulted in a mixed culture. *Escherichia coli* was the most common species, but staphylococci or streptococci were isolated from half of the samples (Backhans et al., 2022b).

Bacteria from farmed fish

In case of outbreaks of disease caused by pathogenic bacteria, up to five isolates from each outbreak are being susceptibility tested within SvarmPat from samples or fish sent to SVA. Bacterial species vary depending on the fish species. In 2021 isolates of *Flavobacterium psychrophilum*, *Flavobacterium columnare*, *Aeromonas* spp., *Aeromonas salmonicida* var. salmonicida, *Aeromonas hydrophila*, *Vibrio anguillarum*, *Yersinia ruckeri* and *Edwardsiella tarda* were susceptibility tested.

References

Backhans A, Matti F, et al. Antibiotic resistance in enterotoxigenic (ETEC) and non-enterotoxigenic Escherichia coli from suckling piglets and weaned piglets with diarrhoea. In Proceedings: 13th European Symposium of Porcine Health Management, Budapest, Hungary, May 11-13, 2022a.

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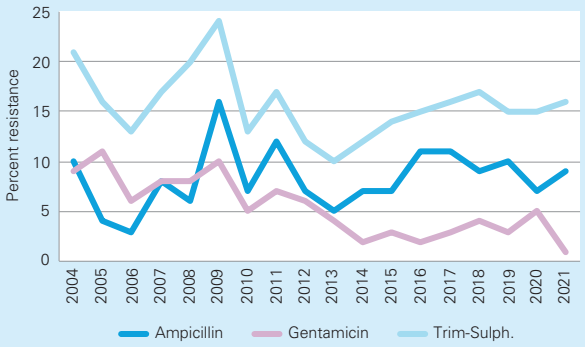
Horses

Escherichia coli

Isolates of *Escherichia coli* are from clinical submissions of the genital tract of mares. As in previous years, resistance to trimethoprim-sulphamethoxazole was the most common trait in 2021. Furthermore, the occurrence has gradually increased from 10 to 17% between 2013 and 2018 but has stabilized the last three years (2019-2021, 15-16%) (Table 4.26 and Figure 4.8). The resistance to gentamicin is continuously low. However, the occurrence of resistance has differed somewhat over the years and trends are difficult to estimate.

Eighty-one percent (252/312) of the isolates were susceptible to all the tested antibiotics. The proportion of multiresistance for the isolates was 5% (15/312), which is comparable to the figures in 2020 (5%) but a slight decline compared to 2019 (9%) (see previous Swedres-Svarm reports). Ten of the fifteen multiresistant isolates were resistant to three antibiotics, three to four antibiotics and two to five. The most common phenotype was resistance to ampicillin, tetracycline and trimethoprim-sulphamethoxazole, occurring in 73% (11/15) of the multiresistant isolates. Resistance to these substances were present in all the isolates resistant to four and five antibiotics. This phenotype was also the most common in *E. coli* isolated from dogs (42%). For comparison of resistance in *E. coli* from other animal species see Comparison of antibiotic resistance in *E. coli* and *Staphylococcus* spp., Table 4.37.

Figure 4.8. Resistance (%) in clinical isolates of *Escherichia coli* from horses 2004-2021. Isolates are from clinical sampling of the genital tract of mares. The number of isolates each year varies (n=124-324, 2021 n=312).



One of the isolates was resistant to cefotaxime. Genes conferring transferable ESC resistance were not detected in the isolate. For more information about ESBL-producing Enterobacterales isolated from horses in Sweden, see Notifiable diseases, ESBL-producing Enterobacterales. None of the isolates were resistant to colistin or meropenem.

Streptococcus equi ssp. *zooepidemicus*

Isolates of *Streptococcus equi* ssp. *zooepidemicus* are from clinical submissions, mainly from the respiratory tract (89%). Over the years, most of the isolates have been susceptible to all

Table 4.26. Distributions of MICs and resistance (%) in *Escherichia coli* from horses, 2021. Clinical isolates from the genital tract of mares.

Antibiotic	Resistance (%) 2021 n=312	≤0.06	0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	9						44.6	42.6	4.2	8.7		
Cefotaxime	<1			99.7		0.3						
Colistin	0					99.7	0.3					
Enrofloxacin	1		98.7	0.6					0.6			
Gentamicin	1						98.7	0.6		0.3	0.3	
Meropenem	0	100										
Neomycin	1							99.0		0.3	0.3	0.3
Tetracycline	6						94.2				5.8	
Trim-Sulph.[a]	16				83.0	0.6			16.3			

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

Table 4.27. Distribution of MICs and resistance (%) in *Streptococcus equi* ssp. *zooepidemicus* isolated from horses, 2021. Clinical isolates mainly from the respiratory tract.

Antibiotic	Resistance (%) 2021 n=98	Distribution (%) of MICs (mg/L) ≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Cephalotin	1						99.0		1.0					
Clindamycin	9					90.8	9.2							
Erythromycin	0					100								
Gentamicin	NR[b]						1.0		3.0	95.9				
Nitrofurantoin	0										100			
Penicillin	0	100												
Tetracycline	NR[b]						4.1	37.8	51.0	7.1				
Trim-Sulph.[a]	0				96.9	3.0								

[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.

relevant tested substances. However, for clindamycin and trimethoprim-sulphamethoxazole the proportion of resistance has varied. For clindamycin between 4 and 11% in 2015-2021, and for trimethoprim-sulphamethoxazole between 0 and 18% during the same period (Table 4.27 and previous Swedres-Svarm reports).

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

Staphylococcus aureus

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

Resistance to penicillin due to penicillinase production is still the most common trait. Although this resistance has varied over the years the proportion has overall declined from 36% in 2008-2009 to 21-22% in 2020-2021 (Figure 4.9 and Table 4.28). The proportions of resistance to gentamicin, tetracycline and trimethoprim-sulphamethoxazole are lower compared to penicillin but have differed slightly over the years and therefore trends are difficult to estimate (Figure 4.9). Resistance to fusidic acid among the tested isolates has varied between 2017 and 2020 with 9, 17, 5 and 6% resistance respectively and the figure for 2021 was 7% (Table 4.28 and previous Swedres-Svarm reports).

Fifty-eight percent (105/182) of the isolates were susceptible to all the tested antibiotics. Eight isolates (4%) were resistant to three or more antibiotics, i.e., multiresistant, which is comparable to the figures in 2015-2020, 0-5% (see previous Swedres-Svarm reports). Three isolates were resistant to three of the tested antibiotics, one to four, three to five and one to six antibiotics. No specific phenotype was noticed among the multiresistant isolates. For comparison of resistance in *Staphylococcus* spp. isolated from other animal species see Comparison of antibiotic resistance in *E. coli* and *Staphylococcus* spp., Table 4.38.

Seven isolates were resistant to cefoxitin (MIC >4mg/L). All the isolates were tested with PCR for detection of the *mecA* and *mecC* genes and three were MRSA. For more information on MRSA in horses in Sweden, see Notifiable diseases, Methicillin resistant *Staphylococcus aureus* (MRSA).

Figure 4.9. Resistance (%) in clinical isolates of *Staphylococcus aureus* 2008-2021 from skin of horses. The number of isolates each year varies (n=75-182, 2021 n=182).

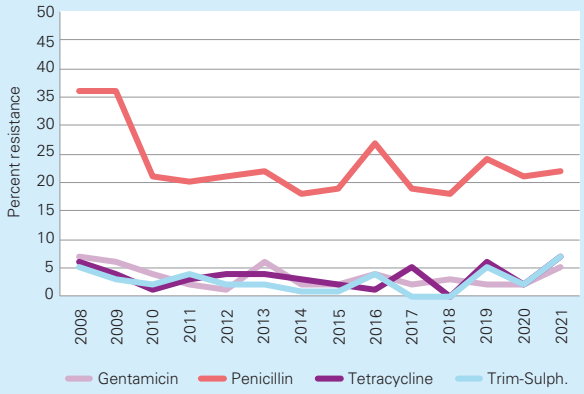


Table 4.28. Distribution of MICs and resistance (%) in *Staphylococcus aureus* isolated from horses, 2021. Clinical isolates from the skin.

Antibiotic	Resistance (%) 2021 n=182	Distribution (%) of MICs (mg/L) ≤0.25	0.5	1	2	4	8	16	32	64	>64
Cefoxitin	4[c]		1.1	0.5	7.7	86.8	2.2	1.6			
Cephalotin	2			97.8	1.1		1.1				
Clindamycin	4		95.6	0.5	2.2	1.6					
Enrofloxacin	3	94.5	2.7	1.1	1.6						
Erythromycin	2		95.1	2.7	1.1	1.1					
Fusidic acid	7		93.4	1.6	1.6	3.3					
Gentamicin	5			91.8	3.3	1.1	3.8				
Nitrofurantoin	3							90.7	6.6	2.7	
Penicillin[a]	22										
Tetracycline	7	56.6	33.0	3.3	2.7	4.4					
Trim-Sulph.[b]	7	90.1	2.7	5.5	0.5	0.5	0.5				

[a]Denotes beta-lactamase production; [b]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphamethoxazole); [c]Seven isolates were resistant to cefoxitin (MIC >4mg/L) and tested with PCR for detection of the *mecA* and *mecC* genes and three were MRSA.

Dogs

Escherichia coli

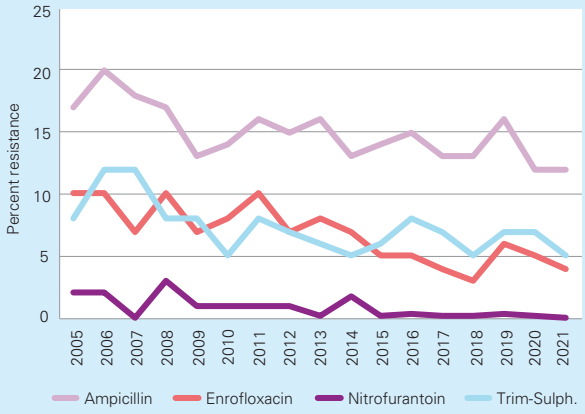
Isolates of *Escherichia coli* are from clinical submissions of urine, submitted either as urine or cultures from dip-slides or other agar plates. As in previous years, resistance to ampicillin was the most common trait in 2021, 12% (Table 4.29 and Figure 4.10). The proportion of resistance to ampicillin, enrofloxacin and trimethoprim-sulphamethoxazole in the tested isolates have declined somewhat throughout the years, but as the figures have differed between years clear trends are difficult to estimate (Figure 4.10).

Eighty-four percent (828/990) of the isolates were susceptible to all the tested antibiotics. The proportion of multiresistance was 2% (22/990) and comparable to 2020 (3%) but has somewhat declined compared to 2015-2019 (6-9%) (see previous Swedres-Svarm reports). Fifty-nine percent (13/22) of the multiresistant isolates were resistant to three antibiotics, 36% (8/22) to four and one isolate to five antibiotics. For comparison of resistance in *E. coli* from other animal species see Comparison of antibiotic resistance in *E. coli* and *Staphylococcus* spp., Table 4.37. The most common phenotype, resistance to ampicillin, tetracycline and trimethoprim-sulphamethoxazole, was detected in 59% (13/22) of the multiresistant isolates. This phenotype was found in all seven isolates resistant to four or more antibiotics, and all seven were also resistant to enrofloxacin. The one isolate resistant to five antibiotics was also resistant to gentamicin.

Fourteen (1%) of the *E. coli* isolates were resistant to cefotaxime (MIC >0.25 mg/L). Genes conferring transferable ESC resistance were detected in four of the isolates. For more information about ESBL-producing Enterobacterales isolated from dogs in Sweden, see Notifiable diseases, ESBL-producing Enterobacterales.

Two isolates were resistant to colistin (MIC >2mg/L). Both isolates were tested with PCR for the *mcr-1* to *mcr-9* genes and found negative.

Figure 4.10. Resistance (%) in clinical isolates of *Escherichia coli* from dog urine 2005-2021. The number of isolates each year varies (n=304-1162, 2021 n=990).



Staphylococcus pseudintermedius

In Swedres-Svarm before 2017, resistance from isolates of *Staphylococcus pseudintermedius* from clinical submissions of sample from skin lesions were reported (see previous Swedres-Svarm reports). From 2017 to 2021 figures of resistance from three different sample collections have been compared, namely skin lesions (S1), wounds (S2) and the external ear canal (S3) (Table 4.30 and previous Swedres-Svarm reports).

Resistance to penicillin due to penicillinase production is high for all three sample collections (71-74%) (Table 4.30). For isolates from skin lesions, where this information was compiled also before 2017, the figure has declined since 2009 (90%) to 74% in 2021. For isolates from wound and ear (figures compared from 2017 and onwards) the proportion of resistance to penicillin has also somewhat declined, from 79% in 2017 for both sample collections to 72% (wound) and 71% (ear) in 2021. Resistance to clindamycin, fusidic acid and tetracycline has differed somewhat over the years but has slightly declined and, in comparison to penicillin, remains at

Table 4.29. Distribution of MICs and resistance (%) in *Escherichia coli* from dogs, 2021. Clinical isolates from urine.

Antibiotic	Resistance (%) 2021 n=990	Distribution (%) of MICs (mg/L) ≤0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	12						54.3	32.3	1.5	0.1	11.7		
Cefalexin	1							10.2	81.1	7.3	0.1	1.3	
Cefotaxime	1[b]			98.6	0.6	0.4	0.1	0.3					
Colistin	<1[c]					98.9	0.9	0.2					
Enrofloxacin	4		96.2	1.3	0.8	0.2	0.1	0.3	1.1				
Gentamicin	1						99.0	0.7			0.3		
Meropenem	0	99.7	0.3										
Neomycin	<1							99.1	0.5	0.1	0.1	0.2	
Nitrofurantoin	0										99.7	0.3	
Tetracycline	3						96.5	0.1			3.4		
Trim-Sulph.[a]	5				94.3	0.7	0.1	0.3	4.5				

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphamethoxazole); [b]All isolates resistant to cefotaxime (n=14) were available for verification. Genes conferring transferable ESC resistance were detected in four of the isolates; [c]The two isolates resistant to colisitin were tested with PCR for the *mcr-1* to *mcr-9* genes and found negative.

lower levels (Table 4.30 and Figure 4.11). In 2021 the cut-offs were adjusted for gentamicin (from MIC 2 to 1 mg/L) and tetracycline (from MIC 1 to 0.5 mg/L) compared to the years before. The change of cut-offs had no impact on the comparison of the yearly figures.

Compared to other staphylococci isolated from animals, the proportion of susceptible isolates is low and the proportion of multiresistance is high. Susceptibility to all the tested antibiotics were observed in 22% of the isolates in all three sample collections. The proportion of multiresistance for the S1 isolates was 24% (139/573), S2 isolates 18% (139/774) and S3 17% (115/681). For comparison of resistance in *Staphylococcus* spp. isolated from other animal species see Comparison of antibiotic resistance in *E. coli* and *Staphylococcus* spp., Table 4.38. The difference in resistance to clindamycin (10-21%) and erythromycin (13-22%) (Table 4.30) between the three sample collections could mirror how various infections are treated. It might also be that some of the individuals are chronically diseased dogs, i.e. relapsing pyoderma, not sampled at the first visit and treated with the same or different antibiotics. A fraction of the isolates from ears (S3) were also tested for florfenicol in 2020 (n=92) and 2021 (n=40), and all were susceptible (data not shown).

Fifty-three percent (74/139) of the multiresistant S1-isolates were resistant to three antibiotics; 29% (40/139) to four; 12% (16/139) to five; 3% (4/139) to six; <1% (1/139) to seven and 3% (4/139) to eight antibiotics. The proportion of isolates resistant to five or more antibiotics has declined from one-third of the multiresistant S1-isolates in 2016 to 20-22% in 2017-2019, 15% in 2020 and 18% (25/139) in 2021. In sample collection S1, where comparisons could go further back than 2017, the proportion of resistance to several of the tested antibiotics have gradually declined (Figure 4.11 and previous Swedres-Svarm reports).

Resistance to penicillin, clindamycin and erythromycin was the most common phenotype, for the multiresistant S1-isolates 81% (112/139), S2 60% (83/139) and S3 52% (60/115). Ninety-seven percent (63/65) of the isolates in sample collection S1 resistant to four or more antibiotics had the common phenotype, combined with resistance to tetracycline 54% (35/65), fusidic acid 42% (27/65), gentamicin 28% (18/65) and/or trimethoprim/sulphamethoxazole 20% (13/65).

A total of 18 isolates (eight S1, nine S2 and one S3) were resistant to oxacillin (MIC >0.25 mg/L). Seventeen isolates were available for testing with PCR for detection of the *mecA* and *mecC* genes and sixteen were MRSP. For more information on MRSP isolated from dogs in Sweden, see Notifiable diseases, Methicillin-resistant *Staphylococcus pseudintermedius* (MRSP).

Figure 4.11. Resistance (%) in clinical isolates of *Staphylococcus pseudintermedius* from dogs 2007-2021. Clinical isolates from skin (S1). The number of isolates each year varies (n=220-573, 2021 n=573).

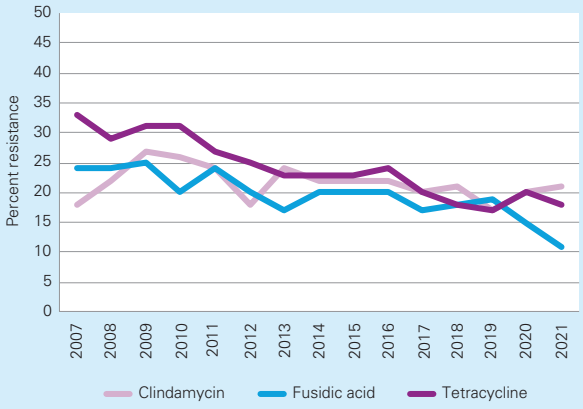


Table 4.30. Distribution of MICs and resistance (%) in *Staphylococcus pseudintermedius* from dogs 2021. Clinical isolates from skin (S1), wounds (S2) and external ear canals (S3).

Antibiotic	Resistance (%)			Distribution (%) of MICs (mg/L), isolates from skin (S1)									
	2021 n=681 S3	2021 n=774 S2	2021 n=573 S1	≤0.25	0.5	1	2	4	8	16	32	64	>64
Cephalothin	<1	<1	<1			99.3	0.5		0.2				
Cefoxitin[a]				24.4	71.6	1.6	1.0	1.0	0.3				
Clindamycin	10	12	21		79.2	0.9	0.3	19.5					
Enrofloxacin	2	1	2	96.3	1.9	0.2	1.6						
Erythromycin	13	14	22		77.7	0.7	0.2	21.3					
Fusidic acid	13	11	11		87.6	1.2	1.0	10.1					
Gentamicin	4	4	5			95.1	0.7	1.2	3.0				
Nitrofurantoin	<1	<1	<1							98.6	1.0	0.3	
Oxacillin	<1[d]	<1[d]	<1[d]	98.6	0.5		0.9						
Penicillin[b]	71	72	74										
Tetracycline	19	20	19	78.9	2.3	0.5		0.3	18.0				
Trim-Sulph.[c]	6	7	7	55.7	37.5	3.5	0.5	0.3	2.4				

[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]Seventeen of eighteen isolates (eight S1, nine S2 and one S3) resistant to oxacillin (MIC >0.25 mg/L) were available for testing with PCR for detection of the *mecA* and *mecC* genes and sixteen were MRSP.

Staphylococcus schleiferi

Isolates of *Staphylococcus schleiferi* are from clinical submissions of samples of various locations, but mainly from the external ear canal (63%), skin (17%) or wound (10%).

The proportion of resistance in isolates of *S. schleiferi* (Table 4.31) was low for most antibiotics compared to isolates of the more common staphylococci, *S. pseudintermedius*, isolated from dogs (Table 4.30). The proportion of penicillinase producing isolates among *S. schleiferi* was 2% which is low compared to other *Staphylococcus* spp. from animals reported in Swedres-Svarm (Table 4.38), and comparable to figures of *S. schleiferi* in 2014-2021 (<1-4%) (see previous Swedres-Svarm reports). Although the proportion of resistance to enrofloxacin is high compared to other *Staphylococcus* spp. from animals, the figures has declined from 20% in 2016 to 10% in 2021 (see previous Swedres-Svarm reports). The proportions of resistance to fusidic acid have differed over the years, between 14% (2016) and 3% (2018), in 2019, 8% and 2020, 12%. In 2021 the figure was 10%, and trends are difficult to estimate. For the other tested antibiotics there is no major difference between years (see Table 4.31 and previous Swedres-Svarm reports). A fraction of isolates from ears were also tested for florfenicol in 2020 (n=14) and 2021 (n=10), and all were susceptible (data not shown). In 2021 the cut-offs were adjusted for gentamicin (from MIC 2 to 1 mg/L) and tetracycline (from MIC 1 to 0.5 mg/L) compared to the years before. The change of cut-offs had no impact on the comparison of the yearly figures.

Seventy percent (146/210) of the *S. schleiferi* isolates were susceptible to all the tested antibiotics and somewhat lower compared to 2018 (81%), 2019 (76%) and 2020 (74%). Multiresistance was detected in 7% (15/210) of the isolates, an increase compared to the figures in 2017-2019 (1-2%) and 2020 (4%) (see previous Swedres-Svarm reports). The figure is based on rather few isolates (n=210) and if it is just random or a trend might be answered by the surveillance to come. Of the fifteen multiresistant *S. schleiferi* isolates, eleven were resistant to three, and four to four of the tested antibiotics. Eight of the fifteen multiresistant isolates were resistant to eryhtromycin, clindamycin and tetracycline. No other specific phenotype was noticed. For comparison of resistance in *Staphylococcus* spp. isolated from other animal species see Comparison of antibiotic resistance in *E. coli* and *Staphylococcus* spp., Table 4.38.

Pseudomonas aeruginosa

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

The bacterium 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, 1% or less of the tested isolates have been resistant to colistin.

The proportion of resistance to enrofloxacin has gradually declined from 25% in 2009 to 8% in 2019-2020 and 4%, in 2021. The figures for gentamicin have stabilized to about <1-2% over the recent years (Table 4.32 and previous Swedres-Svarm reports). Ninety-five percent (280/294) of the isolates were susceptible to all three tested substances. Four percent (13/294) was resistant to one antibiotic, and one isolate was resistant to both colistin and enrofloxacin.

Two isolates were resistant to colistin (MIC >2mg/L). Both isolates were tested with PCR for the *mcr-1* to *mcr-9* genes and found negative.

Table 4.31. Distribution of MICs and resistance (%) in *Staphylococcus schleiferi* from dogs, 2021. Clinical isolates from various locations.

Antibiotic	Resistance (%) 2021 n=210	Distribution (%) of MICs (mg/L) ≤0.25	0.5	1	2	4	8	16	32	64	>64
Cephalothin	<1			99.5	0.5						
Cefoxitin[a]		12.4	82.9	4.3	0.5						
Clindamycin	8		91.9	1.4	1.0	5.7					
Enrofloxacin	10	83.3	6.2	9.0	1.4						
Erythromycin	8		91.9	1.0	1.0	6.2					
Fusidic acid	10		80.5	9.5	8.6	1.0	0.5				
Gentamicin	3			97.1	1.4	1.0	0.5				
Nitrofurantoin	0							98.1	1.9		
Oxacillin	0	100									
Penicillin[b]	2										
Tetracycline	7	90.5	2.4	1.4	0.5	1.4	3.8				
Trim-Sulph.[c]	1	97.1	1.9	1.0							

[a]No cut-off for *S. schleiferi*; [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 *Pseudomonas aeruginosa* from dogs, 2021. Clinical isolates from the external ear canal.

Antibiotic	Resistance (%) 2021 n=294	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	>16
Enrofloxacin	4	2.4	6.5	44.6	32.0	10.9	2.0	1.7		
Colistin[a]	<1				71.1	24.1	4.1	0.3	0.3	
Gentamicin	<1					91.5	6.1	1.7	0.7	

[a]Colistin is equivalent to polymyxin B. The two isolates with MIC >4mg/L were tested with PCR for the *mcr-1* to *mcr-9* genes and found negative.

Pasteurella canis/oralis

Isolates of *Pasteurella* spp. are from clinical submissions of samples from various locations, but mainly, 91%, from the external ear canal, wounds, skin, abscesses, respiratory tract, and synovial fluid.

Pasteurella canis/oralis was the most common *Pasteurella* sp. isolated in samples from dogs, 81% (186/231). The isolates were species identified with MALDI-TOF MS and the species *P. canis* and *P. oralis* cannot be separated by the method. The proportion of resistance to antibiotics in the tested isolates was, as earlier years, low also in 2021 (Table 4.33). *Pasteurella* spp. have a low inherent susceptibility to aminoglycosides, e.g., gentamicin.

The cut-off for *Pasteurella multocida* has been applied for all *Pasteurella* spp. isolates tested. In 2021 the cut-off for *P. multocida* was adjusted for ampicillin compared to the years before, from MIC 1 to 0.5 mg/L. The proportion of resistance in *P. canis/oralis* has been low throughout the years and the change of cut-off had no impact on the comparison of the yearly figures.

The proportion of resistance to enrofloxacin between 2014 and 2021 has slightly increased, from <1% (2014) to 4% in 2020 and was 3% in 2021. Previously (2014-2019), all tested isolates have been susceptible to trimethoprim-sulphamethoxazole but in 2020 and 2021 an isolate each year was resistant (Table 4.33 and previous Swedres-Svarm reports). Of the six isolates resistant to any antibiotic, one was resistant to two (enrofloxacin and tetracycline), and five were resistant to one antibiotic.

Table 4.33. Distribution of MICs and resistance (%) in *Pasteurella canis/oralis* from dogs, 2021. Clinical isolates from various locations.

Antibiotic	Resistance (%) 2021 n=186	Distribution (%) of MICs (mg/L) ≤0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	>8
Ampicillin	0				98.9	1.1						
Enrofloxacin	3	93.0	3.8	0.5	0.5	1.6			0.5			
Gentamicin	NR[b]			4.8	34.9	51.6	5.9	2.2	0.5			
Penicillin	0			96.2	2.7	1.1						
Tetracycline	0			2.2	26.9	60.8	9.7	0.5				
Trim-Sulph.[a]	<1					98.9	0.5			0.5		

[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.

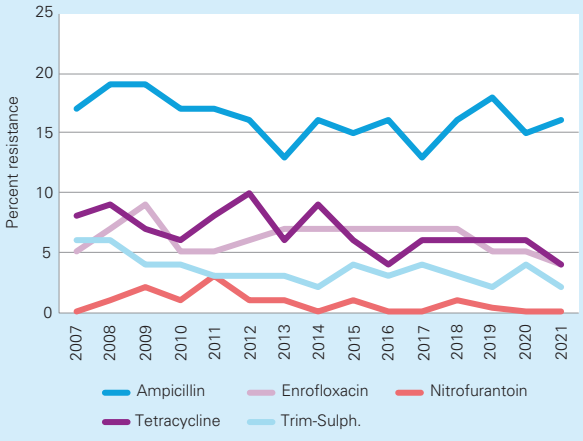
Cats

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 4.29), resistance to ampicillin was the most common trait in 2021 (Table 4.34 and Figure 4.12). In comparison, in *E. coli* from the genital tract of horses (mares) resistance to trimethoprim-sulphamethoxazole was most common (Table 4.26 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-eight percent (356/457) of the *E. coli* isolates were susceptible to all the tested antibiotics. The proportion of multiresistance was <1% (4/457), which is somewhat lower

Figure 4.12. Resistance (%) in clinical isolates of *Escherichia coli* from urine of cats, 2007-2021. The number of isolates each year varies (n=131-545, 2021 n=457).



compared to figures between 2010 and 2020 (2-5%) (see previous Swedres-Svarm reports). Three of the isolates were resistant to three antibiotics and one to four antibiotics. No specific phenotype was noticed. For comparison of resistance in *E. coli* from other animal species see Comparison of antibiotic resistance in *E. coli* and *Staphylococcus* spp., Table 4.37.

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

Two isolates were resistant to colistin (MIC >2mg/L). Both isolates were tested with PCR for the *mcr-1* to *mcr-9* genes and found negative.

Staphylococcus felis

Isolates of *Staphylococcus felis* are from clinical submissions of samples from various locations, but mainly the external ear canal (37%), abscesses and wounds (24%), and urine (24%).

The proportion of resistance to the tested antibiotics in isolates of *S. felis* (Table 4.35) were, as in previous years, less compared to *S. pseudintermedius* in dogs (Table 4.30 and previous Swedres-Svarm reports). For example, resistance to penicillin due to penicillinase production was 19% in *S. felis*, but 71-74% (three different sample collections) in *S. pseudintermedius*. In 2021 the cut-offs were adjusted for gentamicin (from MIC 2 to 1 mg/L) and tetracycline (from MIC 1 to 0.5 mg/L) compared to the years before. The change of cut-offs had no impact on the comparison of the yearly figures.

Seventy-five percent (266/353) of the *S. felis* isolates were susceptible to all the tested antibiotics. Multiresistance was detected in <1% (2/353) of the isolates, and lower compared to the figures in 2015-2020 (4-7%) (see previous Swedres-Svarm reports). The two multiresistant isolates were resistant to three of the tested antibiotics. The most common phenotype in the isolates resistant to two or more antibiotics was resistance to penicillin and erythromycin, 66% (19/29). For comparison of resistance in *Staphylococcus* spp. isolated from

Table 4.34. Distribution of MICs and resistance (%) in *Escherichia coli* isolated from cats, 2021. Clinical isolates from urine.

Antibiotic	Resistance (%) 2021 n=457	Distribution (%) of MICs (mg/L)											
		≤0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	16						60.2	22.3	1.5	1.1	14.9		
Cefalexin	2							15.1	79.0	3.9	2.0		
Cefotaxime	2[b]			98.2	1.1	0.2		0.4					
Colistin	<1[c]					99.1	0.4	0.4					
Enrofloxacin	4		95.8	1.8	1.8	0.2	0.2		0.2				
Gentamicin	<1						99.1	0.7			0.2		
Meropenem	0	99.8	0.2										
Neomycin	<1							99.1	0.2		0.2	0.4	
Nitrofurantoin	0										99.3	0.7	
Tetracycline	4						95.6	0.4	0.2		3.7		
Trim-Sulph.[a]	2				98.0	0.4			1.5				

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphamethoxazole); [b]Eight isolates were resistant to cefotaxime (MIC >0.25 mg/L) and genes conferring transferable ESC resistance were detected in two of the isolates; [c]Two isolates were resistant (MIC >2mg/L), available for PCR detection of the *mcr-1* to *mcr-9* genes and found negative.

Table 4.35. Distribution of MICs and resistance (%) in *Staphylococcus felis* from cats, 2021. Clinical isolates from various locations.

Antibiotic	Resistance (%) 2021 n=353	Distribution (%) of MICs (mg/L)									
		≤0.25	0.5	1	2	4	8	16	32	64	>64
Cephalothin	<1			99.7	0.3						
Cefoxitin[a]		92.1	6.5	0.6	0.6	0.3					
Clindamycin	5		95.2	1.1	0.3	3.4					
Enrofloxacin	<1	97.2	2.3	0.3	0.3						
Erythromycin	7		93.2	0.3	1.1	5.4					
Fusidic acid	2		95.2	3.1	1.4	0.3					
Gentamicin	2			98.3	1.1	0.6					
Nitrofurantoin	0							97.7	2.3		
Oxacillin	0	99.7	0.3								
Penicillin[b]	19										
Tetracycline	3	94.9	2.5	1.4			1.1				
Trim-Sulph.[c]	1	96.9	2.0	1.1							

[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).

other animal species, see Comparison of antibiotic resistance in *E. coli* and *Staphylococcus* spp., Table 4.38.

Pasteurella multocida

Isolates of *Pasteurella* spp. are from clinical submissions of samples from various locations, but mainly from wounds or skin lesions, abscesses, the external ear canal, and the respiratory tract (89%).

Pasteurella multocida was the most common *Pasteurella* sp. isolated in samples from cats, 89% (267/301). The proportion of resistance to antibiotics was low (Table 4.36). *Pasteurella* spp. have a low inherent susceptibility to aminoglycosides, e.g., gentamicin.

The proportion of resistance in *P. multocida* isolated from cats has been low throughout the years. For enrofloxacin the figures have varied between 0 and 3% and for trimethoprim-sulphamethoxazole <1 to 4%. In 2021 the cut-off for *P. multocida* was adjusted for ampicillin compared to the years before, from MIC 1 to 0.5 mg/L. The proportion of resistance in *P. multocida* isolated from cats has been low throughout the years and the change of cut-off had no impact on the comparison of the yearly figures.

Comparison of antibiotic resistance in *Escherichia coli* and *Staphylococcus* spp.

In order to describe the situation regarding antibiotic resistance in different animal species the occurrence of resistance in *E. coli* and different *Staphylococcus* spp. was compared. The occurrence of resistance was assessed as proportion of tested isolates that are susceptible to all tested substances and resistant to one or several substances respectively (Table 4.37 and 4.38). Furthermore, for *Staphylococcus* spp. occurrence of penicillinase production was also compared. All the tested isolates are from clinical submission. For details, see individual reports of animal and bacterial species in earlier sections.

Table 4.36. Distribution of MICs and resistance (%) in *Pasteurella multocida* from cats, 2021. Clinical isolates from various locations.

Antibiotic	Resistance (%) 2021 n=267	Distribution (%) of MICs (mg/L) ≤0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	>8
Ampicillin	0				41.2	58.4	0.4					
Enrofloxacin	3	74.9	21.3	0.4	0.4	0.7	1.1	0.7		0.4		
Gentamicin	NR[b]			0.4		0.7	0.4	5.2	37.1	53.6	2.6	
Penicillin	0			43.1	56.6	0.4						
Tetracycline	0			3.4	9.0	83.5	3.7	0.4				
Trim-Sulph.[a]	<1					99.3	0.4			0.4		

[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 4.37. Resistance (%) and multiresistance (%) in *Escherichia coli* isolated from different animal species tested with a fixed panel of 10 antibiotics. Isolates from clinical submissions 2021.

Animal species	Multiresistance (%)	Resistance (%) to 0->6 antibiotics 0	1	2	3	4	5	6	>6
Cats (urine)	<1	78	17	4	<1	<1			
Cattle, calves (faeces)	23	12	15	49	22	2			
Dogs (urine)	2	84	10	4	1	<1	<1		
Horses (genital tract)	5	81	11	4	3	1	<1		
Pigs (faeces)	16	56	18	11	12	2	2		

Table 4.38. Resistance (%) and multiresistance (%) in *Staphylococcus* spp. isolated from different animal species tested with a fixed panel of 11 antibiotics. Isolates from clinical submissions 2021.

Staphyloccus spp. and origin	Multiresistance (%)	pcas[a]	Resistance (%) to 0->8 antibiotics 0	1	2	3	4	5	6	7	8	>8
S. aureus – horses	4	22	58	30	8	2	<1	2	<1			
S. felis – cats	2	19	75	16	8	<1						
S. pseudintermedius[b] – dogs	24	74	22	36	18	13	7	3	<1	<1	<1	
S. schleiferi – dogs	7	2	70	20	4	5	2					

[a]Penicillinase production; [b]*S. pseudintermedius* from skin, for details see individual report in earlier sections.

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 2021, indicator *E. coli* from fattening pigs as well as from samples of pig and bovine meat were studied. Furthermore, indicator *E. coli* from healthy cattle under one year of age sampled from September 2020 to august 2021 were also studied. Samples of intestinal contents were collected at slaughter and samples of meat were collected at border control posts. The 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.

Escherichia coli

Pigs

Escherichia coli was isolated from 173 (100%) of 173 cultured caecal samples from pigs. The majority of the isolates (64%) was susceptible to all antibiotics tested (Table 4.93). Resistance to ampicillin (25%), sulphonamides (23%), trimethoprim (20%) and tetracycline (17%) were the most common traits (Table 4.39 and 4.40). Thirty-five isolates (20%) were multiresistant, i.e. resistant to three or more antibiotics. All of these had resistance to sulphonamides in their phenotype. Furthermore, most of the multiresistant isolates had resistance to ampicillin and trimethoprim in their phenotype.

Levels of resistance in *E. coli* from pigs are low in an international perspective. The proportion of isolates susceptible to all antibiotics tested has been relatively stable in the latest years (68% in 2015, 71% in 2017, 71% in 2019 and 64% in 2021). However, for some substances the situation has become less favourable in the latest years (Figure 4.13). More precisely, occurrence of resistance to ampicillin, sulphonamides, and trimethoprim in *E. coli* from pigs has increased considerably since 2008. Likewise, occurrence of resistance to tetracycline has increased since 2017. Furthermore, the decrease from 71% to 64% in isolates susceptible to all antibiotics tested seen in 2021 needs to be followed in the upcoming years. Regarding substances in the category B (restrict) of the AMEG classification (EMA, 2019a), resistance to polymyxins (colistin) has been tested since 2011 but has not been detected, and resistance to quinolones and cefotaxime (tested since 2008) has been stable at a low occurrence (Figure 4.13).

One of the isolates was resistant to cefotaxime and ceftazidime. This isolate 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. However, using a more sensitive method, selective culture, ESC resistant *E. coli* was isolated from 25 (8%) of 300 samples. In three of these isolates (1%), transferable genes for resistance to ESC were found. Two isolates had the $bla_{\text{CTX-M-15}}$ gene and the remaining isolate had the $bla_{\text{CTX-M-1}}$ gene. The remaining 22 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. For more details and comments on occurrence of resistance to ESC, see section Antibiotic resistance in animals, Notifiable disease.

Cattle under one year

Escherichia coli was isolated from 56 (98%) of 57 cultured caecal samples from cattle under one year. The majority of the isolates (95%) was susceptible to all antibiotics tested (Table 4.39). Two of the remaining three isolates were resistant to one substance each and the last isolate was resistant to two substances (Table 4.39 and 4.40). Consequently, no isolates were multiresistant, i.e. resistant to three or more antibiotics.

Levels of resistance in *E. coli* from cattle under one year are low in an international perspective. However, the raising conditions of this animal category is not comparable to veal calf production that might make up a large proportion of cattle slaughtered under one year of age in other parts of Europe.

None of the isolates were resistant to cefotaxime or ceftazidime. However, using selective culture, ESC resistant *E. coli* was isolated from 8 (14%) of 57 samples. In seven isolates (12%), transferable genes for resistance to ESC were found. All of these were $ESBL_A$ and carried $bla_{\text{CTX-M-15}}$ (n=6) or $bla_{\text{CTX-M-55}}$ (n=1). The remaining isolate with ESC-resistance 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. For more details and comments on occurrence of resistance to ESC, see section Antibiotic resistance in animals, Notifiable disease.

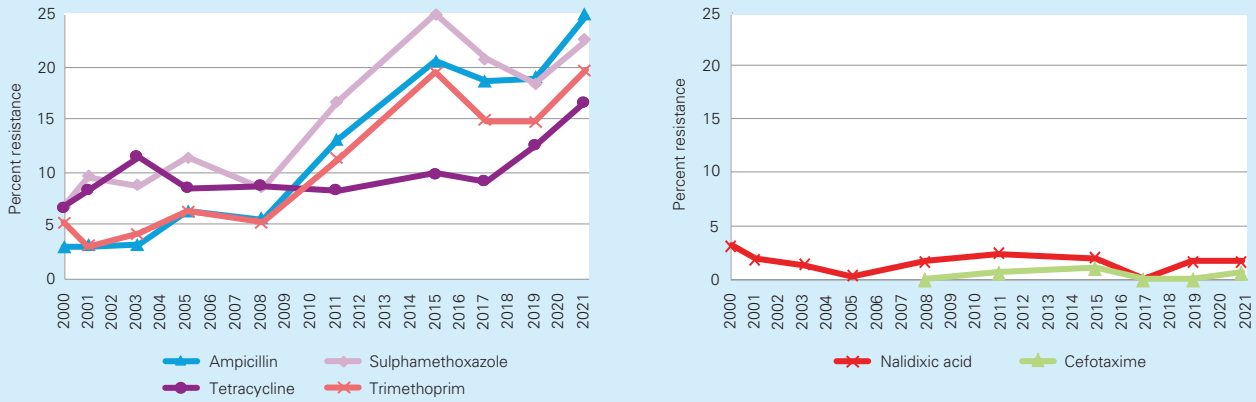
Meat

Regarding meat sampled at border control posts, *E. coli* was isolated from 3 of 15 samples of bovine meat and from 2 of 3 samples of pig meat. The isolates of *E. coli* were from 1 of 5 sampled consignments of bovine meat and from the only sampled consignment of pig meat. All three isolates from bovine meat and one of the two isolates from pig meat were susceptible to all antibiotics tested. The remaining isolate

from pig meat was resistant to ampicillin, chloramphenicol, ciprofloxacin, sulphonamides, and tetracycline. This was the first time that occurrence of resistance among indicator *E. coli* from meat sampled at border control posts was assessed in Svarm. Furthermore, the number of investigated isolates is low. Hence, no real conclusions can be drawn from these results.

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 investigated samples. For more details and comments on occurrence of resistance to ESC, see section Antibiotic resistance in animals, Notifiable disease.

Figure 4.13. Resistance (%) in *Escherichia coli* from fattening pigs 2000-2021. The number of isolates each year varies (n=140-390, 2021 n=175).



Resistance to colistin is not included in the figure showing substances in category B of the AMEG categorisation (EMA, 2019a) as it has not been detected during the years it has been investigated (2011-2021).

Table 4.39. Resistance (%) and multiresistance (%) in indicator *Escherichia coli* from fattening pigs, 2021, and cattle under one year, 2020-2021. 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
		2020 n=172	2012 n=92	2020-21 n=101	2012 n=61	2021 n=175	2006-09 n=115	2020 n=44	2012 n=74	2010-11 n=274
Amikacin	>8	-	-	0	-	0	-	-	-	-
Ampicillin	>8	13	18	2	3	25	2	9	9	2
Azithromycin	>16	0	-	0	-	<1	-	0	-	-
Cefotaxime	>0.25	0	0	0	2	<1	0	0	1	0
Ceftazidime	>0.5	0	-	0	-	<1	-	0	-	-
Chloramphenicol	>16	0	0	0	0	8	0	2	0	<1
Ciprofloxacin	>0.06	12	4	0	5	2	<1	5	3	<1
Colistin	>2	0	1	0	0	0	-	0	0	<1
Gentamicin	>2	<1	3	0	2	0	3	0	0	<1
Meropenem	>0.12	0	-	0	-	0	-	0	-	-
Nalidixic acid	>8	11	4	0	5	2	0	5	0	<1
Sulphamethoxazole	>64	15	16	2	8	23	7	9	4	15
Tetracycline	>8	7	14	2	13	17	<1	9	8	2
Tigecycline	>0.5	0	-	0	-	0	-	0	-	-
Trimethoprim	>2	9	7	2	5	20	2	2	1	16
Resistance (%) to 0->3 antibiotics[a]										
Susceptible to all above		72	66	95	80	64	89	80	84	83
Resistant to 1		15	18	4	7	10	8	14	8	2
Resistant to 2		3	7	2	7	6	3	2	7	12
Resistant to 3		6	3		7	12	<1	2		2
Resistant to >3		4	5			8		2	<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 4.40. Distribution of MICs and resistance (%) in *Escherichia coli* from intestinal content from fattening pigs (n=175), 2021, and cattle under one year (n=56), 2020-2021.

Antibiotic	Source	Resistance %	Distribution (%) of MICs (mg/L)																
			≤0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	>512
Amikacin	Pigs	0									98.3	1.7							
	Cattle <1 year	0									100								
Ampicillin	Pigs	25							8.1	27.7	38.7	0.6	1.2		23.7				
	Cattle <1 year	2							5.4	42.9	48.2	1.8			1.8				
Azithromycin	Pigs	<1								13.3	56.1	29.5	0.6			0.6			
	Cattle <1 year	0								14.3	48.2	37.5							
Cefotaxime	Pigs	<1					99.4		0.6										
	Cattle <1 year	0					100												
Ceftazidime	Pigs	<1					97.7	1.7		0.6									
	Cattle <1 year	0					98.2	1.8											
Chloramphenicol	Pigs	8										91.3	1.2	4.6	2.3	0.6			
	Cattle <1 year	0										100							
Ciprofloxacin	Pigs	2	97.1	1.2		0.6	1.2												
	Cattle <1 year	0	100																
Colistin	Pigs	0							100										
	Cattle <1 year	0							100										
Gentamicin	Pigs	0						91.3	7.5	1.2									
	Cattle <1 year	0						92.9	7.1										
Meropenem	Pigs	0		98.8	0.6	0.6													
	Cattle <1 year	0		100															
Nalidixic acid	Pigs	2									97.7	0.6				1.7			
	Cattle <1 year	0									100								
Sulphamethoxazole	Pigs	23										69.9	7.5						22.5
	Cattle <1 year	2										76.8	19.6	1.8					1.8
Tetracycline	Pigs	17								83.2				0.6	16.2				
	Cattle <1 year	2								98.2					1.8				
Tigecycline	Pigs	0					99.4	0.6											
	Cattle <1 year	0					100												
Trimethoprim	Pigs	20					54.3	24.3	1.7					19.7					
	Cattle <1 year	2					71.4	23.2	3.6					1.8					
			≤0.015	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.

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 2020 was used as a proxy for 2021 (EMA, 2021). This unit roughly corresponds to the total biomass of major animal populations, excluding dogs and cats.

Comparison of sales in tonnes active substance

In 2021, a total of 53.3 and 9.0 tonnes of antibiotics in included ATC classes were consumed in human and veterinary medicine, respectively. Figure 5.1 displays the sales of beta-lactam antibiotics. Substances in this class are by far the most commonly prescribed antibiotics in both human and veterinary medicine and also represent the largest amounts measured in kilograms. Narrow spectrum penicillins (J01CE, J01CF and QJ01CE) represent most of the amount in kg active substance of antibiotics for both humans and animals; 54 and 57%, respectively. There were no sales of carbapenems for animals as no products are authorised for veterinary use. The classes shown in Figure 5.2 are consumed in smaller quantities (n.b. the difference in indexation of the x-axis between the figures), but given their chemical and pharmacological properties, their impact on the emergence of antibiotic resistance and the environment is probably more pronounced than that of the penicillins. In the figures, only antibiotics consumed in a total quantity exceeding 1 000 kg during 2021 are included.

Figure 5.1. Sales of beta-lactam antibiotics for human and veterinary medicine, kg active substance, 2021. Please note the difference in indexation of the horisontal axis between Figures 5.1 and 5.2.

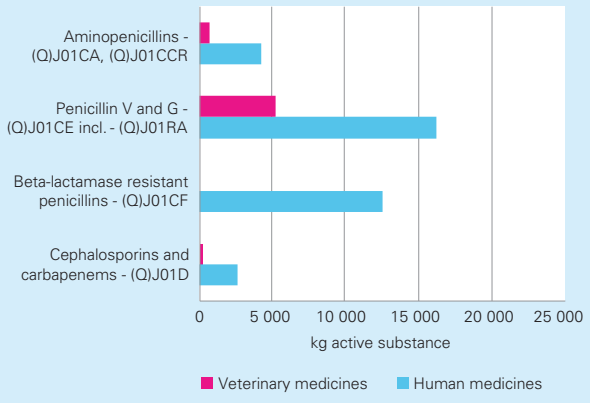
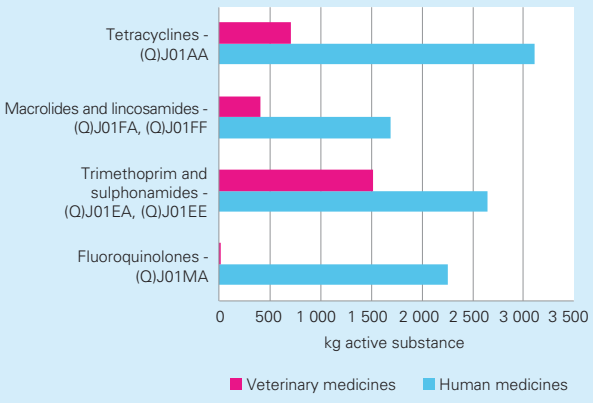


Figure 5.2. Sales of fluoroquinolones, macrolides, lincosamides, trimethoprim and sulphonamides and tetracyclines for human and veterinary medicine, kg active substance, 2021. Please note the difference in indexation of the horisontal axis between Figures 5.1 and 5.2.

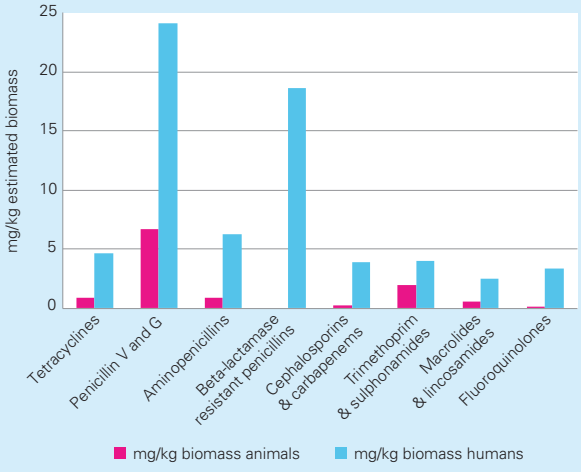


Comparison of sales expressed as mg per kg estimated biomass

In 2021, the sales were 79.3 and 11.8 mg active substance per kg estimated biomass in human and veterinary medicine, respectively. In Figure 5.3, a comparison of sales of antibiotics for use in humans and animals is shown expressed as mg per estimated kg biomass. Data on the total sales do not take the heterogeneity of the 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. This means that the selective pressure in a particular subset of the population (i.e. a particular animal species) can be far larger than in the total population. Nevertheless, in Figure 5.3 the largest differences are noted for beta-lactamase resistant penicillins where the sales for animals are negligible (only sold on license as products for intramammary use), and for the fluoroquinolones, where sales for humans are 140 times higher than for animals.

Both expressed in tonnes active substance and in mg per kg estimated biomass, the number for humans is higher than for animals in Sweden. The sales for humans dominate for all included classes of antibiotics.

Figure 5.3. Sales of antibiotics for humans and animals expressed as mg active substance per estimated kg biomass in 2021.



Comparison of antibiotic resistance in human and veterinary medicine

ESBL-producing Enterobacterales (previously Enterobacteriaceae)

Enterobacterales (previously Enterobacteriaceae) 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. Due to an increased relative occurrence of $bla_{CTX\text{-}M\text{-}1}$ among ESBL-producing *E. coli* from broilers in the last years, this difference is now less clear. Still, 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 (previously Enterobacteriaceae) 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, belonging to CC398, has been and is still commonly detected (n=8 in 2021). Furthermore, in an outbreak at an equine hospital in 2021 involving eight cases a, for horses in Sweden new *spa*-type, t034, belonging to the livestock-associated MRSA clonal complex 398, was detected. All 16 isolates were PVL-negative.

MRSA CC398 acquired in Sweden is uncommon in humans. Among all MRSA cases with available typing results in 2021, there were ten cases with *spa*-types t011 (n=3) and t034 (n=7). Seven of the isolates were PVL-negative while no inormation on PVL status was available for the remaining three 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 2018 and 2019, as part of an ongoing research project there were 14 cases of MRSA with *mecC* from hedgehogs.

In humans, cases of MRSA acquired in Sweden with *mecC* are also uncommon. In 2021, there were seven reported cases with *spa*-types t373 (n=2), t3391 (n=2), t843 (n=1), t9111 (n=1) and t9716 (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. Until 2012, the most common *spa*-type among Swedish dogs and cats was t032. More recently, the epidemiology has become more diverse with several *spa*-types occurring. *Spa*-type t032 was one of the ten most common *spa*-types among human MRSA isolates in Sweden until 2011.

In 2012, PVL-positive MRSA of *spa*-type t002 was isolated from a dairy farmer and from several of the dairy cows and a few other cattle on the farm. Since this *spa*-type is common among MRSA-cases in humans in Sweden, it is likely that transmission has occurred from the farmer to cows (Unnerstad et al., 2018). MRSA of *spa*-types t127 and t008 were detected in milk sample with anonymised origin from 2014 and 2017, respectively. Because also these *spa*-types are common among human MRSA-cases, transmission from humans to cows can be suspected. There is, however, no epidemiological information available about these cases.

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. 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 (17%) 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 45%, 17% and 1% respectively. From animals, 174 *C. coli* from pigs were tested. The only resistance found was against fluoroquinolones (32%).

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 5.1).

Resistance was generally more common in *E. coli* from humans than in isolates from animals (Table 5.1). 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 5.1). This agrees with a very low use of these antibiotic classes in animals (see section on sales of antibiotics above). However,

Table 5.1. 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. 11.0 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	2021	457	16.0	0.2[a]	0.4	0.9	0	0	1.5[b]
Dog (UTI)	Urinary	2021	990	11.8	1.4[a]	0.3	1.0	0	0	4.5[b]
Horse (e.g., endometritis)	Genital tract	2021	312	8.7	0.6[a]	0	1.2	0		16.3[b]
Calf (enteritis)	Faeces/Post-mortem	2019-21	65	55.4	0[a]	0	3.1	0		27.7[b]
Dairy cow (mastitis)	Milk	2021	55	18.2	0[a]	0	0	0		18.2[b]
Laying hens (e.g., salpingitis)	Post-mortem	2018	100	11.0	2.0[a]	0	1.0			3.0[b]
Pig (enteritis)	Faeces/Post-mortem	2021	57	26.3	0[a]	0	1.8	0		28.1[b]
Broiler (healthy)	Intestinal content	2020	172	12.8	0	0	0.6	0		9.3
Cattle under 1 year (healthy)	Intestinal content	2020-21	56	1.7	0	0	0	0		1.8
Pig (healthy)	Intestinal content	2021	175	24.9	0	0	0	0		19.7
Turkey (healthy)	Intestinal content	2020	44	9.1	0	0	0	0		2.3
Humans (UTI)	Urinary	2021	218 100	28.9	10.2	3.6			1.2	18.4
Humans (bloodstream infections)	Blood	2021	10 629		13.7	7.0	5.9	0.1		18.5[b]

[a]Enrofloxacin tested, BP >1mg/L; [b]Trimethoprim-sulphamethoxazole tested, BP >4 mg/L, NordicAST v. 11.0.

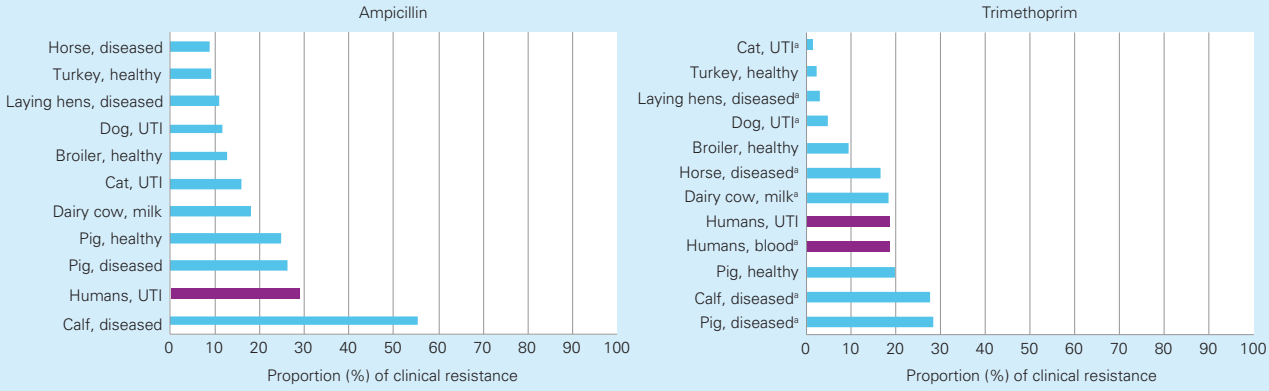
although few isolates of *E. coli* from animals show clinical resistance to fluoroquinolones, reduced susceptibility (i.e. non wild-type) is common in some categories of diseased and healthy animals (See Antibiotic resistance in animals in this and previous reports). Possibly, the selection pressure 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 5.1, Figure 5.4). 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 multi resistant *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 5.4 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 5.1.



[a]Trimethoprim-sulphamethoxazole tested, BP >4 mg/L, NordicAST v. 11.0.

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, 2021. Data from the eHealth Agency.

	<1 years	1-4 years	5-19 years	20-44 years	45-64 years	65-84 years	85 years and older	All age groups
Blekinge	1 513	6 620	27 546	45 423	39 746	33 100	5 108	159 056
Dalarna	2 924	12 699	48 840	80 151	71 591	62 619	8 852	287 676
Gotland	474	2 320	9 543	16 260	15 835	13 816	1 876	60 124
Gävleborg	2 762	12 405	48 650	80 613	73 342	61 255	8 475	287 502
Halland	3 507	15 505	61 695	96 981	84 943	64 506	9 611	336 748
Jämtland Härjedalen	1 276	5 794	22 224	38 252	32 583	27 212	3 814	131 155
Jönköping	4 191	17 440	66 644	112 052	88 433	65 756	10 494	365 010
Kalmar	2 516	10 471	40 951	68 088	61 788	54 100	8 096	246 010
Kronoberg	2 357	9 722	36 707	62 832	47 670	36 975	6 000	202 263
Norrbotten	2 336	9 991	39 299	72 847	64 141	53 409	7 591	249 614
Skåne	15 636	66 403	247 768	451 335	335 444	237 966	34 784	1 389 336
Stockholm	28 384	116 204	429 199	844 097	590 274	338 712	45 120	2 391 990
Sörmland	3 076	14 293	54 783	85 435	74 046	59 592	8 176	299 401
Uppsala	4 163	18 182	68 397	135 330	89 932	63 738	8 652	388 394
Värmland	2 750	12 191	46 100	81 744	71 799	58 978	9 323	282 885
Västerbotten	2 950	12 169	45 619	89 888	63 994	51 224	7 348	273 192
Västernorrland	2 293	10 420	41 707	67 835	62 638	52 298	7 363	244 554
Västmanland	2 973	12 906	48 572	83 625	68 693	52 585	7 787	277 141
Västra Götaland	19 344	80 578	300 287	570 686	423 761	296 043	43 744	1 734 443
Örebro	3 278	14 020	53 485	95 728	73 503	57 678	7 951	305 643
Östergötland	4 886	21 154	81 282	150 935	112 542	83 834	12 525	467 158
Sweden	**113 589**	**481 487**	**1 819 298**	**3 330 137**	**2 546 698**	**1 825 396**	**262 690**	**10 379 295**

Table 6.2. Denominator data (population in Sweden) for calculation of antibiotic sales in humans, 2000-2021. Data from the eHealth Agency.

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

Table 6.3. Number of admissions and patient-days in somatic medical care in Sweden, 2017-2021. Data represent acute care hospitals in all regions except Dalarna for all years and Jämtland Härjedalen for 2020.

Year	Admissions	Patient-days
2017	1 325 969	5 926 402
2018	1 317 455	5 785 393
2019	1 312 524	5 604 882
2020	1 217 430	5 105 100
2021	1 125 967	4 694 552

Table 6.4. Number of admissions and patient-days in somatic medical care in the regions, 2021. Data represent acute care hospitals in all regions except Dalarna.

Region	Admissions	Patient-days
Blekinge	19 974	86 192
Dalarna	8 864	34 331
Gotland	32 209	125 747
Gävleborg	36 875	133 261
Halland	14 355	59 180
Jämtland Härjedalen	43 057	153 845
Jönköping	33 796	109 665
Kalmar	20 015	85 402
Kronoberg	24 752	106 079
Norrbotten	150 297	672 836
Skåne	271 680	1 127 001
Stockholm	33 340	146 133
Södermanland	43 722	218 826
Uppsala	36 547	134 446
Värmland	38 259	176 442
Västerbotten	29 068	118 183
Västernorrland	32 940	134 006
Västmanland	173 779	751 757
Västra Götaland	35 643	147 360
Örebro	55 659	208 191
Sweden	**1 125 967**	**4 694 552**

The denominator data from the microbiological laboratories previously reported in this section is now summarised under "Overview of sampling and culture results including the effect of the COVID-19 pandemic" in the section on antibiotic resistance in humans.

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). The statistics are also as Statistical Messages (SM). Annual figures on number of animals are given in Table 6.5, on animals slaughtered in Table 6.6 and 6.7 and average herd size in Table 6.8.

In brief, the number of dairy cows and pigs has decreased notably over the last three decades while during the same time, herd size has increased. During the same period, the number of beef cows and sheep 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 6.5. Number of livestock and horses (in thousands) 1980-2021. From the statistical database of the Board of Agriculture.

Animal Species	1980[a]	1985[a]	1990	1995	2000	2005	2010	2015	2019	2020	2021
Cattle											
Dairy cows	656	646	576	482	428	393	348	338	305	303	302
Beef cows	71	59	75	157	167	177	197	184	210	207	210
Other cattle >1 year	614	570	544	596	589	527	513	487	500	480	476
Calves <1 year	595	563	524	542	500	509	479	466	451	462	465
Total, cattle	1 935	1 837	1 718	1 777	1 684	1 605	1 537	1 475	1 466	1 453	1 453
Sheep											
Ewes and rams	161	173	162	195	198	222	273	289	280	263	272
Lambs	231	252	244	266	234	249	292	306	269	238	252
Total, sheep	392	425	406	462	432	471	565	595	549	501	523
Pigs											
Boars & sows	290	260	230	245	206	188	156	142	130	131	129
Fattening pigs >20 kg [a]	1 254	1 127	1 025	1 300	1 146	1 085	937	830	943	869	845
Piglets <20kg [b]	1 170	1 113	1 009	769	566	539	427	384	383	368	376
Total, pigs	2 714	2 500	2 264	2 313	1 918	1 811	1 520	1 356	1 456	1 368	1 351
Hens for egg production											
Laying hens	5 937	6 548	6 392	6 100	5 670	5 065	6 061	7 571	8 909	8 403	6 363
Chickens reared for laying	2 636	2 159	2 176	1 812	1 654	1 697	1 647	1 842	2 067	2 420	2 390
Total, hens for egg-production	8 573	8 708	8 568	7 912	7 324	6 762	7 707	9 413	10 976	10 823	8 753
Horses											
Total, horses						283[c]	363	356[d]			

[a]Before 1995, the figure denotes pigs above 3 months of age; [b]Before 1995, the figure denotes pigs below 3 months of age; [c]Data from 2004; [d]Data for 2016.

Table 6.6. Number of animals slaughtered (in thousands) at slaughterhouses, 1980-2021. From the statistical database of the Board of Agriculture.

Animal Species	1980	1985	1990	1995	2000	2005	2010	2015	2019	2020	2021
Cattle											
Cattle >1 year	574	584	523	502	490	433	425	406	418	420	400
Calves < 1 year	130	152	70	30	39	33	27	22	15	13	11
Total, cattle	704	736	593	532	529	466	453	428	433	434	412
Sheep	302	328	280	189	202	206	255	256	252	240	227
Pigs	4 153	4 283	3 653	3 743	3 251	3 160	2 936	2 560	2 573	2 623	2 651
Broilers	40 466[a]	36 410[a]	38 577[a]	61 313	68 617	73 458	78 507	95 974	106 121	110 335	115 629
Turkeys							495	475	508	521	528

[a]Data supplied by the National Food Administration.

Table 6.7. Quantity of livestock slaughtered (in 1000 tonnes) at slaughterhouses, 1990-2021. From the statistical database of the Board of Agriculture.

Animal Species	1990	1995	2000	2005	2010	2015	2019	2020	2021
Cattle									
Cattle >1 year	139.5	140.1	145.4	131.4	133.5	129.7	137.2	138.2	134
Calves < 1 year	6.8	3.2	4.4	4.5	4.3	3.5	2.4	2.2	1.9
Total, cattle	146.3	143.3	149.8	135.9	137.8	133.1	139.7	141.0	136
Sheep	5.0	3.5	3.9	4.1	5.0	4.2	5.1	4.9	4.7
Pigs	293.1	308.8	277.0	275.1	263.5	233.5	240.3	246.5	253
Broilers	44.0[a]	73.6[a]	89.9	96.2	112.0	137.7	159.2	166.8	180
Turkeys					3.2	3.8	4.6	4.7	4.7

[a]Data supplied by the National Food Administration.

Table 6.8. Average number of animals per holding 1995-2021. From the statistical database of the Board of Agriculture.

Animal Species	1995	2000	2005	2010	2015	2019	2020	2021
Cattle								
Dairy cows	27	34	46	62	82	94	98	102
Beef cows	9	12	14	16	18	21	21	21
Ewes and rams	20	25	29	32	32	33	33	32
Boars and sows	31	63	156	156	186	193	185	173
Fattening pigs	157	294	471	664	845	1 053	945	942

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 licence 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 2021 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. In this year's report, Region Dalarna is not included in the statistics showing total sales or the statistics showing hospital care, due to failure to report data for sales of antibiotics to hospitals and other care facilities since 2017.

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 through their database Concise. 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 users per 1 000 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.

Definitions of DDD 2021

Table 6.9. DDD for all antibiotic substances (J01) registered in Sweden in 2021.

	DDD (g)		DDD (g)
J01AA02 - doxycycline	0.1	J01DI54 - ceftolozan and enzyme inhibitor	3
J01AA04 - lymecycline	0.6	J01EA01 - trimethoprim	0.4
J01AA07 - tetracycline	1	J01EC02 - sulfadiazin	0.6
J01AA08 - minocycline	0.2	J01EE01 - sulfamethoxazol 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 - fenoximethylpenicillin	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 - ceftriaxon	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 - ceftazidim 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 - linezolide	1.2
J01DI01 - ceftobiprolmedocaril	1.5	J01XX09 - daptomycin	0.28
J01DI02 - ceftarolinfosamil	1.2	J01XX11 - tedizolid	0.2

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 users per 1 000 inhabitants per year (Users/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 2021 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) 2017-2021 are shown in Table 6.3 and 6.4.

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 includeed. 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

Sampling strategy

Antibiotic resistance as notifiable diseases

ESBL

Screening for $ESBL_A$, $ESBL_M$ and $ESBL_{CARBA}$-producing *Escherichia coli* was performed on caecal samples from healthy pigs and faecal samples from healthy cattle as well as on samples of pig and cattle meat.

Samples from pigs were collected at slaughter under the supervision of the National Food Agency (SLV) at six abattoirs that together processed more than 85% of the total number of pigs slaughtered in Sweden 2021. The number of samples from each abattoir was roughly proportional to the annual slaughter volume of the abattoir. Each sample was randomly selected but represented a unique herd per day. Samples were sent to SVA for culture the same day or the next day after collecting and in meantime kept refrigerated.

Samples from cattle, older than six months, were collected at slaughter for a prevalence study of EHEC at twelve abattoirs, which represented 90% of the total slaughter volume. Samples were collected during September 2020-August 2021.

Samples from broilers were collected at slaughter within the Swedish Campylobacter programme in which whole caeca are collected from each batch of broilers slaughtered. From these samples, 50 were selected in March-April and 50 in September-October. Each sample was from a unique flock but not always from a unique production site. Samples cultured were collected at seven abattoirs that in 2021 accounted for approximately 89% of total volume of broilers slaughtered. The number of samples from each abattoir was roughly proportional to the annual slaughter volume of the abattoir.

Meat samples of fresh pork (305) and beef (303) were collected throughout the year at retail stores by municipal environmental departments in twelve different cities in Sweden. The number of samples from each municipal was roughly proportional to human population.

Clinical isolates from cats, dogs, and horses were submitted to the Dept. of Animal Health and Antimicrobial Strategies, SVA as bacterial strains.

MRSA and MRSP

Clinical isolates from animals were submitted to the Dept. of Animal Health and Antimicrobial Strategies, SVA as bacterial strains.

Findings of MRSA and MRSP in animals are notifiable in Sweden and hitherto most isolates from notified incidents have been confirmed using molecular methods at SVA. As from 2021 (SJVFS 2021:10) all phenotypically suspected MRSA and MRSP isolates must be sent to the Dept. of Animal Health and Antimicrobial Strategies, SVA for verification.

Monitoring of MRSA in dairy cattle was performed by screening isolates of beta-lactamase producing *Staphylococcus aureus* from routine submissions of milk samples sent to SVA. From each submission where beta-lactamase producing *S. aureus* was found, one isolate, selected by convenience, was tested.

Zoonotic pathogens

Salmonella

Salmonellosis in animals is a notifiable disease in Sweden and isolates from each notified incident are confirmed at SVA. Data presented in this report are from susceptibility testing of these isolates. The summary for each year includes one isolate of each serovar from each warm-blooded animal species in notified incidents. An exception is isolates from cats and wildlife from which a subset of isolates is selected by convenience. Isolates from incidents previously notified and still under restrictions are included in the yearly statistics. Also included are isolates obtained in the *Salmonella* surveillance programme from samples collected at slaughter (carcass swabs, neck skins and lymph nodes).

Campylobacter

Screening for *Campylobacter coli* in caecum from pigs were performed on the same samples as for ESBL (see above). Samples from 184 pigs were cultured to isolate 174 *C. coli* and these samples were evenly distributed over the year.

Clinical isolates from animals

Clinical isolates included are from routine bacteriological examinations of clinical submissions or post-mortem examinations. Part of the isolates of *Pasteurella* spp. from calves are, however, isolated from samples collected in surveys initiated within the SvarmPat programme.

In pigs, isolates of *E. coli* are from the gastro-intestinal tract and isolates of *Brachyspira* spp. are from faecal samples. Isolates of *A. pleuropneumoniae* in pigs emanate from tissue samples from lungs sampled post-mortem. Isolates of *Streptococcus suis* are from various tissues sampled at post-mortem examinations.

In cattle, isolates of *E. coli* are from samples from the gastro-intestinal tract from calves or from milk samples. Isolates of *Klebsiella pneumoniae* are from milk samples. Isolates of *Pasteurella* spp. and *Mycoplasma bovis* are from the respiratory tract from calves. In sheep, isolates of *Mannheimia haemolytica* and *Bibersteinia trehalosi* are from tissue samples from lungs sampled post-mortem.

In farmed fish, isolates of *Flavobacterium psychrophilum* and *Flavobacterium columnare* are from post-mortem examinations.

In horses, isolates of *E. coli* are from clinical submissions of samples from the genital tract of mares, isolates of *Streptococcus equi* subsp. *zooepidemicus* are mainly from the respiratory tract, and *S. aureus* are from skin samples.

In dogs, isolates of *E. coli* are from urine, *Staphylococcus pseudintermedius* are from three sampling locations (skin, wounds, and external ear canal) and compared to each other, isolates of *Staphylococcus schleiferi* are from various locations (mainly external ear canal, skin, and wounds), *Pseudomonas aeruginosa* are from the external ear canal and *Pasteurella* spp. are from various locations (mainly external ear canal, wounds, skin, abscesses, the respiratory tract, and synovial fluid).

In cats, isolates of *E. coli* are from urine samples, *Staphylococcus felis* are from various locations (mainly external ear canal, abscesses, and wounds) and *Pasteurella* spp. are from various locations (mainly wounds or skin lesions, abscesses, the external ear canal, and respiratory tract).

Indicator bacteria

The samples from intestinal content from healthy fattening pigs, and cattle under one year as well as the meat sampled at border control posts that were screened for $ESBL_A$, $ESBL_M$ and $ESBL_{CARBA}$-producing *E. coli* were also used to isolate indicator *E. coli*. However, only 175 of the samples from fattening pigs were cultured for indicator *E. coli* and these samples were evenly distributed over the year. From cattle under one year, all collected samples were cultured for indicator *E. coli*. Regarding the shipments of meat sampled at border control posts, the samples from all but one shipment were cultured for indicator *E. coli*.

Isolation and identification of bacteria

Antibiotic resistance as notifiable diseases

ESBL

$ESBL_A$, $ESBL_M$ and $ESBL_{CARBA}$-producing *E. 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 37°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 subcultured 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 subcultured 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 37°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 subcultured 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 subcultured again. *E. 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 *E. coli* 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). Isolates were susceptibility tested using microdilution (see below).

In the screening for MRSA among isolates of beta-lactamase producing *S. aureus* from dairy cows, isolates were tested for presence of *mecA* and *mecC* with PCR (see below). If positive for *mecA* or *mecC*, the isolate was susceptibility tested using microdilution (see below).

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, and isolates allocated to serovar according to White-Kauffmann-Le Minor. For certain isolates, the serovar was verified by whole genome sequencing.

Campylobacter

Campylobacter coli from pigs were isolated and identified at the Dept. of Animal Health and Antimicrobial Strategies, SVA. Samples were cultured direct on mCCDA and Butzler selective agar according to Campylobacter EURL-protocol for isolation, identification and storage of *Campylobacter jejuni* and *Campylobacter coli* for the EU monitoring of antimicrobial resistance. The plates were incubated at 41,5°C in microaerophilic environment for 48h. Isolates were selected based on morphological appearance and the selection of colonies was equally distributed between the selective agars. All isolates were species identified by MALDI-TOF MS.

Clinical isolates from animals

Clinical isolates were isolated and identified with accredited methodology, following standard procedures at SVA. *Mycoplasma bovis* was cultured from PCR positive samples and species identified with MALDI-TOF and/or genome sequencing.

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. coli* was tested according to the CLSI standard M45-3rd ed. for fastidious bacteria (CLSI, 2015).

Susceptibility of *Brachyspira hyodysenteriae* and *Brachyspira 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 (2020b). 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.

Susceptibility of *Mycoplasma bovis* was tested with broth microdilution in Mycoplasma broth with Mycoplasma selective supplement-G (Oxoid). The inoculum density was ($1x10^6$-$5x10^6$ CFU/ml) and the inoculum volume 100 µl per well and incubation was performed in CO_2, 37°C for 72 hours.

Genotyping

Suspected isolates of MRSA and MRSP were confirmed by detection of the *nuc*, *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 then sent to Clinical genomics Stockholm, SciLifeLab (Solna, Sweden) for library preparation and paired-end sequencing using Illumina technologies. Reads were trimmed using Trimmomatic and the specific ESBL-gene was determined using "Antimicrobial Resistance Identification By Assembly (ARIBA)" (Hunt et al., 2017) against the Resfinder (https://cge.cbs.dtu.dk/services/ResFinder/) database. 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. Dept. of Microbiology is accredited for isolation and identification of animal pathogens and of *Salmonella* and Dept. of Animal Health and Antimicrobial Strategies, SVA is accredited for isolation of $ESBL_A$, $ESBL_M$ and $ESBL_{CARBA}$-producing *E. coli* and indicator bacteria at 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, *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), *Aeromonas salmonicida* subsp. *achromogenes* (analogue to ATCC 10801), *Campylobacter jejuni* CCUG 11284^T (analogue to ATCC 33560^T) and *Mycoplasma bovis* Donetta PG45^T ATCC 25523^T were included as quality controls. Relevant control strains were also included and evaluated at least once weekly, when testing, for animal pathogens. 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. 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 (Table 6.11). For some antibiotics, values based on MIC distributions obtained in Svarm are used. This applies e.g. for narasin in *E. faecium* where the ECOFF (>4 mg/L) cuts through the resistant MIC population for some animal categories (e.g. broilers) in a manner not in agreement with the concept of wild-type distributions.

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, 2020a) or epidemiological cut-offs (ECVs) issued by CLSI (CLSI, 2020c) 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.

Table 6.10. Cut-off values (mg/L) for resistance. Values in red are current (March 22) 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	*Campylobacter jejuni*	*Campylobacter coli*	*Enterococcus faecium*	*Escherichia coli* (indicator)	*Escherichia coli* (pathogen)	*Flavobacterium columnare*	*Flavobacterium psychrophilum*	*Klebsiella pneumoniae*	*Mannheimia haemolytica*	*Pasteurella multocida*	*Pseudomonas aeruginosa*	*Salmonella enterica*	*Staphylococcus pseudintermedius*	*Staphylococcus felis, S. schleiferi*	*Staphylococcus aureus*	*Streptococcus suis*	*Streptococcus zooepidemicus*
Amikacin				>8								>4					
Ampicillin			>8	>8	>8				>0.5	>0.5		>8					
Azithromycin				>16								>16					
Cefepime				>0.25													
Cefotaxime				>0.25	>0.25			>0.25				>0.5					
Cefoxitin															>4		
Ceftazidime				>0.5								>2					
Cephalothin													>1	>1	>1	>2	>2
Chloramphenicol	>16	>16	>32	>16								>16			>16		
Ciprofloxacin	>0.5	>0.5	>8	>0.06								>0.06			>1		
Clindamycin													>0.5	>0.5	>0.5[d]	>0.5	>0.5
Colistin				>2	>2			>2			>4						
Daptomycin			>8														
Doxycycline																	
Enrofloxacin				>0.12	>0.12			>0.12	>0.12	>0.06[b]	>2		>0.5	>0.5	>0.5		
Ertapenem		>0.5		>0.03													
Erythromycin	>4	>8	>4										>0.5	>0.5	>1	>0.5	>0.5
Florfenicol						>4	>2		>2	>1							
Fusidic acid													>1	>1	>0.5		
Gentamicin	>2	>2	>32	>2	>2			>2			>8	>2	>1	>1	>2		
Imipenem				>0.5													
Linezolid			>4												>4		
Meropenem				>0.12	>0.12												
Nalidixic acid				>8								>4					
Narasin			>2														
Neomycin					>8			>8									
Nitrofurantoin					>64								>32 (UTI)	>32 (UTI)	>32 (UTI)		
Oxacillin													>0.5	>0.5			
Oxolinic acid						>0.25	>0.25										
Oxytetracycline						>0.25	>0.12		>2								
Penicillin									>0.5	>0.5			[c]	[c]	[c]	>0.25	>0.06
Streptomycin																	
Sulphamethoxazole				>64								>256					
Teicoplanin			>2														
Temocillin				>16													
Tetracycline	>1	>2	>4	>8	>8			>8		>2		>8	>0.5	>0.5	>1	>0.5	
Tiamulin																	
Tigecycline			>0.25	>0.5													
Trimethoprim				>2								>2					
Trim & sulpha[a]					>1			>0.5		>0.5			>0.5	>0.5	>0.5	>0.5	>0.5
Tylosin																	
Tylvalosin																	
Vancomycin			>4														
Valnemulin																	

[a]Concentration of trimethoprim given, tested with sulphamethoxazole in concentration ratio 1/20; [b]Not applied for *Pasteurella* spp. from calves as the range of tested concentrations did not include this cut-off; [c]beta-lactamase production; [d]EUCAST ECOFFs are used for MRSA (clindamycin >0.25).

Svarm 2001–2021

The number of isolates of different matrices reported in Svarm since 2001 is presented in the tables below.

Table 6.11. *Salmonella enterica*, number of isolates 2001-2021.

Source	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Warm-blooded animals	52	49	101	68	105	101	112	122	117	82	71	71	86	77	54	77	63	92	86	135	130
Cold-blooded animals									17												

Table 6.12. *Campylobacter* spp., number of isolates 2001-2021.

Source	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Cattle	67					68							109		23						
Pigs	98		105		100	46		97			83				108		171		171		174
Broilers	50	100		100				38		100		100		102		170		170		183	
Broiler meat													111								
Meat (different sources)	74																				
Water	19																				

Table 6.13. Indicator *Escherichia coli*, number of isolates 2001-2021.

Source	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Cattle						314			223				197		101		85				101
Cattle meat																					3
Pigs	308		303		390			349			167				200		140		174		175
Pig meat								19			20										2
Broilers	296	306		300			296			181		194		197		175		178		172	
Broiler meat										77		92									
Laying hens												61									
Turkeys													55	59		85		66		44	
Horses										274											
Dogs						257						74									
Willow grouse					19																
Wild boars	87																				

Table 6.14. Indicator *Enterococcus faecalis* and *E. faecium*, number of isolates 2001-2021 *(E. faecalis/E. faecium)*.

Source	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Cattle						13/98			10/24				11/42								
Pigs	52/106		87/71		55/47			68/39			22/23										
Pig meat								17/3			29										
Broilers	49/204	57/189		48/163			28/197			35/136		44/136		27/187							
Broiler meat										81/17		78/10									
Laying hens												20/36									
Turkeys																41/70					
Horses										34/27											
Dogs						135/29															
Wild boars	12/35																				
Sheep								24/15													

Table 6.15. Clinical isolates from farmed animals, number of isolates 2001-2021.

Animal species & bacterial species	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Cattle																					
Escherichia coli (enteric)		220		87	39	24			40	15	15	58	30	29	36	29	31	14	19	18	29
Escherichia coli (uterine)													60								
Escherichia coli (milk)			169										142	95	113	74	79	100	74	60	55
Klebsiella spp. (milk)			44			24							41	39	41	36	34	52	34	45	39
Pasteurella spp.			100				27	32	14	27	80	37	39	39	46	104	86	79	63	65	24
Staphylococcus aureus (milk)	100	100			96			87						74							
Streptococcus dysgalactiae (milk)		100																			
Streptococcus uberis (milk)		100																			
Fusobacterium necrophorum									41								24				
Mycoplasma bovis																					38
Pigs																					
Actinobacillus pleuropneumoniae							84	39	24	16	57	33	36	37	33	18	23	16	16	15	
Brachyspira hyodysenteriae	75	109	100		31	26	23	15	24	9	7	7	8	7	7	11	15	5	7	12	8
Brachyspira pilosicoli			93		57	72	44	31	24	13	16	17	12	13	7	17	21	22	27	22	17
Escherichia coli (enteric)	82	340	340	386	325	298	93	83	102	94	91	74	142	118	84	67	222	52	75	66	57
Pasteurella spp.	75						38	25	24	10	17	24	95	19	7	8	10	9			
Staphylococcus hyicus				20													65				
Streptococcus equisimilis											82										
Streptococcus suis																	72			27	25
Poultry (laying hens)																					
Escherichia coli (infection)							70											100			
Sheep																					
Staphylococcus aureus (udder)							25								30						
Fusobacterium necrophorum									24												
Mannheimia haemolytica and *Bibersteinia trehalosi*														44							34
Fish																					
Aeromonas salmonicida subsp. *achromogenes*							67	20	23	8	14	5	10	9	1	8				30	
Aeromonas salmonicida subsp. *salmonicida*																				30	
Flavobacterium columnare							30	16	10	5	8	3	5	9	4	3					42
Flavobacterium psychrophilum							42	27	24	21	27	31	23	61	31	16	26	21	8	18	12

Table 6.16. Clinical isolates from companion animals and horses, number of isolates 2001-2021.

Animal species & bacterial species	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Horses																					
Actinobacillus spp.	40																				
Escherichia coli (genital)	103	166	188	188	161	124	273	174	210	236	174	196	140	229	188	324	240	309	244	253	312
Rhodococcus equi	20			187																	
Streptococcus equi ssp. *zooepidemicus*	174	163	150	185	175	174	180	159	152	43	131	140	123	129	82	114	81	97	52	64	98
Staphylococcus aureus									308	131	135	145	139	132	116	75	127	118	104	131	182
Fusobacterium spp.																		40			
Dogs																					
Escherichia coli (urinary)	183	204	234	247	304	366	425	503	599	803	661	407	840	943	1 112	1 162	1 038	1 082	1 082	1 078	990
Pasteurella canis														207	194	253	152	232	157	248	186
Pasteurella multocida				231										29	46	23					
Pseudomonas aeruginosa			234						261	313	353	178	309	389	355	349	306	366	349	324	294
Staphylococcus pseudintermedius (skin)	156	133	102	159	126	89	220	258	381	444	388	229	566	513	393	376	417	515	507	567	573
Staphylococcus pseudintermedius (external ear)																	648	784	827	792	682
Staphylococcus pseudintermedius (wound)																	844	1 005	932	826	792
Staphylococcus schleiferi														297	201	163	175	240	233	236	210
Cats																					
Escherichia coli (urinary)		46	52	55	74	95	131	170	245	236	274	310	404	461	455	537	539	545	495	470	457
Betahemolytic streptococci											184										
Pasteurella dagmatis														20	22	19					
Pasteurella multocida														244	340	349	301	392	216	382	267
Staphylococcus felis														244	227	277	287	310	312	403	353

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SWEDRES | SVARM 2021

This annual report describes the monitoring of antibiotic resistance and antibiotic sales in human and veterinary medicine in Sweden in 2021.

During 2021 the COVID-19 pandemic continued in Sweden. Its impact is discussed where relevant in each section, and in a special In Focus-text after the Summary.

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 in 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. All the same, the risk of introducing $ESBL_{CARBA}$ among vulnerable patients is very concerning because this would have serious consequences. So far, $ESBL_{CARBA}$ has never been confirmed from domestic animals in Sweden.

For humans the COVID-19 pandemic had considerable impact on antibiotic resistance. The number of reported cases of all mandatory-reported resistance, except VRE, continued to decrease during 2021. In contrast, resistance proportions surveilled in clinical cultures, such as for *Escherichia coli* isolated from blood, generally followed the previous trends.

Work against antibiotic resistance has naturally been delayed during the pandemic. The efforts to optimise antibiotic use, prevent infections, and minimise dissemination of antibiotic resistance are now being gradually resumed. It is increasingly important to address the slow pandemic that antibiotic resistance constitutes.

Focus areas:
- Effects of the COVID-19 pandemic
- Swedish antibiotic prescribing according to the WHO AWaRe classification
- Antibiotics in digital health
- Clinical trial – comparing the effect of temocillin versus cefotaxime on the intestinal microbiota
- Microbiological diagnoses and antibiotic resistance for bovine mastitis pathogens
- SvarmPat – monitoring of resistance in pathogens from farm animals

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 area of public health, including infectious disease prevention.

The National Veterinary Institute (SVA) is an expert authority within the field of risk assessment, diagnostics, and 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.