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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 and Vendela Bergfeldt,
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

Since 2002, the Swedish public health and veterinary sectors have jointly published the Swedres-Svarm report on the monitoring of antibiotic resistance and antibiotic sales in human and veterinary medicine, presenting data from humans, animals, and food in a comparative analysis. This reflects decades of proactive, interdisciplinary work to mitigate the effects of antibiotic resistance where Sweden has been in the lead, long before the term One Health was coined.

The year 2020 has been unique due to the pandemic spread of SARS-CoV-2. This has had a major impact on the prevalence of communicable disease in society, as well as in the areas of antibiotic resistance and use. The national average for antibiotic prescriptions in humans has decreased dramatically, and in 2020 the long-term target of 250 prescriptions/1 000 inhabitants per year was reached. There are several plausible reasons for this, for example, changed behaviour, introduced recommendations and restrictions, fewer health care visits, reduced travel and migration, and necessary changes of prioritisation within health care. The impact of the COVID-19 pandemic is commented on in the summary and, where relevant, in the separate sections. This is also described in an In Focus-text directly after the summary.

The COVID-19 pandemic has also had a direct impact on this report. Normally it is published in early June, but this year the publication has been delayed till after the summer.

It is positive and reassuring that internationally there has been a high level of activity regarding antimicrobial resistance despite the COVID-19 pandemic. For example, the WHO has published several documents concerning surveillance, including documents on the inclusion of *Candida* spp. in the global antimicrobial resistance and use surveillance system (GLASS), on estimating attributable mortality of antimicrobial resistance in bloodstream infections, on national systems for monitoring antimicrobial consumption in hospitals, and on the application of genome sequencing for AMR surveillance. The Public Health Agency of Sweden, as a WHO Collaborating Centre for Antibiotic Resistance Containment, participates in the implementation of GLASS.

On the veterinary side, there are also positive signs. A decreasing trend in overall sales of antibiotics is noted at the EU level, as reported by the European surveillance of veterinary antimicrobial consumption. A decrease in sales at the global level has also been reported by the World Organisation for Animal Health, OIE. Some decreases in the occurrence of antibiotic resistance among food-producing animals are noted in a joint report by the ECDC and EFSA. Furthermore, steps have been taken to initiate a network for surveillance of antibiotic resistance in animal pathogens in Europe.

At the time when this preface is written, COVID-19 is fortunately decreasing in Sweden, and successive adjustments of the restrictions are planned. Several evaluations of the pandemic and the pandemic responses have been initiated. Suggested improvements from these will probably also influence the ways we work within the field of antibiotic resistance as well as other fields within public health. It is important to include, and emphasise the work against antibiotic resistance in the continued discussions. Although not as dramatic as COVID-19, antibiotic resistance also spreads globally and causes an ever increasing burden of disease.

Solna and Uppsala, June 2021

Johan Carlson

Director General
The Public Health Agency of Sweden

Ann Lindberg

Director General
National Veterinary Institute

Contributors and participants

Editors

Olov Aspevall and Vendela Bergfeldt,
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, Vendela Bergfeldt, Hanna Billström, Jessica Darenberg, Ulrica Dohnhammar, Petra Edquist, Nazanin Hashemi, Jenny Hellman, Cecilia Jernberg, Jerker Jonsson, Eva Morfeldt, Barbro Mäkitalo, Ragda Obeid, Kristina Rizzardi, Karin Westmo, Gunilla Skoog Ståhlgren, Tomas Söderblom, Anders Ternhag and Lina Thebo

Medical Products Agency
Maria Larsson

Strama Stockholm
Annika Hahlin

National Reference laboratory for Antibiotic Resistance, Växjö Hospital
Gunnar Kahlmeter

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
Anna-Karin Ohlsson

Authors Svarm

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

National Food Agency
Maria Egervärn, Catarina Flink and Hilde Riedel

Swedish Board of Agriculture
Kinfe Girma

Other contributors in Svarm

National Veterinary Institute
Björn Bengtsson, Boel Harbom and Paulina Hysing

Farm & Animal Health
Maria Lindberg

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Contributions to Svarm
The environmental departments in several municipalities are acknowledged and thanked for collecting samples of fresh meat from retail for ESBL-screening.

Content

Sammanfattning/Summary

Sammanfattning

Under covid-19 pandemin har både antibiotikaförsäljningen och anmälningarna av antibiotikaresistenta bakterier hos människor minskat. Det ses även i annan rapportering av de flesta anmälningspliktiga infektioner hos människor. I övervakningen av resistensnivåer bland kliniska isolat från människor ses däremot inte denna påverkan, 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 en 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 minska under 2020, efter att stadigt ha pekat nedåt under de senaste årtiondena. Följsamheten till behandlingsrekommendationer ökar, därmed minskar användningen av bredspektrumantibiotika.

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 2020

- Den totala antibiotikaförsäljningen inom humanmedicin i Sverige minskade med 13 procent jämfört med 2019, mätt i DDD per 1 000 invånare och dag.
- Generellt ses en minskad försäljning i alla delar av vården mellan 2019 och 2020, vilket är en effekt av pandemin med covid-19.
- Det nationella genomsnittet för antibiotikaförsäljning till människor har minskat ytterligare och ligger nu under det långsiktiga nationella målet på 250 recept per 1 000 invånare och år.
- Andelen MRSA bland Staphylococcus aureus från blododling har ökat till 2,3 procent, från 1,8 procent 2019.
- Antalet vårdrelaterade, mindre kluster av ESBL-CARBA har ökat, tre kluster 2020 jämfört med ett 2019.
- I samband med pandemin har antalet fall minskat av all anmälningspliktig antibiotikaresistens, utom pneumokocker med nedsatt känslighet för penicillin. 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.
- Den minskade förekomsten av ESBL-bildande E. coli i prov från slaktkyckling som setts de senaste åren stabiliserades under 2020.
- Bakterier som bildar ESBL-CARBA har inte konfirmerats hos djur i Sverige.

Försäljning av antibiotika

Antibiotikaförsäljning inom humanmedicin

Den totala mängden antibiotika som såldes i Sverige minskade med 13 procent under 2020 och ligger nu på 9,7 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. Antibiotikaförsäljningen under 2020 påverkades stort av covid-19 pandemin och en minskad försäljning ses inom alla vårdformer och framförallt öppenvården.

Öppenvård

Antalet antibiotikarecept som hämtades ut på apotek minskade påtagligt (17 procent) under 2020. Försäljningen minskade i samtliga åldersgrupper, men mest bland de yngre, jämfört med 2019. Minskningen var störst för antibiotika som ofta används vid luftvägsinfektioner (28 procent). Antalet recept per 1 000 invånare under 2020 var 237, vilket innebär att det nationella målet på 250 recept per 1 000 invånare och år uppnåddes under året. Bland de 21 regionerna låg försäljningen i 19 regioner under 250-målet under 2020.

Försäljningen av antibiotika på recept inom tandvården fortsatte att minska under 2020 och var 3,2 procent lägre än år 2019. Sedan år 2007 har antibiotikaförsäljningen inom tandvården minskat med hälften.

En tendens till ökad försäljning av antibiotika via digitala vårdgivare ses under 2020.

Sjukhus och andra vårdformer

Den totala försäljningen av antibiotika på rekvisition till vårdinrättningar sjönk till 1,36 DDD per 1 000 invånare och dag under 2020 och minskade därmed med 4 procent från 2019. Antibiotikaförsäljningen till akutsjukhusen har minskat mätt i DDD per 100 vårddagar och ligger kvar på samma nivå som 2019 mätt i DDD per 100 vårdtillfällen.

Den totala försäljningen på slutenvårdsrekvisition och uppdelat på försäljning till akutsjukhus minskade framförallt bland betalaktamaskänsliga och -resistenta penicilliner (J01CE och J01CF). Dessa fortsätter trots detta att vara

bland de största antibiotikaklasserna. Försäljningen av cefalosporiner och kombinationer av penicilliner har fortsatt att öka till akutsjukhus. Användningen av bredspektrumpreparat – cefalosporiner (J01DB-DE), karbapenemer (J01DH), fluorokinoloner (J01MA) och piperacillin-tazobactam (J01CR05) – visar stora regionala variationer. Även andelen penicilliner, mätt i DDD, varierar stort mellan regionerna.

Antibiotikaförsäljning inom veterinärmedicin

Statistiken för 1980–2019 har uppdaterats avseende mängden aktiv substans bensylpenicillin. En faktor som används vid beräkning har ändrats och det resulterar i generellt något lägre siffror än vad som tidigare publicerats.

Den rapporterade försäljningen av antibiotika för djur uppgick 2020 till 9 306 kilogram, varav 53 procent var penicillin med smalt spektrum. Motsvarande värden för 2011 var 12 220 kilogram och 52 procent.

Den totala försäljningen av antibiotika för djur har minskat med över två tredjedelar sedan 1986 då användningen av tillväxtbefrämjande antibiotika upphörde, korrigerat för att antalet av vissa djurarter har förändrats över tid. 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 2020 såldes 54,0 ton antibiotika för behandling av människor och 9,1 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 79,8 milligram per kilogram för människor och 11,9 milligram per kilogram för djur. Försäljning inom humanmedicin dominerade för alla inkluderade antibiotikaklasser utom för 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 2020, Enterobacterales (tidigare Enterobacteriaceae) med ESBL

- Antal rapporterade fall: 8 230 (föregående år 10 717), relativ förändring: 23 procent minskning.
- Antal fall med blodförgiftning: 727 (föregående år 835), relativ förändring: 13 procent minskning.
- Som tidigare år var E. coli den vanligaste arten, 87 procent, följt av Klebsiella pneumoniae, 9 procent.

Resultat 2020, Enterobacterales (tidigare Enterobacteriaceae) med ESBL-CARBA

- Antal rapporterade fall: 128 (föregående år 201), relativ förändring: 36 procent minskning.
- Antal fall med blodförgiftning: 11 (föregående år 6).
- Antal vårdrelaterade kluster av ESBL-CARBA har ökat, tre mindre kluster 2020 jämfört med ett 2019.
- Även bland Enterobacterales (tidigare Enterobacteriaceae) med ESBL-CARBA var E. coli den vanligaste arten, 61 procent, följt av K. pneumoniae, 26 procent.

Bakterier som bildar ESBL är inte anmälningspliktiga vid fynd hos djur. Sådana bakterier är ovanliga hos djur i Sverige. Tidigare var förekomsten hos slaktkyckling hög men den har minskat under senare år. Under 2020 undersöktes förekomsten av ESBL-bildande E. coli i tarm- och köttprov från slaktkyckling samt i tarmprov från kalkon med selektiva metoder. Sådana bakterier hittades i 3 respektive 0 procent av tarmproven från slaktkyckling respektive kalkon och i 2 procent av kycklingköttsproven med svenskt ursprung. Bakterier som bildar ESBL-CARBA har inte konfirmerats hos djur i Sverige.

Staphylococcus aureus resistenta mot meticillin (MRSA)

Samhällsförvärvad smitta är sedan länge den vanligaste typen hos människor smittade med MRSA i Sverige, med två tredjedelar av fallen. Från 2015 rapporteras familje-/hushållssmitta och samhällsförvärvad smitta separat. Familje-/hushållssmitta och samhällsförvärvad smitta utgjorde vardera 32 procent av fallen.

Resultat 2020

- Antal rapporterade fall: 3 112 (föregående år 3 858), relativ förändring: 19 procent minskning.
- Antal fall med blodförgiftning: 98 (föregående år 72), relativ förändring: 36 procent ökning.
- Andelen MRSA bland S. aureus från blododling har ökat till 2,3 procent, från 1,8 procent 2019.

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 27 fall av MRSA, vilket är en tredubbling jämfört med den tidigare högsta noteringen, 9 fall år 2014. Delvis förklaras ökningen av MRSA-utbrott på två hästsjukhus, totalt 18 fall. Det ena utbrottet, 7 fall, var av den hittills vanligaste varianten, *spa*-typ t011, tillhörande lantbruksdjurstypen MRSA CC398. Det andra utbrottet, 11 fall, var av *spa*-typ t1971 som första gången konstaterades hos hästar i Sverige 2019 (1 fall).

Staphylococcus pseudintermedius resistenta mot meticillin (MRSP)

Under 2020 var antalet anmälda fall av meticillinresistenta Staphylococcus pseudintermedius (MRSP) hos djur på samma nivå som de senaste åren. Totalt anmäldes 49 fall av MRSP till Jordbruksverket, varav isolat från 47 hundar 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 2020

- Antal rapporterade fall: 112 (föregående år 118), relativ förändring: 5 procent minskning.
- Antal fall med blodförgiftning: 4 (föregående år 9).

Enterococcus faecium och Enterococcus faecalis resistenta mot vankomycin (VRE)

Resultat 2020

- Totalt antal rapporterade fall: 79 (föregående år 232), relativ förändring: 66 procent minskning.
- Antal rapporterade fall av E. faecium med vankomycinresistens: 77 (föregående år 221), relativ förändring: 65 procent minskning.
- Antal rapporterade fall av E. faecalis med vankomycinresistens: 4 (föregående år 11).
- Två fall rapporterades med både E. faecium och E. faecalis.
- Antal fall med blodförgiftning: 4 (föregående år 10).
- Åtta sjukhusrelaterade smittspridningar rapporterades under året med 2-7 fall vardera. År 2019 rapporterades 22 sjukhusrelaterade smittspridningar.

Under 2020 undersöktes förekomsten av VRE i tarmprov från slaktkyckling med selektiva metoder. Sådana bakterier hittades i 6 procent av proven. Därmed fortsätter den minskning i förekomsten av VRE hos slaktkyckling som setts sedan 2005. Alla isolat tillhörde den klon av E. faecium med *van*A som är vanligast bland VRE från slaktkyckling i Sverige.

Resistens hos zoonotiska smittämnen

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 faeces-isolat från människor högst mot fluorokinoloner, 20 procent. Ingen resistens mot meropenem rapporterades. Salmonellaisolat från invasiva infektioner hos människor är mycket mer resistenta än isolat från djur i Sverige. Detta beror troligen på att en stor andel av fallen hos människor är smittade utomlands.

Campylobacter-stammar 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 43 procent och mot tetracyklin 24 procent 2020. En procent var resistenta mot erytromycin.

Vanligtvis behandlas inte infektioner som orsakas av Salmonella eller Campylobacter med antibiotika, varken hos människor eller hos djur. Hos människor resistensbestäms därför endast en liten andel av isolaten, varav de flesta gäller allvarliga infektioner. Se vidare avsnittet ”Comparative analysis” och ”Antibiotic resistance in humans” för respektive bakterie.

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 6–8 procent. Antalet anmälningar av E. coli ESBL från blod 2020 var 601. Resistens mot ciprofloxacin är nu 14 respektive 11 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 (16-20 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 2020 var 104. Liksom för E. coli är resistensen mot ciprofloxacin nu relativt hög, 10 respektive 8 procent hos isolat från blod och urin, ett observandum vid val av empirisk behandling av febril urinvägsinfektion.
- Staphylococcus aureus: Resistens mot cefoxitin (som indikerar MRSA) hos isolat från blod och prover från hud- och mjukdelar var 2,3 procent respektive 2,2 procent. Antalet anmälningar av MRSA från blod 2020 var 98.
- Enterococcus faecalis och Enterococcus faecium: Vankomycinresistensen hos isolat från blod är fortsatt låg (0 respektive 0,3 procent) och för höggradig aminoglykosidresistens ses en fortsatt minskning.
- Clostridioides difficile: Incidensen har minskat med 9 procent från 2016 till 2020, och är nu 60 fall per 100 000 invånare och år. Antibiotikaresistens har inte undersökts 2020.

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 och S. felis från katter. 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 djurslag och situationen är gynnsam ur ett internationellt perspektiv.

Summary

During the COVID-19 pandemic, both antibiotic sales and mandatory reported antibiotic resistance in humans have decreased. This is also seen in most Swedish reports of notifiable infectious diseases in humans. In contrast, the resistance levels among clinical isolates from humans in general have followed previous trends and do not seem to have been especially affected by the pandemic. The extensive impact of the COVID-19 pandemic on society and health care has also affected the sampling for resistant bacteria, the number of hospital admissions, the number of visits as well as the type of visits to health care facilities 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 $ESBL_{CARBA}$.

The reduction of antibiotic sales for humans continued in 2020, after several years of decreasing trends. Compliance with treatment recommendations is increasing, thus decreasing the use of broad-spectrum antibiotics.

In veterinary medicine, sales of antibiotics have decreased markedly since the mid 80s. During the last 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 the occurrence of ESBL producing *Escherichia coli* among broilers that has declined significantly. 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 2020

- The total sales of antibiotics for humans in Sweden decreased by 13% in 2020 compared to 2019, as measured in DDD per 1 000 inhabitants per day.
- Overall, there are substantial reductions in sales of antibiotics in all care sectors between 2019 and 2020, which can be put in relation to the COVID-19 pandemic.
- The national average for antibiotic prescriptions to humans has decreased further and in 2020 the long-term target of 250 prescriptions per 1 000 inhabitants per year was reached nationally.
- The proportion of MRSA among *Staphylococcus aureus* isolated from blood has increased to 2.3%, compared to 1.8% 2019.
- There was an increasing number of health care-related, smaller clusters of $ESBL_{CARBA}$, from one in 2019 to three in 2020.
- In relation to the pandemic, all mandatory reported antibiotic resistance, except pneumococci with decreased susceptibility to penicillin, has decreased. This is not seen for resistance levels among clinical isolates, where trends 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.
- The decreased occurrence of ESBL-producing *E. coli* in samples from broilers that has been seen in the latest years was stabilised in 2020.
- $ESBL_{CARBA}$-producing bacteria have not been confirmed in animals in Sweden.

Sales of antibiotics

Sales of antibiotics for humans

The total sales of antibiotics for humans in Sweden were 13% lower in 2020 and are now 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 care facilities. The sales of antibiotics in 2020 were largely affected by the COVID-19 pandemic and a decrease in sales was seen in all health care sectors, especially in outpatient care.

Outpatient care

The sales of prescriptions dispensed at pharmacies in Sweden decreased by 17% in 2020. The sales decreased in all age groups compared to 2019, but the decrease was most noticeable among children. The most substantial decrease was seen among antibiotics commonly used to treat respiratory tract infections (28%). The national average number of sales in prescriptions per 1 000 inhabitants per year was 237 in 2020, which means that the national long-term target of 250 prescriptions per 1 000 inhabitants per year was reached nationally and in 19 out of 21 regions in 2020.

The sales of antibiotics in dentistry continued to decrease in 2020 by an additional 3.2%, compared with 2019. Since 2007, the sales in dentistry have been reduced by half.

A tendency for increased sales of antibiotics prescribed by digital care providers was seen in 2020.

Hospitals and other health and social care facilities

In 2020, the sales of antibiotics on requisition decreased to 1.36 DDD per 1 000 inhabitants per day, a decrease of 4.1% compared with 2019. This includes all antibiotics sold to hospitals, other healthcare facilities and some nursing homes. The sales to acute care hospitals decreased compared to 2019, as measured in DDD per 100 admissions, but remained at the same level as in 2019 as measured in DDD per 100 patient-days.

The sales of antibiotics in hospital care in total and to acute care hospitals decreased, especially among beta-lactamase sensitive and resistant penicillins (J01CE and J01CF). Despite the decrease, these classes are still among the most sold. The sales of cephalosporins and combinations of peni-

cillins to acute care hospitals have continued to increase. The use of broad-spectrum antibiotics – cephalosporins, carbapenems, fluoroquinolones and piperacillin-tazobactam – shows large regional variations in terms of which substances are used. The relative use of penicillins measured in DDD also varies between the regions.

Sales of antibiotics for animals

Data for procaine benzylpenicillins from 1980 to 2019 have been recalculated following a change in a factor used for the calculation of active substance. As a result, the figures are generally somewhat lower than what have been published in previous years.

In 2020, reported sales of antibiotics for animals were 9 306 kg, of which 54% were penicillins with narrow spectrum. The corresponding figures for 2011 were 12 220 kg and 52%, respectively.

Since the withdrawal of growth-promoting antibiotics from the Swedish market in 1986, the total sales of antibiotics have decreased by more than two thirds when corrected for population sizes over time. 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 54.0 tonnes of antibiotics were sold for human use and 9.1 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 79.8 and 11.9 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 one of the antibiotic resistance types for which notification is required.

Results 2020, Enterobacterales (previously Enterobacteriaceae) with ESBL

- Number of reported cases: 8 230 (previous year 10 717), relative change –23%.
- Number of bloodstream infections: 727 (previous year 835), relative change –13%.
- As in previous years, *Escherichia coli* was the most common species, (87%), followed by *Klebsiella pneumoniae*, (9%).

Results 2020, Enterobacterales (previously Enterobacteriaceae) with $ESBL_{CARBA}$

- Number of reported cases: 128 (previous year 201), relative change –36%.
- Number of bloodstream infections: 11 (previous year 6).
- The number of health care related, clusters of $ESBL_{CARBA}$ increased, from one in 2019 to three in 2020.
- Among Enterobacterales (previously Enterobacteriaceae) with $ESBL_{CARBA}$, *E. coli* was the most common species, (61%) followed by *Klebsiella pneumoniae* (26%).

ESBL-producing Enterobacterales (previously Enterobacteriaceae) are rare among animals in Sweden. Previously, the occurrence in intestinal samples from broilers was high but it has decreased in recent years. In 2020, the occurrence of ESBL-producing *E. coli* in intestinal samples from broilers and turkeys, as well as samples of broiler meat was investigated with screening methods. Such bacteria were isolated from 3% and 0% of the intestinal samples from broilers and turkeys respectively, and 2% of the broiler meat samples of Swedish origin.

$ESBL_{CARBA}$-producing bacteria were not confirmed in animals in Sweden.

Methicillin-resistant *Staphylococcus aureus* (MRSA)

Community-acquired infection has long been the most common type in humans, with two-thirds 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 both accounted for 32% of the cases.

Results 2020

- Number of reported cases: 3 112 (previous year 3 858), relative change -19%.
- Number of bloodstream infections: 98 (previous year 72), relative change +36%.
- The proportion of MRSA among *Staphylococcus aureus* isolated from blood has increased to 2.3% in 2020, compared to 1.8% in 2019.

The occurrence of MRSA in animals in Sweden is still low, which limits the spread from animals to humans. MRSA was found sporadically in horse, dog and cat. However, the number of MRSA cases in horses was tripled in 2020, compared to the previous highest figure of nine cases in 2014. The increase could be explained by outbreaks in two equine hospitals with a total of 18 cases. In companion animals, the same types of MRSA as in humans dominate, indicating a human source of MRSA in these animals. In horses, livestock-associated MRSA clonal complex 398 used to be the most common, but in 2020 *spa*-type t1971 dominated (14 of 27 cases). This variant is since 2019 a new finding in horses in Sweden.

Methicillin-resistant *Staphylococcus pseudintermedius* (MRSP)

In 2020, the number of reported cases of methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) in animals was around the same level as in previous years. In total 49 cases of MRSP were notified to the Swedish Board of Agriculture, and isolates from 47 cases from dogs were available for further investiga-

tions. The epidemiology of MRSP is more diverse compared to earlier years with several sequence types occurring.

MRSP in humans is not notifiable.

Streptococcus pneumoniae with reduced susceptibility to penicillin (PNSP)

Results 2020

- Number of reported cases: 112 (previous year 118), relative change –5%.
- Number of bloodstream infections: 4 (previous year 9).

Vancomycin-resistant enterococci (VRE)

Results 2020

- Total number of reported cases: 79 (previous year 232), relative change –66%.
- Number of reported cases of *E. faecium* with vancomycin resistance: 77 (previous year 221), relative change –65%.
- Number of reported cases of *E. faecalis* with vancomycin resistance: 4 (previous year 11).
- There were two cases infected with both *E. faecium* and *E. faecalis*.
- Number of bloodstream infections: 4 (previous year 10).
- Eight hospital-related outbreaks were reported during the year with 2-7 cases each. In 2019, 22 hospital-related outbreaks were reported.

In 2020, the occurrence of VRE in intestinal samples from broilers was investigated with screening methods. Such bacteria were isolated from 6% of the samples. This shows that the decrease in occurrence of VRE among broilers in Sweden since 2005 has continued. All of the isolates belonged to the clone of *E. faecium* with *vanA* that is the most common among VRE in broilers in Sweden.

Zoonotic pathogens

Salmonella is rare in animals in Sweden. Furthermore, only a few of the incidents involve antibiotic-resistant strains. Resistance to fluoroquinolones is rare. For *Salmonella* species isolated from human faeces, the highest occurrence of resistance was against fluoroquinolones, (20%). 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 43% and resistance to tetracycline was 24% in 2020. One percent 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 are tested for antibiotic susceptibility, most of which are related to serious infections. See the "Comparative analysis" section of each bacterium.

Human clinical isolates

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

- *Escherichia coli*: Resistance in blood isolates to ceftazidime and cefotaxime was 6-8%. The number of reported *E. coli* ESBL from blood was 601 cases in 2020. Resistance to ciprofloxacin is now 14% and 11%, respectively, in isolates from blood and urine. This needs to be noted when choosing empirical treatment for febrile urinary tract infection.
- When *E. coli* from urine are age and gender distributed, some differences in resistance are seen. Most prominent is the high ciprofloxacin resistance (16-20%) 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 104 in 2020. As for *E. coli*, resistance to ciprofloxacin is now relatively high, 8-10% 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 2.3% and 2.2% respectively. The number of reported MRSA from blood was 98 in 2020.
- *Enterococcus faecalis* and *Enterococcus faecium*: Vancomycin resistance in isolates from blood remains low (0% and 0.3%, respectively) and the high-lewel aminoglycoside resistance has decreased.
- *Clostridioides difficile*: The incidence has decreased by 9% from 2016 to 2020 (60 cases per 100 000 inhabitants). No isolates were tested for antibiotic resistance.

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 bensylpenicillin, but penicillin resistance is common in *Staphylococcus pseudintermedius* from dogs and occurs in *S. aureus* from horses and *S. felis* from cats. Resistance 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.

Effects of the COVID-19 pandemic

In 2020 the COVID-19 pandemic appeared in Sweden in two waves, starting in March and October respectively. There were approximately 455 000 cases notified during the year but the actual number of individuals infected with COVID-19 was, due to limited testing capacity in the spring, not identified and estimated to be much higher than what was reported. 4 200 individuals required intensive care, and 9 800 died within 30 days after having being diagnosed with COVID-19. The pandemic, and the actions to handle and counteract it, have of course had enormous impact on the whole society, and especially on public health and the health care sector. Here we summarise and discuss these effects, and some factors contributing to them. This is also commented on, where relevant, in each separate section of the report. Additional analyses of effects on health care, infections, and antibiotic consumption will be carried out.

Effect on human medicine

Findings related to the pandemic

The total sales of antibiotics decreased by 13% in 2020 compared to 2019, as measured in DDD per 1 000 inhabitants per day.

- The most substantial decrease was seen among antibiotics commonly used to treat respiratory tract infections (28%), and for children 0-4 years old.
- Overall, there are substantial reductions in sales of antibiotics in all healthcare sectors between 2019 and 2020.
- The national average for antibiotic prescriptions to humans has decreased further, and in 2020 the long-term target of 250 prescriptions per 1 000 inhabitants per year was reached nationally.
- All mandatory reported antibiotic resistance pathogens, except pneumococci with decreased susceptibility to penicillin, have decreased. A corresponding decrease is however not seen for resistance levels among clinical isolates, where trends are relatively unaffected.
- The total number of cultures from blood, urine, nasopharynx, and throat decreased by 12% between 2019 and 2020. For blood cultures the decrease was 2%, for urine cultures 6%, for nasopharyngeal cultures 28% and for throat cultures 34%.

Factors affecting data

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 other communicable diseases as well. 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 surgery.

Changes in incidence of communicable diseases

The incidence has decreased for most of the surveyed communicable diseases. 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 as compared to prior years.

Changes in health care consumption

There were fewer visits in outpatient care and less elective surgery performed during 2020 compared to 2019 (SALAR, 2020).

In addition there were fewer hospital admissions in 2020. The number of patient-days was at the same level as in 2019. For further information on treatment in hospital care in relation to the COVID-19 pandemic, please visit the website of the National Board of Health and Welfare.

In April 2020 acute care visits decreased by 30% compared to the same month last year. In June the acute care visits were 15% fewer. Visits in outpatient care decreased by 36% during January to May 2020, compared to the same five months in 2019 (SALAR, 2020).

A survey regarding the influence of the pandemic on visits to health care during spring 2020 showed that one out of five people did not seek health care even if needed or had cancelled a planned visit (Public Health Agency, 2020).

Effect on veterinary medicine

Although primarily a human pandemic, COVID-19 has also had both direct and indirect consequences for animal health and veterinary medicine. One direct effect on animal health was the spread of SARS-CoV-2 among minks. During the autumn of 2020 active surveillance of the occurrence of the virus at mink farms in Sweden was performed and antibodies were detected in many of the samples (SVA, 2021). There was also a great demand for information regarding SARS-CoV-2 in other animals and the potential for spread of the virus from humans to animals and vice versa. Examples of indirect consequences are shortage of both personnel and consumables, in all parts of the veterinary and food sector. However, the effects of these are difficult to estimate. Especially this soon after the outbreak of the pandemic.

The consequences with a direct impact on SVA are however easier to evaluate. One of these is that the impact on human healthcare triggered the diagnostic department at SVA to initiate changes in order to be able to analyse samples from humans for SARS-CoV-2. During the year, SVA performed such analyses for some regions in Sweden and over 160 000 samples were analysed. This, together with additional workload due to outbreaks of both avian influenza and *Salmonella* Choleraesuis among animals in Sweden put a lot of pressure on the laboratory capacities at SVA. All in all, this forced down prioritisation of other, less acute, analyses. However, the analyses necessary for the Svarm part could in fact be performed.

Yet another effect of the COVID-19-pandemic that possibly have had a direct impact on the accuracy of the data presented in this report is the number of dogs in Sweden. 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 during the COVID-19 pandemic. The population estimate for 2020 used for the analyses in the report does not reflect that, and it is possible that the number of packages per 1000 individuals for 2020 given in the report is an overestimate.

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Guidance for readers

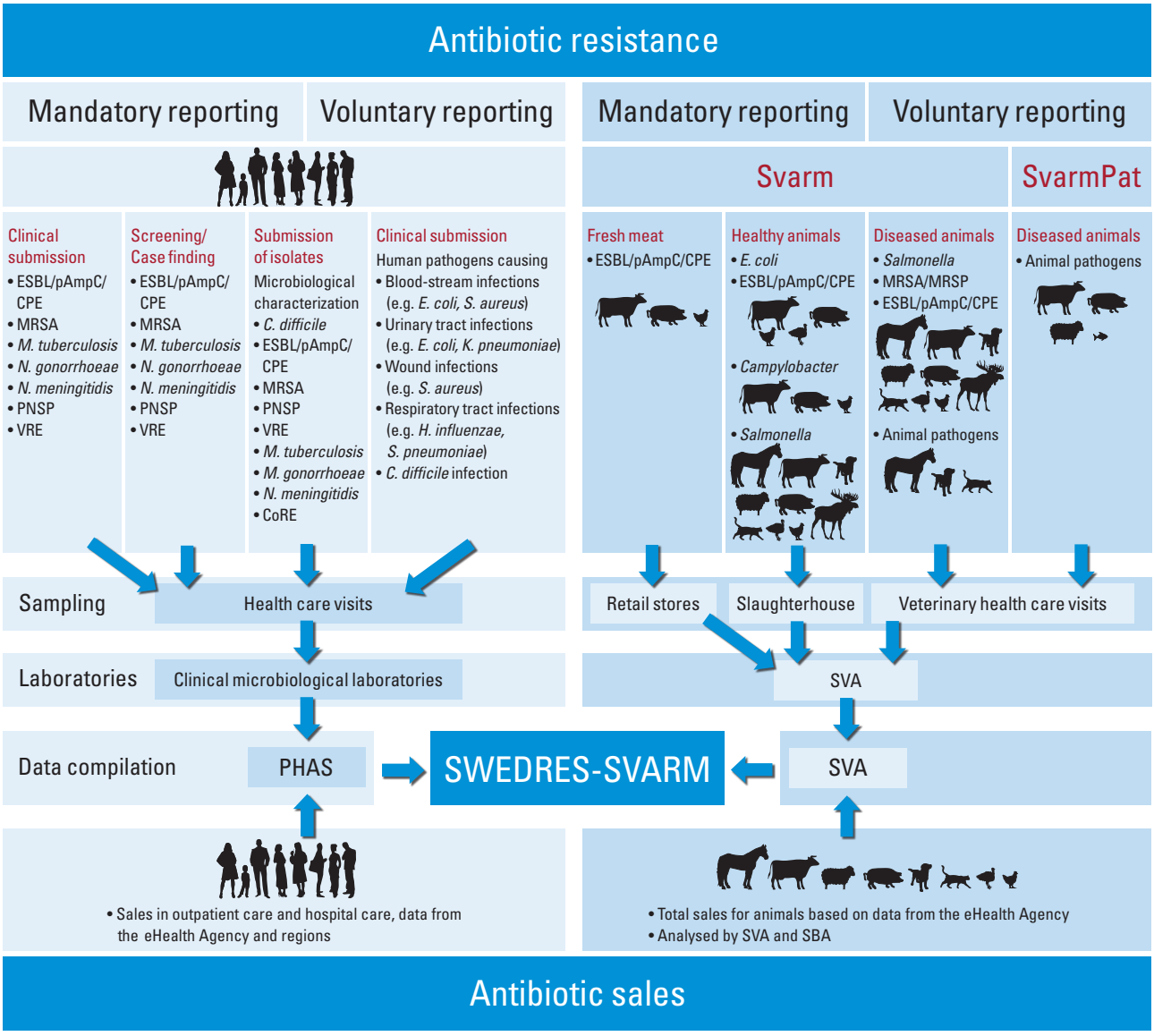
The Swedres-Svarm report is the result of a cooperation between the Public Health Agency of Sweden and the National Veterinary Institute with the aim to present data relating to both humans and animals on the sales of antibiotics and on antibiotic resistance in a joint report.

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 2020.

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

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.

Comparison of sales of antibiotics between regions and to the elderly 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 get their medication by prescription, whereby data are included in outpatient sales. However, there are also nursing homes where medicines are bought 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 elderly people is not entirely reliable.

Wherever sales of antibiotics to a certain group of people are displayed (children 0-6 years, women 15-79 years, inhabitants in a region), the denominator is the total number of individuals in the same 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 hospital care. Therefore, data on sales exclusively to acute care hospitals have been provided by pharmacists in local Strama groups in all regions.

Treatment recommendations are adopted locally by the regional Drug and Therapeutics Committee and therefore the prescribed daily doses for certain indications can vary between regions. This should be kept in mind as it may affect comparisons.

Antibiotic resistance

Swedres - Humans

Most of the data on resistance in Swedres is derived from routine diagnostic samples sent for testing at clinical 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. In Swedres, only MIC results for *Clostridioides difficile* were interpreted using ECOFFs.

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 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, some interpretive criteria (ECOFFs) have been changed by EUCAST. 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 used for isolates with phenotypically identified acquired resistance to three or more antibiotic classes. This implies, for example, that resistance to ciprofloxacin, enrofloxacin and nalidixic acid represents resistance to one class of antibiotics.

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

AST	Antimicrobial susceptibility testing
ATC	Anatomical therapeutic chemical classification system
BSI	Blood stream 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
EPIS AMR-HAI	Epidemic Intelligence Information System for Antimicrobial Resistance and Healthcare-associated Infections
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 Susceptibility Testing
GAS	*Streptococcus pyogenes* (Group A streptococci)
GBS	*Streptococcus agalactiae* (Group B streptococci)
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
MRB	Multi-resistant bacteria
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
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)
Svarm	Swedish veterinary antibiotic resistance monitoring programme
Swedres	Swedish utilisation and resistance in human medicine
TB	Tuberculosis
UTI	Urinary tract infection
VRE	Vancomycin-resistant enterococci
XDR	Extreme drug resistance (used for *Mycobacterium tuberculosis*)

Sales of antibiotics for humans

The impact of the COVID-19 pandemic on antibiotic sales

The changes in antibiotic sales during the COVID-19 pandemic in 2020 were exceptional and in stark contrast to earlier years of monitoring. Apart from the big decrease in sales, other parts of the health care system were also affected, such as fewer surgeries performed and less visits in outpatient care (SALAR, 2020). Because the antibiotic sales during 2020 were strongly affected by COVID-19, the analyses in the sales chapter in Swedres-Svarm 2020 are made in relation to this. In the outpatient care section, there is also a chapter focusing specifically on the sales in 2020 by month and quarter, which aims to highlight the sales in relation to the COVID-19 pandemic.

The analyses of data for 2020 are focused on sales in outpatient care and the number of prescriptions per 1 000 inhabitants. Because antibiotics in hospital care are sold on requisition, this measure is not as reliable in short term analyses, as all antibiotics that were bought might not have been used. This is particularly true in 2020, where several regions made larger purchases in the beginning of the pandemic (INSIKT, 2020). Despite a noted shortage of some substances, mainly cephalosporins, no distribution was made from the national preparedness stockpile of antibiotics.

In hospital care, a decrease in the number of admissions was seen during 2020, Figure 6.3 in the section *Background data, material, methods and references.* The number of patient-days was at the same level as in 2019. These changes in the denominator affects the results in the section on acute hospital care. For further information on treatment in hospital care in relation to the COVID-19 pandemic, please visit the website of the National Board of Health and Welfare.

There are several factors that might have contributed to the drop in sales in outpatient care. Sweden had a decrease in the spread of common viral infections, such as influenza and respiratory syncytial virus (Public Health Agency, 2020a & 2020b), which indicates a reduction in infection spread in general. There was also a change in behaviour of the public in accordance with national COVID-19 regulations. Apart from this, the lower number of visits in primary health care facilities was also most likely a contributing factor to the number of prescriptions issued. In April 2020, acute care visits decreased by 30% compared to the same month last year. In June, the acute care visits were 15% fewer. Visits in outpatient care decreased by 36% during January to May 2020 compared to the same five months in 2019 (SALAR, 2020). In May 2020, the Public Health Agency sent out a questionnaire to the online panel Folkhälsorapport regarding visits to health care. The result showed that one out of five people did not seek health care even if needed or had cancelled a planned visit (Public Health Agency, 2020c). However, the decrease in antibiotic sales has not had any impact on the number of serious infections that can occur as a complication of untreated upper respiratory tract infections, which was shown in a study conducted by the Public Health Agency and the National Board of Health and Welfare in December 2020 (read more in In Focus about reduced dispension of antibiotic prescriptions). This study also showed a decrease in the number of treated respiratory tract infections in hospital care.

Further studies are needed to establish the connection of the above mentioned factors to the lowered number of sales, but the overall tendency is that behavioural changes in accordance with the COVID-19 regulations have probably also affected the spread of common respiratory infections and thereby the need for antibiotics.

The interpretation of Swedish data is on-going and studies are being conducted in 2021 to further understand the impact of the COVID-19 pandemic and the consequences of the reduction in the sales of antibiotics. Moreover, international studies are in the pipeline to compare the Swedish situation with other European countries. Because data are still being gathered and registers for 2020 still being updated, further studies and in-depth analyses of the effects of COVID-19 will follow. In the 2021 Swedres-Svarm edition there will be possibilities to present more results on the long-term effects of the pandemic. The monitoring of sales continues and the Public Health Agency is following the trends in sales over a longer period of time, not least to see the effects on sales after the COVID-19 restrictions have been lifted.

International studies present a trend of wide antibiotic prescribing among COVID-19 patients, despite the low risk for bacterial infections. For COVID-19 patients antibiotics are only indicated to treat secondary bacterial infections and co-infections. The inappropriate use of antibiotics could result in increased antimicrobial resistance, and it is therefore important to monitor and work to promote the responsible use of antimicrobials in this patient group (ECDC, 2021).

Total sales of antibiotics for humans

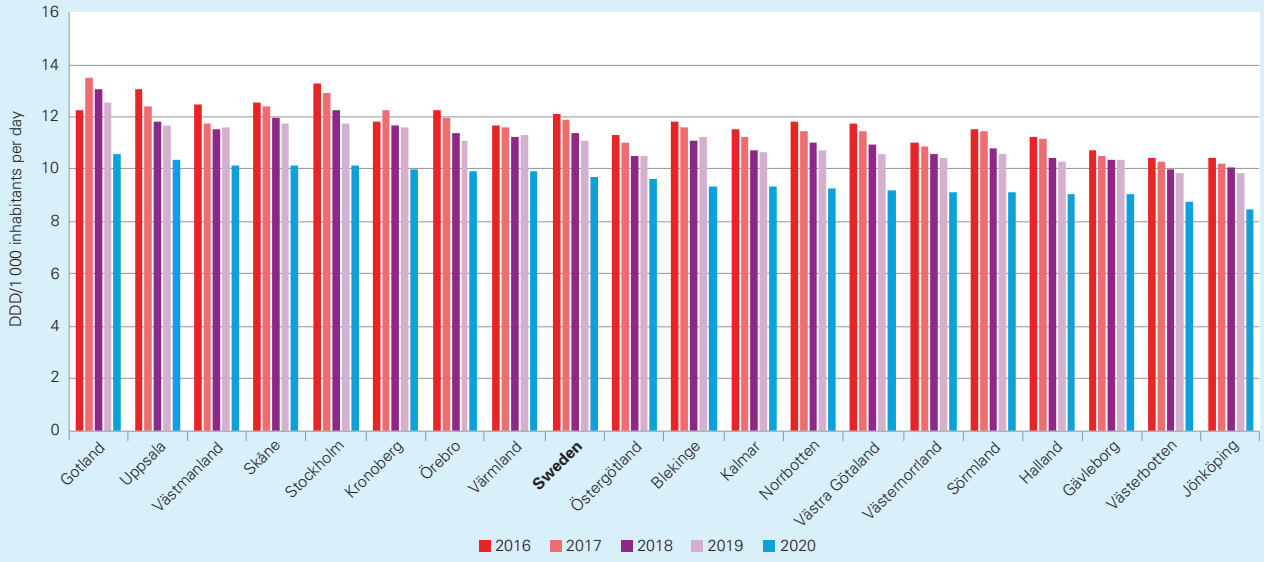
Results

- The total sales of antibiotics (J01 excl. methenamine) decreased by 13% compared to 2019 (from 11.1 DDD to 9.7 DDD per inhabitants per year), Figure 1.1.
- The sales of fluoroquinolones, cephalosporins and combinations of penicillins have decreased slightly in 2020 compared to the previous year, Figure 1.2.
- Beta-lactamase sensitive penicillins and tetracyclines were the two most sold antibiotic classes in Sweden during 2020, though a substantial decrease in the sales of beta-lactamase sensitive penicillins was seen, Figure 1.2.

Comments

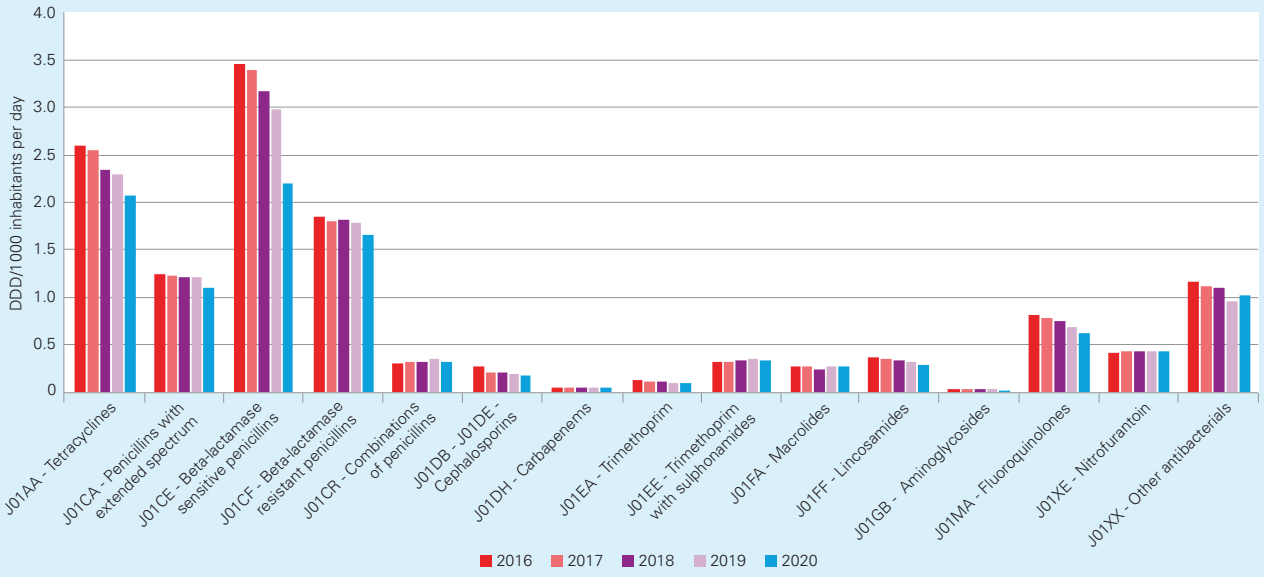
The 2020 data on antibiotic sales present a pronounced decrease and add to a downward trend in Sweden. Compared to the average total consumption in the EU/EEA in 2019; 19.4 DDD/1 000 inhabitants per day (ECDC, 2020), Figure 1.1 gives an indication of Sweden's restrictive position regarding antibiotic prescribing. However, there are considerable differences between the regions in Sweden, with total sales ranging from 10.6 to 8.5 DDD per 1 000 inhabitants per day. Figure 1.1 and 1.2 show prescriptions to individuals as well as antibiotics dispensed in hospitals, nursing homes etc. Region Dalarna and Jämtland Härjedalen are not included in the statistics showing total sales.

Figure 1.1. Sales of antibiotics (J01 excl. methenamine), humans, per region, 2016-2020, DDD/1 000 inhabitants per day.



Source: The Public Health Agency of Sweden

Figure 1.2. Sales of antibiotics, humans, ATC-5, 2016-2020, DDD/1 000 inhabitants per day.



Source: The Public Health Agency of Sweden

Antibiotics in outpatient care

Total sales

Results

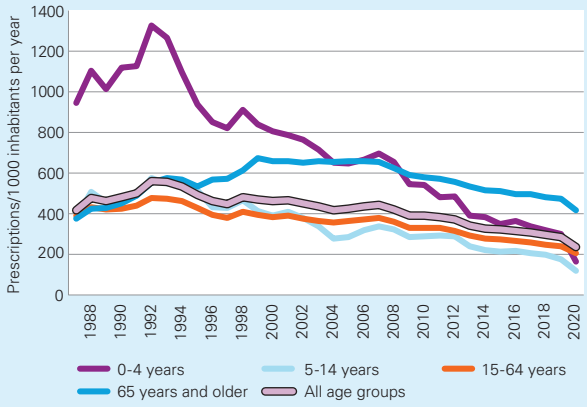
- The sales of antibiotics in outpatient care were 17% lower in 2020 than in 2019.
- A decrease can be seen in most antibiotic classes and for all age groups, with the biggest decrease among antibiotics commonly used to treat respiratory tract infections (RTIs) and for children 0-4 years old.
- The trend towards increased use of first-line antibiotics against urinary tract infections continues.

Comments

The statistics for outpatient care includes all sales of antibiotics on prescription issued to individuals; both from health care centres in the community and from hospitals. Since 1992, when the sales of antibiotics on prescriptions peaked, the sales have decreased by 58%, Figure 1.3. The greatest change during these years is seen among young children in the age group 0-4 years, where sales decreased from 1 328 prescriptions per 1 000 inhabitants per year in 1992 to 165 in 2020. This group also displays the biggest decrease in the last year, with a decrease of 45%. The total number of prescriptions per 1 000 inhabitants per year for all age groups was 237 in 2020.

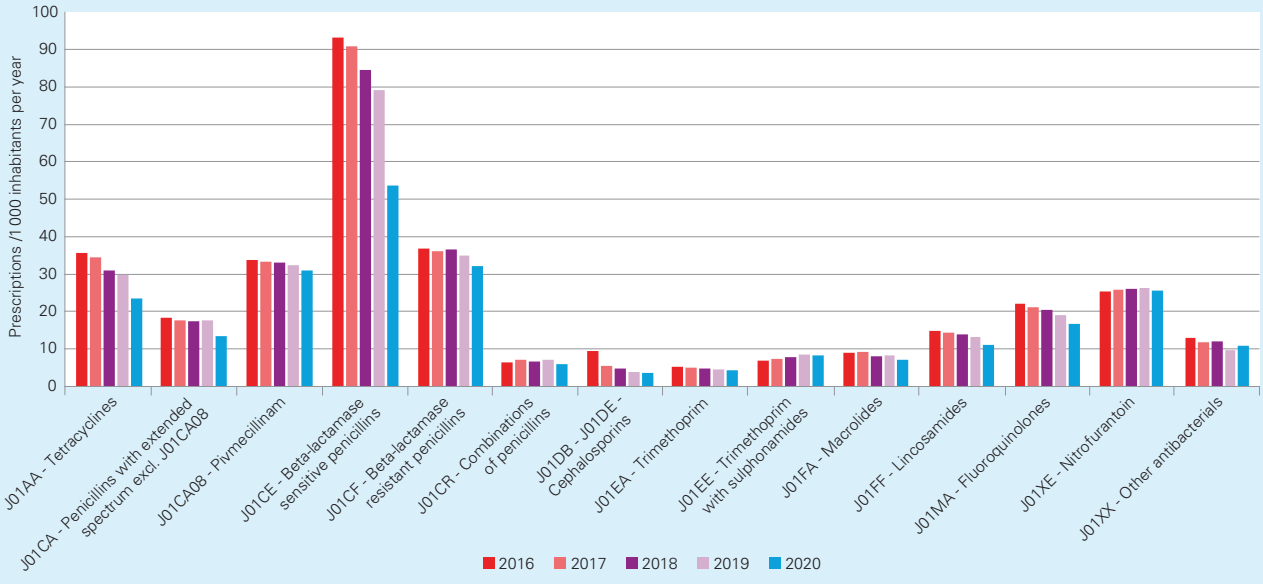
Less seasonal variation in sales of antibiotics is seen over the years, data available at https://www.folkhalsomyndigheten.se/folkhalsorapportering-statistik/statistikdatabaser/folkhalsodata-och-folkhalsostudio/, which could indicate increased adherence to prescribing guidelines (Coenen S, Ferech M, et al. 2007). The sales of antibiotics in Sweden in 2020 were strongly affected by the COVID-19 pandemic, more about this in the section below. Measured in prescriptions, beta-lactamase sensitive penicillins (J01CE) and beta-lactamase resistant penicillins (J01CF) were the most commonly sold antibiotics in 2020, Figure 1.4. If measured in DDD per 1 000 inhabitants per day, beta-lactamase sensitive penicillins (J01CE) and tetracyclines (J01AA) were the most commonly sold antibiotics in 2020, Table 1.1.

Figure 1.3. Sales of antibiotics (J01 excl. methenamine), humans, per age group, 1987-2020, prescriptions/1 000 inhabitants per year.



Source: The Public Health Agency of Sweden

Figure 1.4. Sales of antibiotics, humans, ATC-5, 2016-2020, prescriptions/1 000 inhabitants per year.



Source: The Public Health Agency of Sweden

Table 1.1. Sales of antibiotics in outpatient care, humans, by antibiotic class or substance, age groups, per year, 2016-2020, DDD/1 000 inhabitants per day, prescriptions/1 000 inhabitants per year, users/1 000 inhabitants per year.

Age groups (years)	DDD/1 000 per day					Prescriptions/1 000 per year					Users/1 000 per year				
	2016	2017	2018	2019	2020	2016	2017	2018	2019	2020	2016	2017	2018	2019	2020
Tetracyclines (J01AA)															
0-6	0.00	0.01	0.01	0.01	0.01	0.07	0.28	0.30	0.31	0.33	0.06	0.22	0.23	0.23	0.23
7-19	2.67	2.65	2.59	2.72	2.74	23.18	22.77	21.24	21.96	21.37	14.79	15.04	14.09	14.59	14.12
20-64	2.55	2.47	2.26	2.21	2.01	37.54	35.75	32.00	30.47	24.98	29.09	27.84	25.09	23.98	19.11
65-79	2.78	2.82	2.54	2.44	1.82	54.30	54.90	49.12	45.74	30.26	41.62	42.27	38.10	35.45	22.76
80+	1.90	2.05	1.90	1.80	1.29	43.79	46.88	42.47	40.11	25.96	35.20	37.41	34.25	32.19	19.93
All age groups	2.40	2.35	2.16	2.14	1.92	35.57	34.59	31.06	29.69	23.50	26.75	26.27	23.77	22.72	34.78
Penicillins with extended spectrum (J01CA) excl. pivmecillinam (J01CA08)															
0-6	0.67	0.63	0.65	0.61	0.30	40.12	37.56	38.73	35.82	17.58	30.22	28.35	29.08	27.07	13.66
7-19	0.21	0.21	0.21	0.20	0.14	8.14	7.81	7.89	7.22	4.78	6.39	6.06	6.08	5.63	3.74
20-64	0.35	0.34	0.34	0.36	0.32	12.16	11.75	11.36	11.96	10.68	9.57	9.25	8.90	9.39	7.98
65-79	0.94	0.96	0.95	0.99	0.80	31.10	31.02	30.01	30.71	23.43	23.87	24.11	23.14	23.67	17.48
80+	1.17	1.24	1.23	1.36	1.11	36.18	37.65	37.04	39.09	29.93	28.67	29.99	29.45	30.54	22.89
All age groups	0.49	0.49	0.49	0.51	0.41	18.23	17.69	17.34	17.70	13.53	13.92	13.63	13.31	13.49	19.98
Pivmecillinam (J01CA08)															
0-6	0.02	0.02	0.02	0.02	0.02	1.21	1.42	1.71	1.60	1.34	1.13	1.28	1.56	1.47	1.23
7-19	0.19	0.19	0.19	0.18	0.18	12.69	12.89	12.71	12.36	12.00	11.06	11.24	11.13	10.86	10.49
20-64	0.47	0.47	0.46	0.45	0.43	29.49	29.12	28.80	28.30	27.21	24.33	24.04	23.84	23.57	22.61
65-79	1.02	1.00	1.00	0.98	0.92	59.05	58.28	58.31	56.68	53.66	43.66	43.27	43.37	42.26	40.02
80+	1.94	1.92	1.92	1.90	1.86	114.21	113.02	112.75	111.29	107.57	81.61	81.04	80.78	80.17	76.62
All age groups	0.56	0.55	0.54	0.53	0.51	33.83	33.33	33.07	32.42	31.07	26.23	25.99	25.87	25.48	48.82
Beta-lactamase sensitive penicillins (J01CE)															
0-6	2.89	2.68	2.53	2.33	1.13	209.30	196.07	185.01	171.14	82.12	155.69	147.11	139.97	130.92	66.45
7-19	2.72	2.63	2.43	2.20	1.34	96.85	92.47	86.04	76.35	45.35	77.04	73.43	68.72	61.39	36.91
20-64	3.19	3.17	2.93	2.76	2.06	76.54	75.78	70.27	66.47	49.11	65.21	64.67	59.89	56.69	41.97
65-79	3.51	3.61	3.36	3.26	2.63	81.39	83.98	77.92	75.51	59.59	68.14	70.50	65.60	63.41	49.70
80+	3.05	3.10	3.05	2.97	2.38	73.38	74.34	72.69	70.74	55.00	62.27	63.46	62.12	59.69	45.68
All age groups	3.20	3.15	2.93	2.76	1.99	93.22	90.77	84.43	79.09	53.58	74.78	73.67	68.84	64.71	89.12
Beta-lactamase resistant penicillins (J01CF)															
0-6	0.24	0.27	0.28	0.24	0.19	23.91	27.26	28.35	24.06	18.62	19.01	21.61	22.27	18.94	14.54
7-19	0.74	0.72	0.73	0.72	0.62	25.43	25.20	26.24	24.97	21.25	20.42	20.04	20.95	19.88	16.72
20-64	1.25	1.21	1.22	1.20	1.11	30.31	29.57	29.98	29.14	27.16	24.07	23.43	23.87	23.14	21.30
65-79	2.64	2.54	2.60	2.54	2.42	53.36	51.95	53.19	51.03	47.93	35.38	34.39	35.67	33.92	31.22
80+	5.26	5.23	5.21	5.13	4.89	100.41	99.14	98.77	94.99	90.41	61.19	59.86	60.88	58.73	54.89
All age groups	1.53	1.48	1.49	1.46	1.36	36.73	36.05	36.61	35.06	32.18	26.67	26.25	26.92	25.71	46.53
Combinations of penicillins (J01CR)															
0-6	0.12	0.13	0.10	0.12	0.08	11.52	12.85	9.25	10.98	6.98	6.90	7.68	5.70	6.45	3.87
7-19	0.10	0.11	0.11	0.11	0.08	4.21	4.76	4.07	4.42	3.32	2.73	2.81	2.56	2.56	1.90
20-64	0.17	0.18	0.19	0.19	0.16	5.32	5.59	5.71	5.80	4.99	4.27	4.45	4.54	4.66	3.96
65-79	0.30	0.33	0.35	0.38	0.33	8.81	9.90	9.96	10.57	9.08	6.39	7.15	7.23	7.57	6.27
80+	0.29	0.35	0.39	0.42	0.41	8.79	10.14	10.97	12.19	11.23	6.55	7.46	8.03	9.01	7.80
All age groups	0.18	0.20	0.21	0.22	0.18	6.47	7.02	6.72	7.12	5.87	4.69	5.03	4.92	5.15	8.36
Cephalosporins (J01DB-DE)															
0-6	0.24	0.03	0.01	0.01	0.01	24.25	2.94	1.03	0.74	1.99	19.99	2.55	0.81	0.54	1.63
7-19	0.13	0.05	0.04	0.03	0.02	8.95	3.73	2.62	1.84	1.46	7.10	3.11	2.20	1.53	1.21
20-64	0.11	0.08	0.07	0.06	0.05	6.38	5.09	4.61	3.82	3.36	5.14	4.09	3.71	3.01	2.66
65-79	0.17	0.12	0.10	0.09	0.08	9.37	7.48	6.67	5.83	5.30	6.89	5.57	4.92	4.20	3.78
80+	0.30	0.21	0.19	0.16	0.14	17.64	13.61	12.54	10.54	9.79	13.17	10.39	9.65	8.15	7.33
All age groups	0.14	0.08	0.07	0.06	0.05	9.40	5.55	4.76	3.94	3.61	7.33	4.36	3.72	3.02	5.54

Age groups (years)	DDD/1 000 per day					Prescriptions/1 000 per year					Users/1 000 per year				
	2016	2017	2018	2019	2020	2016	2017	2018	2019	2020	2016	2017	2018	2019	2020
Trimethoprim (J01EA)															
0-6	0.06	0.06	0.06	0.05	0.04	7.51	7.80	8.22	7.00	6.16	5.59	5.80	6.15	5.22	4.44
7-19	0.03	0.03	0.03	0.02	0.02	1.94	1.87	1.73	1.50	1.40	1.56	1.39	1.29	1.14	1.01
20-64	0.07	0.06	0.06	0.05	0.05	2.56	2.22	2.02	1.88	1.75	1.91	1.65	1.49	1.37	1.25
65-79	0.25	0.24	0.23	0.22	0.21	9.48	8.95	8.26	8.36	7.99	6.49	5.91	5.57	5.55	4.88
80+	0.62	0.58	0.54	0.55	0.52	30.30	28.37	26.38	27.70	26.63	14.21	12.92	12.36	12.78	11.76
All age groups	0.12	0.11	0.10	0.10	0.09	5.35	4.98	4.67	4.54	4.29	3.47	3.16	3.00	2.86	5.12
Trimethoprim with sulphonamides (J01EE)															
0-6	0.07	0.09	0.09	0.09	0.08	8.06	10.32	10.96	10.12	8.91	4.56	6.60	7.03	6.46	5.12
7-19	0.10	0.11	0.11	0.11	0.10	3.80	4.62	4.77	4.72	4.26	1.81	2.25	2.29	2.22	1.95
20-64	0.20	0.20	0.21	0.22	0.20	4.87	5.11	5.32	5.67	5.49	2.66	2.78	2.89	3.15	2.90
65-79	0.62	0.62	0.67	0.73	0.69	13.66	14.53	15.57	17.82	17.66	8.86	9.23	9.81	11.15	10.57
80+	0.55	0.54	0.62	0.74	0.70	13.98	14.92	16.74	20.87	20.22	10.25	10.68	11.51	13.84	13.05
All age groups	0.26	0.26	0.28	0.30	0.28	6.85	7.44	7.86	8.55	8.22	3.99	4.37	4.61	5.01	9.21
Macrolides (J01FA)															
0-6	0.25	0.26	0.24	0.19	0.10	11.61	12.45	11.55	9.89	5.41	8.97	9.54	8.61	7.23	3.52
7-19	0.22	0.22	0.19	0.18	0.15	8.70	9.35	7.79	7.06	5.40	6.09	6.49	5.13	4.71	3.14
20-64	0.23	0.21	0.19	0.23	0.24	8.39	8.23	7.48	7.86	7.04	6.30	6.30	5.66	6.10	5.41
65-79	0.29	0.32	0.28	0.35	0.38	8.34	9.04	8.33	9.18	8.71	5.40	5.65	4.98	5.80	5.20
80+	0.22	0.22	0.21	0.27	0.31	6.33	6.61	6.40	7.63	7.45	3.97	4.45	3.87	4.91	4.63
All age groups	0.24	0.24	0.22	0.25	0.25	8.91	9.19	8.16	8.35	7.15	6.24	6.41	5.63	5.88	9.69
Lincosamides (J01FF)															
0-6	0.02	0.04	0.03	0.04	0.01	5.03	7.66	7.07	7.76	3.21	3.70	5.70	5.40	6.01	2.32
7-19	0.11	0.12	0.11	0.11	0.09	7.22	7.72	7.37	7.26	5.26	5.70	6.00	5.75	5.61	4.06
20-64	0.30	0.29	0.28	0.26	0.23	14.34	13.64	13.06	12.34	10.61	11.38	10.80	10.28	9.78	8.25
65-79	0.56	0.56	0.53	0.48	0.45	22.52	21.94	21.39	19.54	17.81	15.57	15.10	14.56	13.51	12.03
80+	0.72	0.75	0.72	0.71	0.66	30.05	29.99	29.39	28.37	26.19	18.83	18.48	18.15	17.62	16.09
All age groups	0.32	0.31	0.30	0.28	0.25	14.76	14.48	13.90	13.20	11.16	10.91	10.70	10.24	9.80	16.19
Fluoroquinolones (J01MA)															
0-6	0.02	0.02	0.02	0.02	0.02	0.83	0.98	1.09	0.99	1.00	0.50	0.55	0.64	0.60	0.48
7-19	0.10	0.10	0.09	0.10	0.08	3.25	3.47	3.30	3.27	2.92	2.51	2.69	2.56	2.52	2.21
20-64	0.55	0.52	0.49	0.45	0.38	17.62	16.78	16.07	14.71	12.68	12.83	12.24	11.69	10.71	9.13
65-79	1.53	1.47	1.41	1.31	1.15	51.73	49.97	48.17	44.49	39.53	35.22	33.97	32.59	30.15	26.55
80+	1.90	1.82	1.83	1.70	1.55	70.11	67.28	67.51	62.76	57.10	49.10	47.22	46.72	43.38	39.12
All age groups	0.66	0.63	0.60	0.56	0.49	22.11	21.20	20.49	18.93	16.65	15.45	14.84	14.28	13.19	23.03
Nitrofurantoin (J01XE)															
0-6	0.06	0.06	0.07	0.07	0.06	7.37	8.04	7.49	8.66	8.50	5.46	6.11	6.11	6.80	6.47
7-19	0.12	0.12	0.11	0.11	0.10	9.12	9.21	8.71	8.85	8.35	7.72	7.83	7.41	7.50	7.10
20-64	0.31	0.32	0.33	0.32	0.32	20.88	21.51	21.86	21.70	21.40	16.84	17.22	17.45	17.29	17.00
65-79	0.76	0.78	0.80	0.81	0.78	45.21	45.72	46.23	46.58	44.10	32.22	32.42	32.53	32.29	30.47
80+	1.38	1.44	1.46	1.49	1.47	87.65	90.38	91.64	93.85	92.56	53.10	53.66	53.61	54.07	50.85
All age groups	0.39	0.40	0.40	0.41	0.40	25.32	25.86	26.02	26.24	25.56	18.68	19.01	19.08	19.05	36.80
All agents (J01 excl. methenamine)															
0-6	4.66	4.30	4.13	3.80	2.06	350.96	325.85	310.94	289.25	162.33	213.20	200.20	193.33	181.09	105.93
7-19	7.46	7.29	6.97	6.83	5.69	214.06	206.47	194.98	182.28	137.85	138.87	133.58	127.80	118.96	89.34
20-64	9.78	9.54	9.04	8.78	7.59	267.17	260.87	249.19	240.72	207.10	168.36	164.83	158.05	152.70	130.27
65-79	15.44	15.44	14.88	14.62	12.73	449.99	449.06	434.48	423.12	366.17	235.37	236.19	228.14	221.15	189.67
80+	19.37	19.50	19.32	19.25	17.33	634.73	634.08	626.87	621.40	561.21	301.19	301.50	298.15	293.00	258.98
All age groups	10.52	10.28	9.81	9.58	8.20	317.65	308.95	295.86	285.50	237.08	184.49	180.70	173.97	167.30	275.17

Antibiotic sales in 2020 during the COVID-19 pandemic

Results

- The sales of antibiotics in outpatient care were 25% lower in the second quarter of 2020 compared to the second quarter of 2019.
- Antibiotics commonly used to treat RTIs decreased by 40% during the second quarter of 2020 compared to the second quarter of 2019.
- Antibiotic sales to children 0-6 years decreased by 63% in the second quarter of 2020, compared to the same period in 2019.

Comments

During the COVID-19 pandemic, the sales of antibiotics in outpatient care plummeted. After several years of decreasing 1-5% per year (Public Health Agency, 2021), the sales of antibiotics (J01 excl. methenamine) were 17% lower in 2020 than in 2019, Figure 1.3. COVID-19 was declared a pandemic in March 2020 (WHO, 2020) and in the following quarters of 2020 a big difference is seen compared to previous years. Taking a closer look at some of the infections for which antibiotics are prescribed, the difference in sales is bigger in the group of RTI antibiotics, which decreased by 40% in the second quarter of 2020 compared to the same period in 2019, Figure 1.6. The sales in antibiotics often used for UTIs, SSTIs and acne were roughly at the same level as in 2019. This corresponds well to the overall trend in Sweden of a decreased number of RTIs (see more in the section on the impact of the COVID-19 pandemic). The age group that has had the biggest decrease in sales is children 0-6 years. In quarter two, three and four in 2020, the sales in this group decreased by 63%, 38% and 61% respectively, compared to the corresponding periods in 2019, Figure 1.7. A similar trend is seen in this group concerning antibiotics used to treat RTIs, Figure 1.8.

Figure 1.5. Sales of antibiotics (J01 excl. methenamine), humans, per quarter, 2016-2020, prescriptions/1 000 inhabitants per quarter.

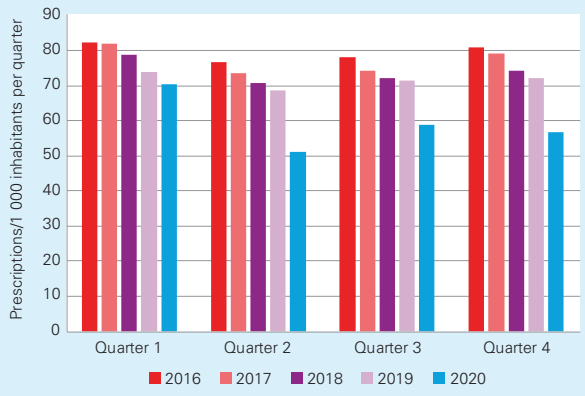


Figure 1.6. Sales of antibiotics commonly used to treat respiratory tract infections, urinary tract infections, skin and soft tissue infections and skin and soft tissue infections (acne), humans, per month, 2016-2020, prescriptions/1 000 inhabitants per month.

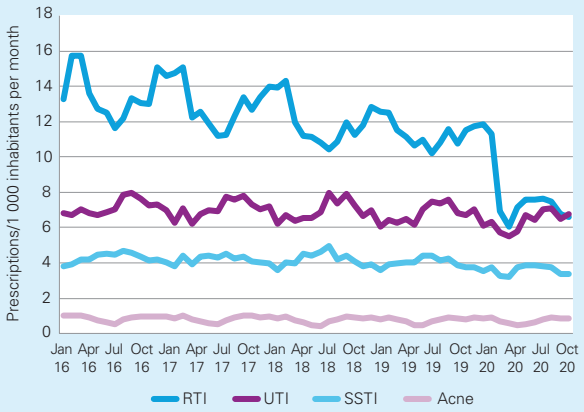


Figure 1.7. Sales of antibiotics (J01 excl. methenamine), humans, **children 0-6 years**, per quarter, 2016-2020, prescriptions/1 000 children per quarter.

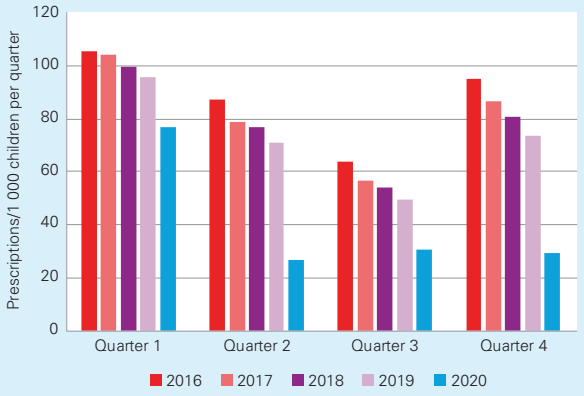
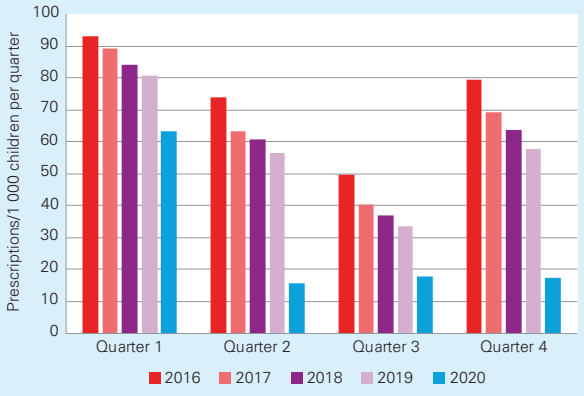


Figure 1.8. Sales of antibiotics commonly used to treat respiratory tract infections, humans, **children 0-6 years**, per quarter, 2016-2020, prescriptions/1 000 children per quarter.



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

Results

- Beta-lactamase sensitive penicillins (J01CE) decreased by 32% in 2020 and the overall sales of RTI antibiotics decreased by 28% compared to 2019.
- Antibiotics commonly used to treat UTIs in women 15-79 years have decreased by 5.1% in the last year.

Comments

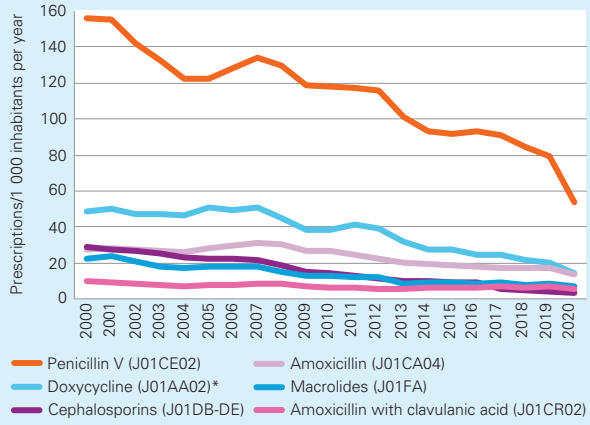
Antibiotics commonly used to treat RTIs are generally the most frequently prescribed antibiotics in Sweden. The antibiotics included in this measure are doxycycline (J01AA02; excluding packages larger than 50 tablets), penicillin V (J01CE02), amoxicillin (J01CA04), amoxicillin with enzyme inhibitor (J01CR02), cephalosporins (J01DB-DE) and macrolides (J01FA), Figure 1.9. The sales of all these antibiotic classes have decreased significantly ($p < 0.001$) in the latest years, except for amoxicillin with enzyme inhibitor (J01CR02), for which trend analysis shows an increase since 2017. However, in 2020 the sales were lower than in 2019 for all antibiotics commonly used to treat RTIs.

Beta-lactamase sensitive penicillin (J01CE) is the recommended first-line antibiotic for treatment of lower RTIs in Sweden (Swedish Medical Products Agency, 2008) and the most frequently prescribed antibiotic in outpatient care, measured both in DDD per 1 000 inhabitants per day and in prescriptions per 1 000 inhabitants per year, Figure 1.9 and Table 1.1. Beta-lactamase resistant penicillin (J01CF) was the second most frequently prescribed antibiotic in outpatient care measured in prescriptions per 1 000 inhabitants per year.

National treatment recommendations for urinary tract infections (Swedish Medical Products Agency, 2017), recommend pivmecillinam (J01CA08) and nitrofurantoin (J01XE01) over trimethoprim (J01EE01) against UTIs in women 15 years or older and the trend towards increased use of first-line antibiotics continues, Figure 1.10. A decrease in the past years is seen for the overall sales of antibiotics used to treat UTIs in women older than 15 years, with a total decrease of 15% since the year 2000.

The sales of antibiotics commonly used to treat UTIs in men 65 years and older have decreased since 2000, with a change in use from trimethoprim and fluoroquinolones (that have decreased) to nitrofurantoin and pivmecillinam (that have increased). Fluoroquinolones continued to decrease (significant change, $p < 0.001$), by 9.1% from 2019 to 2020. As nitrofurantoin and pivmecillinam are recommended as first-line antibiotics for treatment of symptomatic UTI without fever in men (Swedish Medical Products Agency, 2017), the increased use in the mentioned classes is in line with treatment recommendations. The increase in sales of first-line antibiotics since 2020 is significant ($p < 0.001$) and the rate of increase gets higher over time, Figure 1.11.

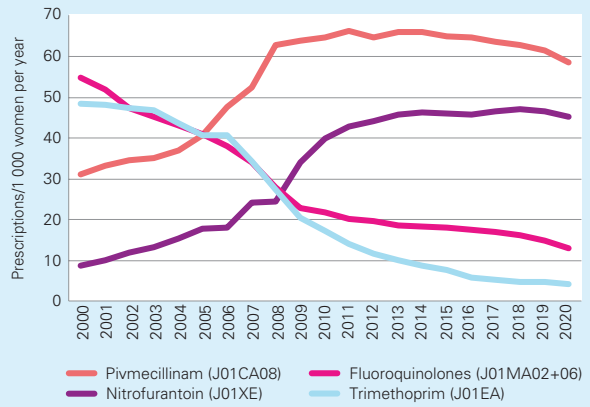
Figure 1.9. Sales of antibiotics commonly used to treat respiratory tract infections, humans, 2000-2020, prescriptions/1 000 inhabitants per year.



*Doxycycline (J01AA02) excl. packages with more than 50 tablets.

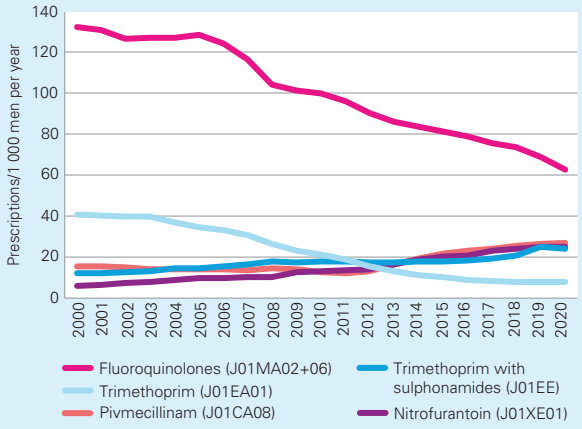
Source: The Public Health Agency of Sweden

Figure 1.10. Sales of antibiotics commonly used to treat urinary tract infections, humans, women, 15-79 years, 2000-2020, prescriptions/1 000 women per year.



Source: The Public Health Agency of Sweden

Figure 1.11. Sales of antibiotics commonly used to treat urinary tract infections, humans, men 65 years and older, 2000-2020, prescriptions/1 000 men per year.



Source: The Public Health Agency of Sweden

Age and gender comparisons

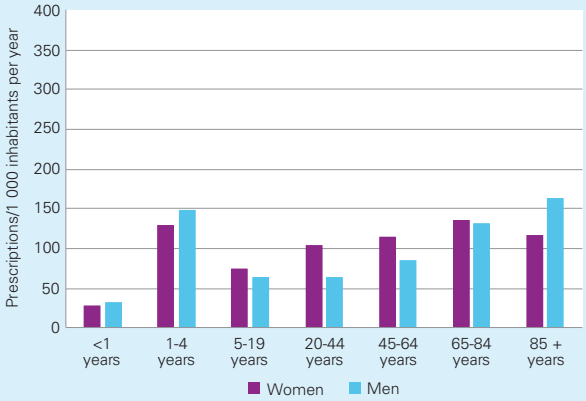
Results

- The most frequently sold antibiotics in the age group 1-4 years are the antibiotics commonly used to treat RTIs. They represent 73% of the total antibiotic sales in this age group.
- RTI antibiotics are prescribed more to women than to men, except in the youngest and the oldest population, Figure 1.12.
- Antibiotics commonly used to treat UTIs are mostly prescribed to women and the older age groups, Figure 1.13.
- The sales of antibiotics that are commonly used to treat skin and soft tissue infections are similar for men and women and between age groups, with higher sales in the older age groups, Figure 1.14.
- Antibiotics commonly used to treat acne are mainly used in the age groups 5-44 years and predominately by women, Figure 1.15. In the age group 20-44 most of the prescriptions are found among 20-29 year-olds (data not shown).
- 61% of all antibiotic prescriptions in Sweden during 2020 were issued to women, Figure 1.16.

Comments

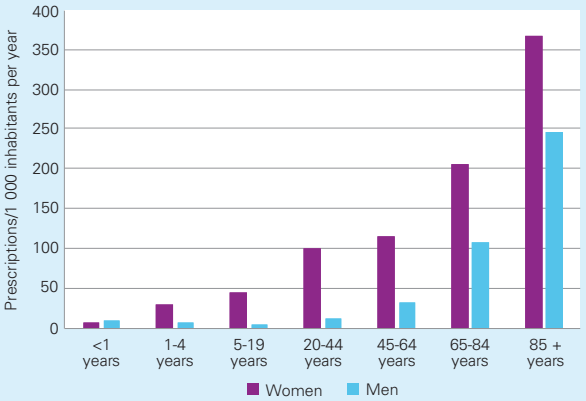
Concerning antibiotics that are commonly used to treat skin and soft tissue infections and acne, people in the older age groups are more often prescribed longer treatments, which impacts the amount of antibiotics used. The elderly are also prescribed the same antibiotics that are used for acne, but treated for other indications, such as rosacea and other skin conditions.

Figure 1.12. Sales of antibiotics commonly used to treat respiratory tract infections, humans, 2020, prescriptions/1 000 inhabitants per year. This measure includes doxycycline (J01AA02; excluding packages larger than 50 tablets), penicillin V (J01CE02), amoxicillin (J01CA04), amoxicillin with enzyme inhibitor (J01CR02), cephalosporins (J01DB-DE), and macrolides (J01FA).



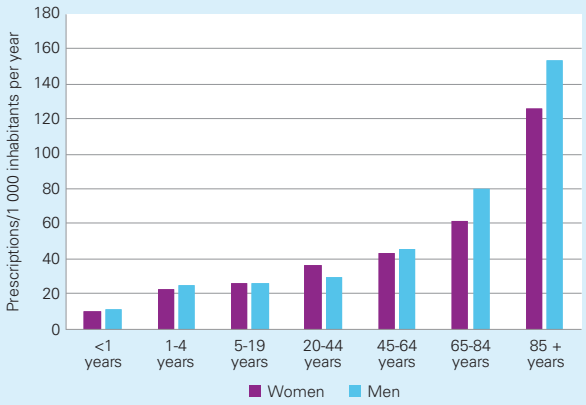
Source: The Public Health Agency of Sweden

Figure 1.13. Sales of antibiotics commonly used to treat urinary tract infections, humans, 2020, prescriptions/1 000 inhabitants per year. This measure includes pivmecillinam (J01CA08), trimethoprim (J01EA01), ciprofloxacin (J01MA02) and nitrofurantoin (J01XE01).



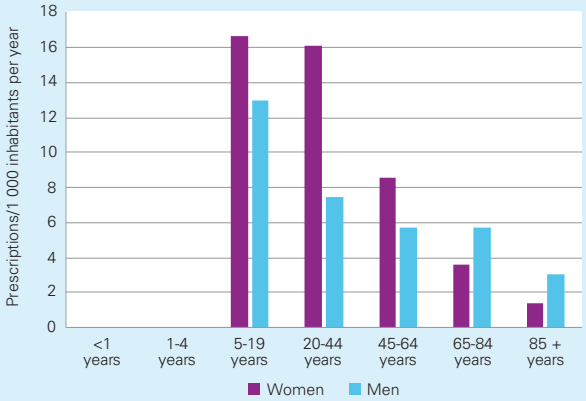
Source: The Public Health Agency of Sweden

Figure 1.14. Sales of antibiotics commonly used to treat skin and soft tissue infections, humans, 2020, prescriptions/1 000 inhabitants per year. This measure includes clindamycin (J01FF01) and flucloxacillin (J01CF05).



Source: The Public Health Agency of Sweden

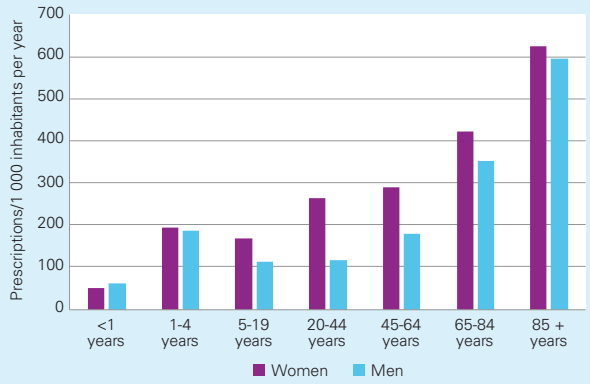
Figure 1.15. Sales of antibiotics commonly used to treat skin and soft tissue infections (acne), humans, 2020, prescriptions/1 000 inhabitants per year. This measure includes doxycycline (J01AA02; packages over 50 tablets), lymecycline (J01AA04), oxytetracycline (J01AA06) and tetracycline (J01AA07).



Source: The Public Health Agency of Sweden

In general, comparisons across age groups show that the use of antibiotics is greatest among people that are 85 years and older. As mentioned in the chapter "Guidance for readers", part of the antibiotic use among the elderly are not included in the statistics for outpatient care, as it is sold on requisition and included in hospital data. Therefore a possible underestimation in the age group 85 years and older cannot be ruled out.

Figure 1.16. Sales of antibiotics (J01 excl. methenamine), humans, age and gender, 2020, prescriptions/1 000 inhabitants per year.



Source: The Public Health Agency of Sweden

Antibiotic sales for children

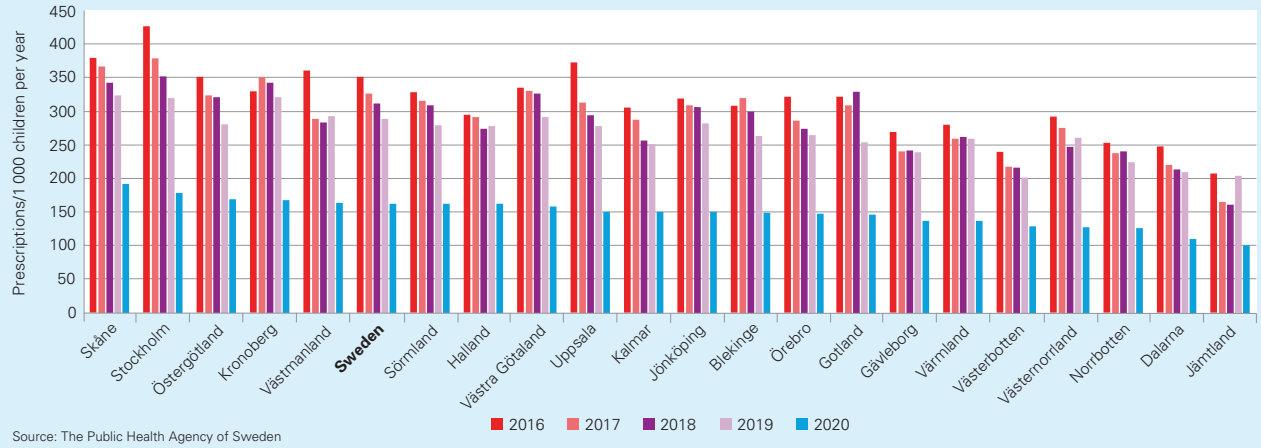
Results

- Sales of antibiotics for children 0-6 years were 44% lower in 2020 than in 2019, Figure 1.17.
- The most sold antibiotic for children 0-6 years was beta-lactamase sensitive penicillin (J01CE), which accounted for 51% of the sales, Table 1.1.
- The proportion of children 0-6 years treated with at least one course of antibiotics decreased in 2020.

Comments

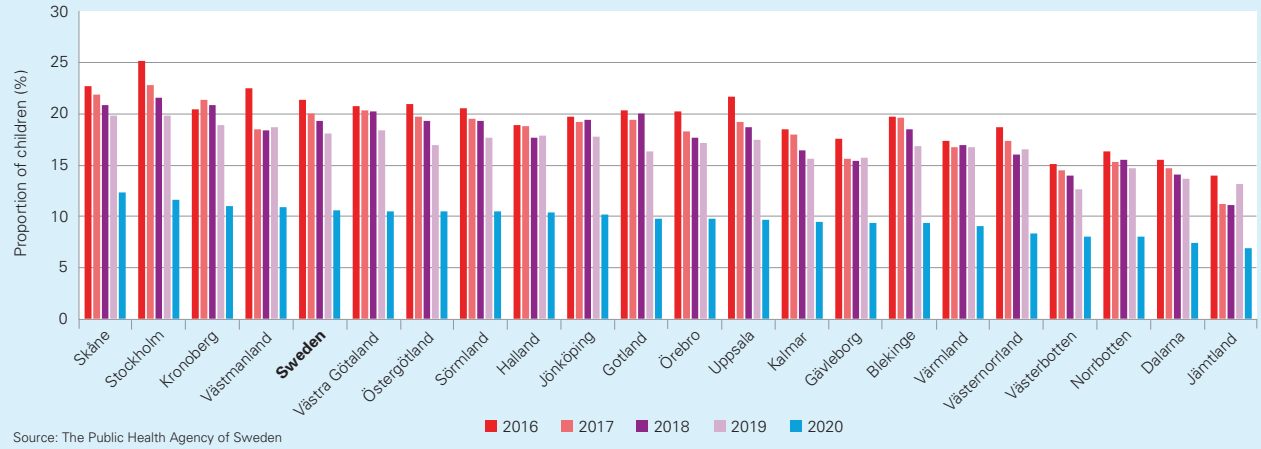
The decrease in sales of antibiotics for children 0-6 years was seen in all of the 21 regions in Sweden. There are large variations; from 192 prescriptions per 1 000 children and year in Region Skåne to 100 in Region Jämtland Härjedalen, Figure 1.17. Several regions show substantial changes in sales compared to 2019. The proportion of children (0-6 years) treated with at least one course of antibiotics in 2020 was 11%, Figure 1.18. The proportion decreased in all of the 21 regions during 2020, which corresponds well to the decrease in the regional sales of antibiotics, Figure 1.17.

Figure 1.17. Sales of antibiotics (J01 excl. methenamine), humans, children 0-6 years, per region, 2016-2020, prescriptions/1 000 children per year.



Source: The Public Health Agency of Sweden

Figure 1.18. Proportion (%) of children aged 0-6 years treated with at least one course of antibiotics (J01 excl. methenamine), humans, per region, 2016-2020.



Source: The Public Health Agency of Sweden

Regional comparisons

Results

- The annual average sales of antibiotics were 237 prescriptions per 1 000 inhabitants in 2020.
- 14% of the Swedish population was treated with at least one course of antibiotics in 2020, Figure 1.20.

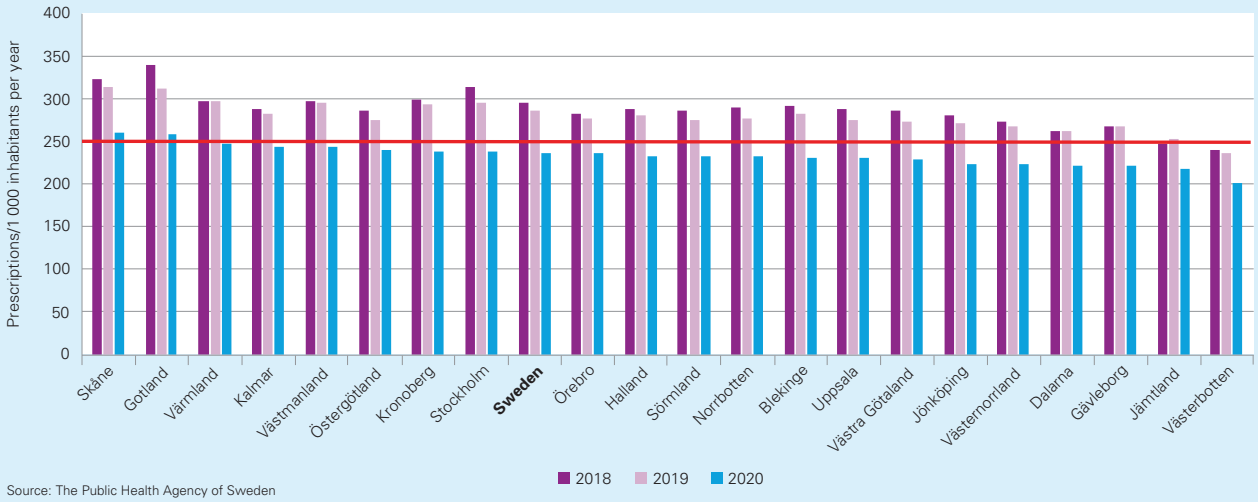
Comments

The proportion of people using antibiotics varies between the regions, from 15% in Region Skåne to 11% in Region Västerbotten, Figure 1.20. Both the proportion of people and of children treated with antibiotics during the last five years have decreased on a national level.

In 2018, the national annual average sales of antibiotics were for the first time below 300 prescriptions per 1 000 inhabitants 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 reached nationally and in 19 out of 21 regions. Equivalently to the proportion of the population treated with at least one course of antibiotics, there are also large regional variations in sales, ranging from 261 prescriptions per 1 000 inhabitants per year in Region Skåne to 201 in Region Västerbotten, Figure 1.19. These numbers need to be interpreted carefully and in relation to the COVID-19 pandemic.

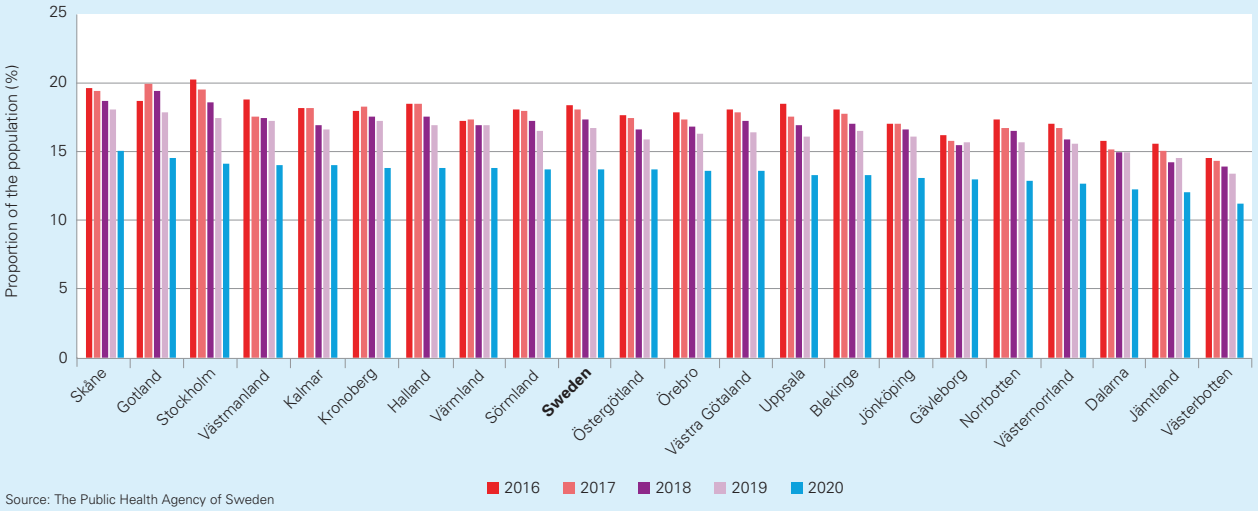
The Swedish strategic programme against antibiotic resistance (Strama) has proposed quality targets for antibiotic prescribing in outpatient care, focusing on the use of penicillin V in children and fluoroquinolones in the treatment of UTIs in women. The target for penicillin V in children 0-6 years of age is set to 80% or more of prescriptions, with penicillin V (J01CE02) as the numerator and amoxicillin (J01CA04), penicillin V (J01CE02), amoxicillin with clavulanic acid (J01CR02), cephalosporins (J01DB-DE) and macrolides (J01FA) as the denominator. In 2020 the proportion of penicillin V among children was 72% on a national level, Figure 1.21.

Figure 1.19. Sales of antibiotics (J01 excl. methenamine), humans, per region, 2018-2020, prescriptions/1 000 inhabitants per year.



Source: The Public Health Agency of Sweden

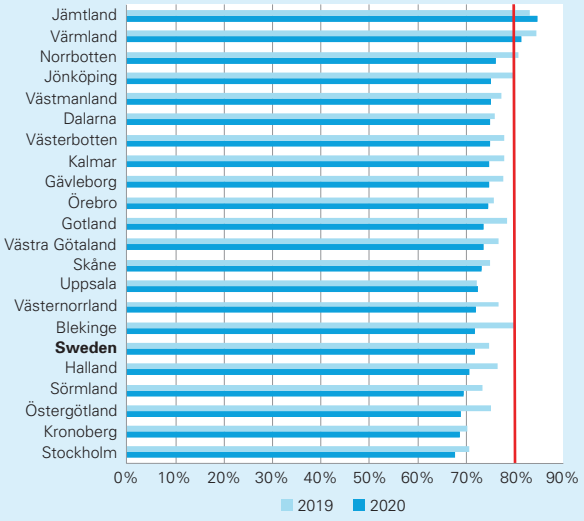
Figure 1.20. Proportion (%) of the population treated with at least one course of antibiotics (J01 excl. methenamine), humans, per region, 2016-2020.



Source: The Public Health Agency of Sweden

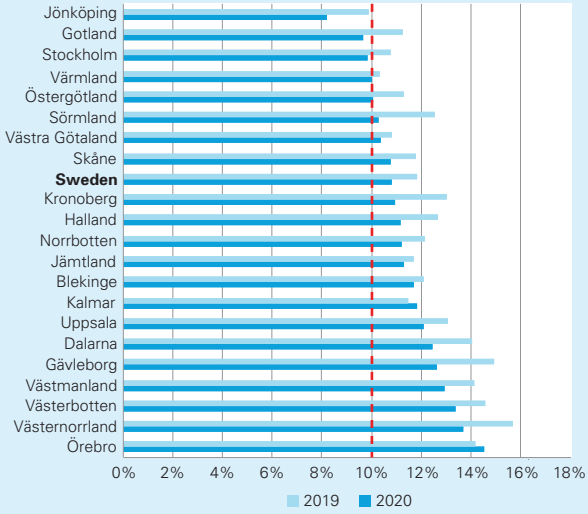
The target for prescribed fluoroquinolones to women is set to the age group 18-79 years, though the treatment recommendations for UTIs concern women >15 years. In Figure 1.22, the proportion of fluoroquinolones is shown for women 15-79 years, which corresponds well to women 18-79 years. Data on both age groups are found in the embedded file. The target is set to a maximum of 10% fluoroquinolones. Here, the numerator is ciprofloxacin (J01MA02) and norfloxacin (J01MA06) and the denominator is pivmecillinam (J01CA08), trimethoprim (J01EA01), ciprofloxacin (J01MA02), norfloxacin (J01MA06) and nitrofurantoin (J01XE01). In 2020, the proportion of fluoroquinolones was 11% on a national level, Figure 1.22.

Figure 1.21. Proportion penicillin V of antibiotics that are commonly used to treat respiratory tract infections in children 0-6 years, humans, per region, 2019 and 2020. The red line indicates Strama's target at a minimum of 80%.



Source: The Public Health Agency of Sweden

Figure 1.22. Proportion fluoroquinolones of antibiotics commonly used to treat urinary tract infections in women 15-79 years, humans, women, per region, 2019 and 2020. The dashed line indicates Strama's target of maximum 10% fluoroquinolones for women 18-79 years.



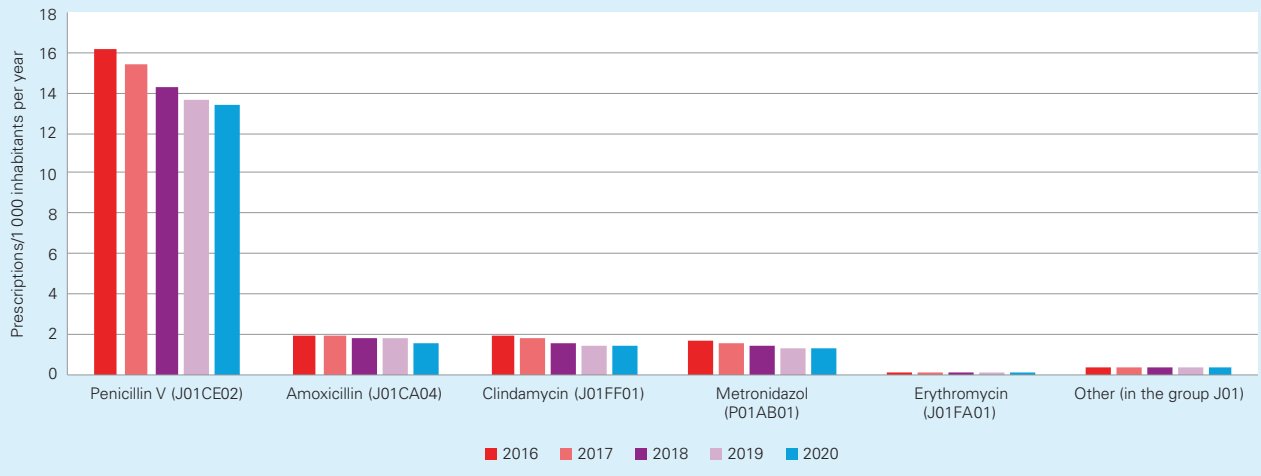
Source: The Public Health Agency of Sweden

Antibiotics in dentistry

Results

- Dentists now account for around 6.6% of all antibiotics prescribed in Sweden, excl. metronidazole (P01AB01), compared to 5.9% in 2019.
- The sales of antibiotics (J01 excl. methenamine; metronidazole P01AB01) decreased by 3.2% in 2020, from 19 to 18 prescriptions per 1 000 inhabitants per year. The sales of amoxicillin and clindamycin decreased by 12% and 4.4% respectively, Figure 1.23.
- The most commonly prescribed antibiotic by dentists was penicillin V (74% of the total sales), which decreased by 2.3% compared to 2019.

Figure 1.23. Antibiotics prescribed by dentists in outpatient care, humans, 2016-2020, prescriptions/1 000 inhabitants per year.



Source: The Public Health Agency of Sweden

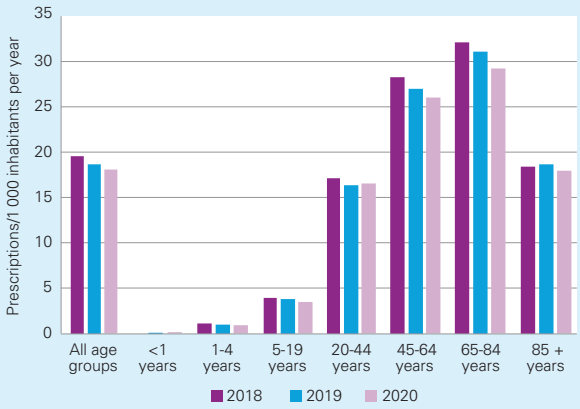
Comments

Most prescriptions of antibiotics issued by dentists are found in the age group 65-84 years, followed by the age group 45-64 years. Between 2000 and 2007, an increase was seen in all age groups, but since 2007 there has been an overall decreasing trend, Figure 1.24 (data found in the embedded file). 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, for a broader anaerobic spectrum, metronidazole is also recommended as first-line treatment in dentistry and therefore included in the measure of sales.

The sales of antibiotics in dentistry (J01 excl. methenamine; metronidazole P01AB01), measured in prescriptions per 1 000 inhabitants per year, were lower in 16 of 21 regions in 2020 compared to 2019, Figure 1.25. There are regional differences; dentists in Region Skåne prescribed the most, with 23 prescriptions per 1 000 inhabitants. This is more than twice as much as dentists in Region Västerbotten, who prescribed the least (11 prescriptions per 1 000 inhabitants) in 2020. These regional differences correspond to some extent to the differences in sales in total outpatient care, Figure 1.19.

The effects of the COVID-19 pandemic are not yet pronounced in the number of antibiotic prescriptions issued by dentists. The trend of a continuous decrease in the sales continued during 2020. Nonetheless, a decrease is seen in the number of dental care visits, mostly in the age group 70 years and older, compared to previous years (National Board of Health and Welfare, 2020a). Data on dental care subsidy show a big decrease in the allowance paid to the dental care clinics as subsidy for the patient's dental care (Swedish Social Insurance Agency, 2020). National dental care subsidy is provided for people who are 24 years and older. In 2020, 3 704 035 people received dental care subsidy compared to 4 037 368 people in 2019. This reduction is due to fewer people visiting dental care clinics and thus not using the allowance. The decline in the number of visits during 2020 is seen across all types of visits to dental care. Preventive dental care at dental hygienists has decreased the most. This is attributable to fewer appointments as well as clinics having to cancel, restrict or pause non-urgent care during the pandemic. The impact of this decline in the number of visits is hard to establish at the moment and therefore continuous monitoring of both the sales of antibiotics and the number of visits is important. Studies on the short-term and long-term consequences of the COVID-19 pandemic on dental care are needed.

Figure 1.24. Antibiotics (J01 excl. methenamine; metronidazole P01AB01) prescribed by dentists in outpatient care, humans, age group, 2018-2020, prescriptions/1 000 inhabitants per year.



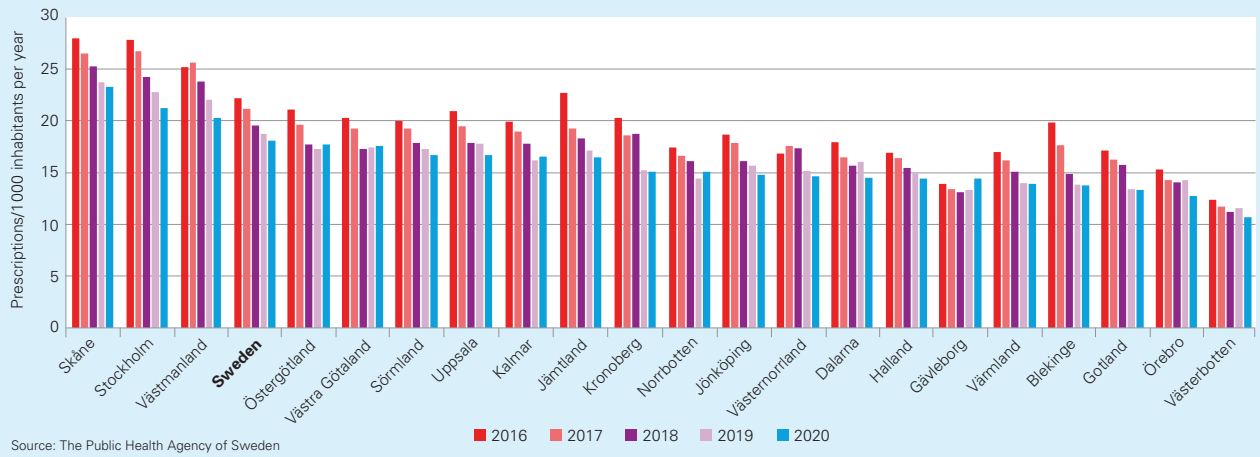
Source: The Public Health Agency of Sweden

Antibiotics in digital care

In this report, digital care refers to digital consultations provided through applications for telephones and web-based consultations.

The Swedish digital care sector has grown in recent years and in 2020, the digital health care services had a rapid development. A large portion of the health care centres that previously only offered visits in person, have now developed platforms for digital consultations. Simultaneously, several health care centres that before only provided digital care

Figure 1.25. Antibiotics (J01 excl. methenamine; metronidazole P01AB01) prescribed by dentists in outpatient care, humans, 2016-2020, prescriptions/1 000 inhabitants per year.



Source: The Public Health Agency of Sweden

have also opened facilities for visits where the patient is physically present. Overall, in 2020, the total number of consultations in digital care for all types of health issues has increased (SALAR, 2020).

In Sweden, registration codes are issued to all health care providers and can for example give the opportunity to measure prescribing trends. Prescriptions issued by health care centres that provide care both in their facilities and through digital consultations are accounted for under the same registration number, regardless of the kind of visit. Consequently, it has become more complex to separate data and specifically measure prescriptions in digital care. To follow and analyse the antibiotic prescribing patterns in digital care is therefore not possible at this point and the surveillance of sales in this sector needs to be developed further.

However, for Swedres-Svarm 2020, efforts were made to compile data on prescriptions from digital consultations. Data were aggregated by the eHealth Agency, based on registration numbers for 12 digital care providers in 2019 and 2020. The sample from these providers shows a clear increase in dispensed antibiotic prescriptions from 2019 to 2020. Taking a closer look at the different age groups, the individuals in the group 20-44 years received most antibiotic prescriptions via digital care providers, which might indicate that this age group seeks digital health care to a larger extent. Showing the data separated into different antibiotic classes, a large proportion of the prescribed antibiotics are the class J01X. Here nitrofurantoin (J01XE01) is found, one of the first-line treatment recommendations of urinary tract infection in non-pregnant women.

These compilations do not reflect the data with full accuracy, but give an indication of the situation in 2020. In the future, it is important to be able to analyse digital care in the same manner as outpatient care, dentistry and hospital care, to give a comprehensive view of antibiotic prescribing trends in this sector.

Antibiotics in hospital care

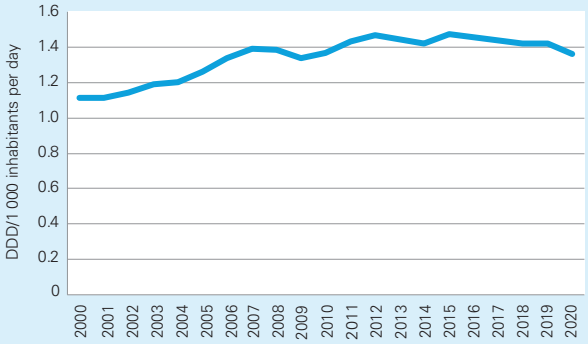
Data shown in this section include sales on requisition to all Swedish hospitals and other facilities, covering acute care hospitals, some nursing homes and other institutions within health and social care that order antibiotics for dispensing to patients or residents. To provide a more detailed picture of antibiotic use in secondary care, there are also displays of sales to acute care hospitals only, related to number of admissions and patient-days. The amount of nursing homes that purchase antibiotics (and other medicines) to dispensaries, whereby the sales are included in hospital care data, varies between regions. On a national level, the proportion of antibiotics in hospital care sold to acute care hospitals is about 70%. Region Dalarna is not included in the statistics showing hospital care and admissions and patient-days from Dalarna are excluded. Requisition data from Region Jämtland Härjedalen are excluded from 2020, as well as admissions and patient-days from the same year. Data from 2014 from Jönköping are incomplete.

Antibiotic sales in hospitals and other health and social care facilities

Results

- The total sales of antibiotics (J01 excl. methenamine) in hospital care in Sweden were 1.36 DDD per 1 000 inhabitants per day in 2020, which is 4.1% lower compared to 2019.
- Beta-lactamase resistant and beta-lactamase sensitive penicillins (J01CF and J01CE) have decreased in hospital care and combinations of penicillins (J01CR) have increased in 2020, Figure 1.27.
- Sales in hospital care represent 14% of the total sales of antibiotics for humans in Sweden (outpatient care, hospitals and other health care facilities) measured in DDD per 1 000 inhabitants per day.

Figure 1.26. Sales of antibiotics (J01 excl. methenamine) in hospital care, humans, 2000-2020, DDD/1 000 inhabitants per day.



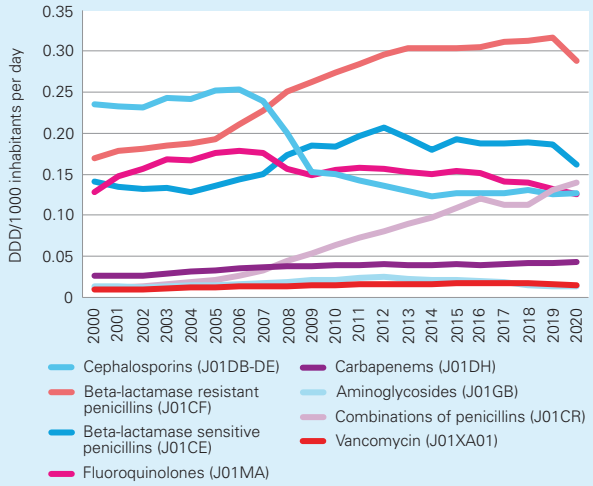
Source: The Public Health Agency of Sweden

Comments

The total sales of antibiotics (J01 excl. methenamine) in hospital care have decreased significantly since 2015 ($p < 0.001$) and the decrease continued in 2020, Figure 1.26. Taking a closer look at the different classes of antibiotics, there have been several changes in the last years. The change in the sales of cephalosporins around 2006-2009 is explained by a shift in the use of substances, meaning the number of DDDs appear lower, and by an altered prescribing that has continued since. Simultaneously, beta-lactamase sensitive penicillins (J01CE) and combinations of penicillins (J01CR), mainly piperacillin-tazobactam (J01CR05), have gradually replaced the cephalosporins. Combinations of penicillins have increased significantly ($p < 0.001$) since 2000 and beta-lactamase resistant penicillins show an upward trend up until 2019, which turned downwards in 2020. Even as the beta-lactamase sensitive penicillins have replaced the cephalosporins, at the same time the sales of this class have decreased significantly ($p < 0.001$) since 2016. One reason behind the dip in sales of penicillins (J01CE and J01CF) in 2020 might be the decreased number of surgeries that has been performed (National Board of Health and Welfare, 2020b) and that these substances often are used as prophylaxis (Skoog et al., 2016). In the summer of 2020 a shortage of cefotaxim (J01DD01) was noted and other

substances were recommended as an alternative. However, the shortage was brief and cefotaxim became available quickly. As several of the alternative antibiotics were other cephalosporins, the changes are not visible in the data in this report. A varying availability of substances might also be the cause of fluctuations in the data, Figure 1.27. Further and more detailed analyses on the effects of the COVID-19 pandemic on hospital care in Sweden need to be conducted in order to get an accurate picture of the changes in sales.

Figure 1.27. Sales of antibiotics in hospital care, humans, ATC-5 and ATC-7, 2000-2020, DDD/1 000 inhabitants per day.



Source: The Public Health Agency of Sweden

Antibiotic sales in Swedish acute care hospitals

Results

- Data from acute care hospitals show that the sales of antibiotics decreased in 2020 compared to 2019 as measured in DDD per 100 admissions and were at the same level as in 2019 measured in DDD per 100 patient-days, Table 1.2.
- Beta-lactamase resistant penicillins (J01CF) are the most common antibiotics, making up 21% of the sales.
- Cephalosporins (J01DB-DE) increased in 2020.
- The proportion of beta-lactamase sensitive antibiotics of all antibiotics in acute care hospitals decreased in 17 of 19 regions in 2020 compared to 2019.
- The proportion of cephalosporins of all antibiotics in acute care hospitals varied between the regions from 16% to 3.4% during 2020 and the corresponding numbers for fluoroquinolones were 12% and 5.5%. Piperacillin-tazobactam varied between 15% and 4.2% and carbapenems between 7.2% and 2.0%, Figure 1.29.

Comments

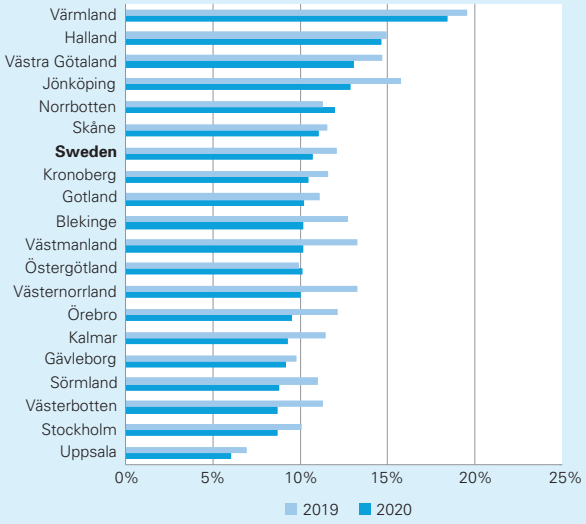
The major classes in sales are the beta-lactamase resistant penicillins (J01CF), beta-lactamase sensitive penicillins (J01CE), cephalosporins (J01DB-DE), fluoroquinolones (J01MA) and combinations of penicillins (J01CR), which mainly consist of piperacillin-tazobactam (J01CR05). Cephalosporins (J01DB-DE) and carbapenems (J01DH) have shown increasing sales in the last few years and continued to do so in 2020. They now represent 12% and 4.1% respectively, Table 1.2. There are substantial variations in

Table 1.2. Sales of antibiotics to acute care hospitals. humans. ATC-5 & ATC-7, 2016-2020, DDD/100 admissions and DDD/100 patient-days. Some substances are displayed on ATC level 7 as they are valuable to follow separately. The substances in question are also included in the ATC level 5. The table is sorted on highest to lowest DDD/100 admissions in 2020.

	DDD/100 admissions					DDD/100 patient-days				
	2016	2017	2018	2019	2020	2016	2017	2018	2019	2020
Beta-lactamase resistant penicillins (J01CF)	58.2	61.3	63.7	64.0	60.9	12.9	13.7	14.5	15.0	14.5
Combinations of penicillins (J01CR)	28.9	28.1	28.8	33.5	37.4	6.4	6.3	6.6	7.8	8.9
Cephalosporins (J01DB-DE)	29.7	31.2	32.5	31.3	33.2	6.6	7.0	7.4	7.3	7.9
Beta-lactamase sensitive penicillins (J01CE)	32.3	35.2	35.7	35.0	30.3	7.2	7.9	8.1	8.2	7.2
Piperacillin-tazobactam (J01CR05)	24.4	22.8	23.2	27.2	29.6	5.4	5.1	5.3	6.4	7.1
Fluoroquinolones (J01MA)	27.4	27.0	26.9	25.5	24.6	6.1	6.0	6.1	6.0	5.9
Penicillins with extended spectrum (J01CA)	22.9	23.8	23.6	23.4	22.1	5.1	5.3	5.4	5.5	5.3
Benzylpenicillin. PcG (J01CE01)	18.9	21.3	21.7	22.1	19.5	4.2	4.8	4.9	5.2	4.7
Tetracyclines (J01AA)	21.5	21.1	20.1	19.2	17.5	4.8	4.7	4.6	4.5	4.2
Trimethoprim with sulphonamides (J01EE)	11.1	11.3	11.9	12.8	12.7	2.5	2.5	2.7	3.0	3.0
Carbapenems (J01DH)	9.6	10.1	10.8	10.9	11.6	2.1	2.3	2.4	2.5	2.8
Phenoximethylpenicillin. PcV (J01CE02)	13.3	13.8	13.8	12.8	10.6	3.0	3.1	3.1	3.0	2.5
Pivmecillinam (J01CA08)	8.4	8.3	8.3	7.7	7.7	1.9	1.9	1.9	1.8	1.8
Lincosamides (J01FF)	8.3	8.6	8.5	7.7	7.1	1.8	1.9	1.9	1.8	1.7
Macrolides (J01FA)	5.1	5.5	5.1	5.5	7.0	1.1	1.2	1.2	1.3	1.7
Glycopeptides (J01XA)	4.6	4.7	4.8	4.6	4.6	1.0	1.0	1.1	1.1	1.1
Imidazole derivates (J01XD)	3.8	4.6	4.7	4.2	4.1	0.9	1.0	1.1	1.0	1.0
Aminoglycosides (J01GB)	5.0	4.7	4.0	3.7	3.6	1.1	1.1	0.9	0.9	0.9
Nitrofurantoin (J01XE)	2.2	2.3	2.3	2.1	2.1	0.5	0.5	0.5	0.5	0.5
Moxifloxacin (J01MA14)	2.2	2.2	2.2	2.0	1.9	0.5	0.5	0.5	0.5	0.5
Methenamine (J01XX05)	1.8	1.9	1.8	1.5	1.3	0.4	0.4	0.4	0.4	0.3
Linezolid (J01XX08)	0.8	0.8	0.8	1.0	1.2	0.2	0.2	0.2	0.2	0.3
Vancomycin (A07AA09)	0.3	0.5	0.5	0.5	1.0	0.1	0.1	0.1	0.1	0.2
Trimethoprim (J01EA)	1.0	0.7	0.7	0.7	0.6	0.2	0.2	0.2	0.2	0.1
All agents (J01)	**275.7**	**283.9**	**287.8**	**288.7**	**283.1**	**61.1**	**63.5**	**65.5**	**67.6**	**67.5**

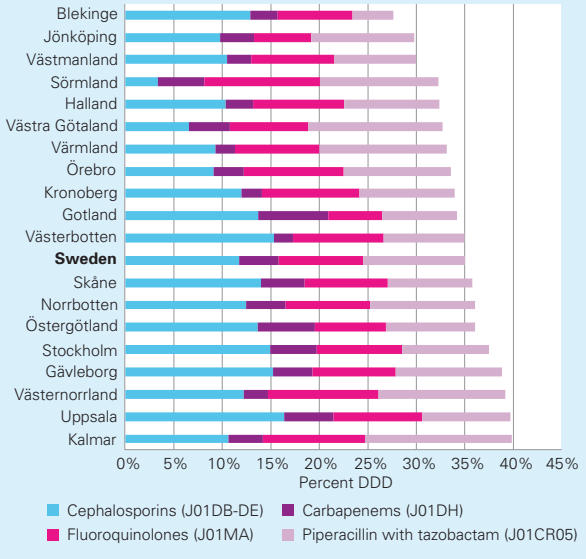
sales of antibiotics between Swedish acute care hospitals in the different regions, both in number of DDD per 1 000 inhabitants per day and in proportion and distribution of the different antibiotic classes, Figure 1.28 and Figure 1.29. These differences are to an extent explained by differences in dosages of drugs, types of hospital, case mix and patient demographics and should be taken into account in comparisons. For example, the regions Uppsala, Stockholm, Västerbotten, Västra Götaland, Skåne, Östergötland and Örebro all have tertiary referral hospitals with more advanced care, which impacts the amount of antibiotics used. It may also be noted that the denominators admissions and patient-days have decreased over the years, Figure 6.3, and thus affect the results accounted for in the section of acute care hospitals. Read more about the impact of the COVID-19 pandemic on Swedish health care and admissions and patient-days in the Swedish Association of Local Authorities and Regions' (SALAR) report (SALAR, 2020).

Figure 1.28. Proportion (%) of beta-lactamase sensitive penicillins (penicillin V and G, J01CE01-02) of all antibiotics in Swedish acute care hospitals, humans, per region and Sweden, 2019 and 2020.



Source: The Public Health Agency of Sweden

Figure 1.29. Proportion (%) of broad-spectrum antibiotics (cephalosporins, carbapenems, fluoroquinolones and piperacillin-tazobactam) of all antibiotics in Swedish acute care hospitals, humans, per region and Sweden, 2020.



Source: The Public Health Agency of Sweden

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. In this section, adverse reactions between 2016 and 2020 related to antibiotics were analysed for various groups of agents.

There were 2 989 reports of side effects caused by the use of antibiotics during this period.

The following organ system groups received most reports during 2016-2020 related to the use of systemic antibiotic drugs: skin- and subcutaneous tissue disorders (n=1 353), gastrointestinal disorders (n=717), nervous system disorders (n=442), general disorders (n=431), respiratory disorders (n=197), musculoskeletal disorders (n=187), immune system disorders (n=133), investigations (n=126), hepatobiliary disorders (n=123), renal and urinary disorders (n=117), psychiatric disorders (n=99) and reproductive system and breast disorders (n=96). The majority of the reports (66%) 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 2016-2020.

Antibiotic	Total number of adverse drug reaction reports 2016-2020	Number of 'serious' reports	Number of fatal cases
Phenoxymethylpenicillin (J01CE02)	419	115	0
Flucloxacillin (J01CF05)	282	135	6
Ciprofloxacin (J01MA02)	269	171	6
Nitrofurantoin (J01XE01)	231	82	2
Clindamycin (J01FF01)	227	86	4
Sulfamethoxazole and trimethoprim (J01EE01)	196	115	3
Amoxicillin (J01CA04)	159	52	0
Doxycycline (J01AA02)	143	36	0
Piperacillin-tazobactam (J01CR05)	104	63	3
Metronidazole (P01AB01)	102	53	0

Reduced dispension of antibiotic prescriptions has not resulted in increased complications

Introduction

A substantial decrease in the sales of antibiotics was seen in outpatient care during 2020. A study was conducted to explore whether the decline seen in prescribed dispensed antibiotics during 2020 has resulted in an increase in complications to common infections resulting in a higher number of hospital admissions or visits to specialist care.

Methods

The study was based on national registers in which the whole population was included. Data on prescribed and dispensed drugs were obtained from the Swedish Prescribed Drug Register. Information on the number of health care events due to selected infection diagnoses was obtained from the National Patient Register. Both registries are kept by the National Board of Health and Welfare. Prevalence was calculated for different age groups, for antibiotic prescriptions and for diagnostic groups.

The antibiotics were categorized in classes of antibiotics used to treat respiratory tract infections, urinary tract infections and skin and soft tissue infections. The classification of the diagnoses was according to the international classification of diseases (ICD-10). Diagnostic groups reflecting complications to infections usually treated in primary care, such as quinsy after tonsillitis, mastoiditis after otitis and meningitis/brain abscess following sinusitis were identified and chosen for the study; other severe potential complications such as pneumonia, blood-stream infections and necrotizing fasciitis were also included.

Results

The decrease in antibiotic sales during 2020 was most evident in the age group 0-4 years and for antibiotics used to treat respiratory tract infections. The sales of antibiotics used to treat urinary tract infections and skin infections remained largely unchanged.

At the same time there was a decrease in the number of visits to specialist care for common infections as well as hospital admissions related to complications to respiratory infections. The number of hospital admissions and visits due to severe urinary tract infections and skin and soft tissue infections remained unchanged. No increase was seen in the number of hospital admissions or specialist care for blood-stream infections or meningitis in this study.

Discussion

The reductions seen in the number of prescriptions and in the prevalence of complications to common infections is likely due to an overall decrease of transmission of respiratory infections. This in return is a result of recommendations and restrictions issued to mitigate the pandemic, such as physical distancing and increased infection control measures. Other factors that reduced the spread of infections include that people have stayed at home to a larger extent while feeling ill. An increase in the disbursement for temporary parental benefit for the care of sick children during 2020 compared to the previous years, suggests that parents have stayed home with sick children.

Conclusion

There was a dramatic decrease in the number of dispensed prescriptions of antibiotics 2020 compared to previous years. This decrease could be attributed to a number of reasons related to the COVID-19 pandemic. Simultaneously, we could not see any increase in treatments for complications to common infections.

Reference

The National Board of Health and Welfare. Minskad antibiotikaanvändning under covid-19-pandemin har inte lett till fler allvarliga infektioner, 2020, https://www.socialstyrelsen.se/globalassets/sharepoint-dokument/artikelkatalog/ovrigt/2020-12-7119.pdf

Primary Care Quality – Diagnosis-linked indicators for best practice in primary care

Primary Care Quality (PVQ) is a quality system developed by the Swedish Association of Local Authorities and Regions (SALAR) for the primary care setting (SALAR, 2021). The system consists of a number of national diagnosis-linked quality indicators, a specification for user-friendly feedback and a national function receiving, calculating and returning statistical reference values. The main purpose is easy follow-up and continuous local quality improvement for primary care professionals, without causing any extra administrative work.

Data for the last 12 months are collected automatically, based on existing stored data from the electronic medical records, and is transferred to a national service function for calculation of average values, and then returned to the local level. These data are also available as a basis for discussion on overall aims and challenges to primary care in Sweden. Some indicators can be obtained through the national website for health care data, www.vardenisiffror.se.

At the health care centre, updated data from one's own patients are provided and national average numbers are given as a reference and benchmark. This stimulates local reflection and dialogue among colleagues. Individual patients are also possible to find and follow at the local level.

Support for local learning and improvement in handling common infections

The infectious disease indicators are developed by the Public Health Agency in collaboration with representatives for the primary care professions, and are created to give meaningful information and support quality improvement.

At the end of 2020, there were almost 70 indicators in PVQ for common infections in primary care. Most indicators measure incidence of the most common infection diagnoses respectively, the percentage of patients treated with antibiotics for each diagnosis and the percentage of patients treated with first-line antibiotics according to current treatment recommendations. There are also indicators for testing group A streptococci in tonsillitis, testing CRP in upper and lower respiratory infections, percentage of quinolone use in lower urinary tract infections and whether the antibiotic was prescribed after a physical examination or not. The indicators can also be shown for different age groups and genders. A key to reliable data is the registration of the diagnosis and efforts must be made to register the most correct diagnosis in each case. Benchmarks can be shown for each indicator on local, regional and national levels.

Practical use

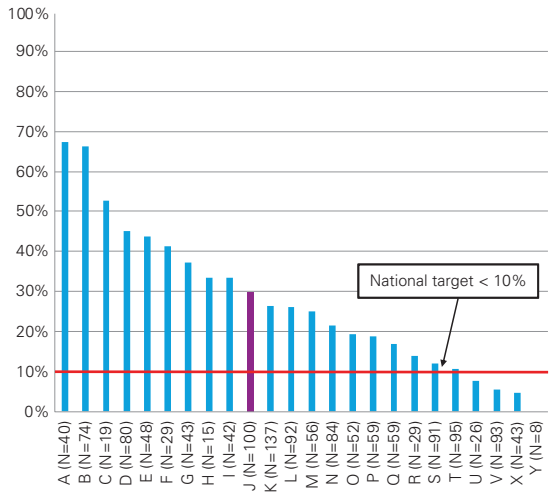
In total, almost 1 000 primary health care centres in Sweden (> 80%) are at this point connected to the system. Activities at national level are ongoing to support implementation and increase the use in all regions.

At the regional level, Strama groups use the system in their communication with the health care centres. Some Strama groups send out annual reports while others have regular individual meetings with the health care centres, where feedback on the indicators is provided. Such educational outreach visits have been shown to change how health care professionals prescribe medications (O'Brien et al., 2007; Arnold & Straus, 2005). The indicators are used as a starting point for a dialogue with the doctors and nurses. A multifaceted approach is more likely to achieve behavioral change in prescribing.

The health care centres can also use PVQ to improve health care quality, evaluation and use it for operational planning. It is also possible to focus on patients who have not been treated according to the treatment recommendations and discuss why and how they can improve. In this way PVQ is a useful and valuable tool for local quality improvement in primary care.

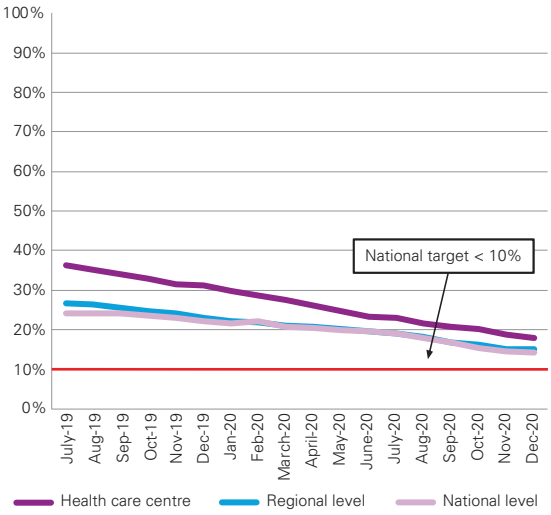
Figure 1 and 2 exemplify how data from PVQ can be displayed in the system. In figure 1 the purple bar represents the health care centre that has extracted the data for comparison with other health care centres and in figure 2 the same health care centre is displayed over time.

Figure 1. Health care centres in Northwestern Stockholm. Patients with acute bronchitis treated with antibiotics 2020 (N=number of patients with acute bronchitis).



Source: Primary Care Quality

Figure 2. Benchmark for a local health care centre, regional and national levels. Patients with acute bronchitis treated with antibiotics 2019-2020.



Source: Primary Care Quality

References

Swedish Association of Local Authorities and Regions (SALAR). 2021, Primary Care Quality. https://skr.se/skr/tjanster/englishpages/activities/primarycarequality.10073.html

O'Brien MA, Rogers S, et al. 2007, Educational outreach visits to change health care professional care for patients. *Cochrane Database Syst Rev*, 4 No.: CD000409.

Arnold SR, Straus SE. 2005, Interventions to improve antibiotic prescribing practices in ambulatory care. *Cochrane Database Syst Rev*, 4 No.: CD003539.

Sales of antibiotics for animals

Statistics on total sales of antibiotics for use in animals in Sweden are available since 1980. For a review of data from 1980-2000, see Svarm 2000 and for the following years the relevant Svarm and Swedres-Svarm reports.

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 are collected through a separate system, and information is given under Comments by animal species, Aquaculture.

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

Updates with new conversion factors for procaine benzylpenicillin

The protocol for the European surveillance of veterinary antimicrobial consumption (ESVAC) has been updated with regard to conversion factors for certain benzylpenicillins (EMA, 2021). Benzylpenicillins, in particular procaine benzylpenicillin, constitute a large proportion of the total sales of antibiotics for animals in Sweden. Data for procaine benzylpenicillins from 1980 and onwards have therefore been recalculated with the new conversion factor (0.57 compared to previously 0.6).

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. Data from 2016 and onwards are likely to be complete in this respect.

Trends in animal populations

Changes in the numbers of animals may affect trends in statistics on sales of antibiotics. Compared to 2011, the number of pigs slaughtered in 2020 has decreased by 7%, while the number of broilers has increased by 39%. The number of dairy cows decreased by 12% 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 2020, the total reported sales from Swedish pharmacies of antibiotics authorised for veterinary use were 9 306 kg, of which 53% was benzylpenicillin. The corresponding figures for 2011 were 12 220 kg and 52%, respectively.

Since 2011, sales of all classes of antibiotics except aminopenicillins have decreased notably. The sales of aminopenicillins decreased from 2011 to 2019, but in 2020 an increase was noted (Table 2.1). This is explained by increased sales for pigs, while the sales of tablets intended for companion animals continued to deacrease (see comments by animal species, Pigs). In addition, in the past five years (since 2015), sales of aminoglycosides have increased. This is explained by a shift from polymyxins (colistin) to aminoglycosides for treatment of weaning diarrhoea (see comments by animal species, Pigs). Sales of other classes have decreased also over the last five years period.

During 2014-2018, the total sales were comparatively stable but in 2019 and 2020 the figures were 8 and 7% lower than in 2018 (Table 2.1). The decrease derives from most classes and in most cases a downward trend can be seen over time.

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

ATCvet code		2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
QJ01AA, QG01A	Tetracyclines	1 073	881	935	787	685	515	529	516	522	609
QJ01CE, -R, QJ51	Benzylpenicillin[c]	6 310	5 983	5 592	5 148	5 479	5 620	5 553	5 594	5 242	5 006
QJ01CA, QJ01CR	Aminopenicillins	723	649	645	635	642	677	640	683	648	765
QJ01D	Cephalosporins	498	410	330	299	267	242	210	187	161	162
QA07AA, QJ01G, -R, QJ51R	Aminoglycosides	427	408	264	298	322	312	302	376	343	393
QA07AB, QJ01E	Sulphonamides	1 867	1 812	1 707	1 699	1 634	1 643	1 678	1 539	1 445	1 462
QJ01E	Trimethoprim & derivatives	338	329	320	314	313	318	326	297	281	285
QJ01F	Macrolides & lincosamides	648	632	564	484	485	472	515	578	486	447
QJ01MA	Fluoroquinolones	120	106	52	45	34	30	25	29	20	25
QA07AA,QJ01BA, QJ01XQ	Others[d]	216	174	205	201	224	337	147	237	115	151
	Total sales	**12 220**	**11 385**	**10 614**	**9 910**	**10 086**	**10 165**	**9 925**	**10 037**	**9 263**	**9 306**

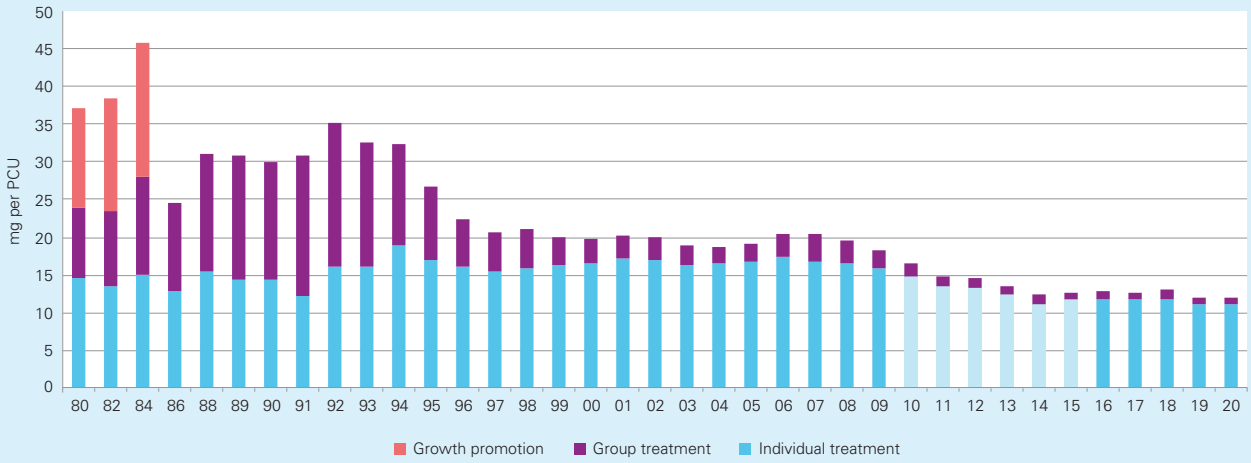
[a]Data for penicillins have been updated with new conversion factors applied by ESVAC, resulting in lower figures for penicillins and lower total compared to data in previous Swedres-Svarm reports. [b]Data from 2010-2015 are uncertain because of a lack of completeness mainly affecting injectable products. [c]Also includes small amounts of phenoxymethylpenicillin and penicillinase stable penicillins. [d]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 2019 as a proxy for PCU in 2020. 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.

Measured as mg per PCU, the overall sales have decreased by more than two thirds 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. Sales of antibiotics for animals 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 2011, the sales of these antibiotics, expressed as mg/PCU, have decreased by 83%, 78% and 92%, 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 Sweden (an organisation providing animal health services for dairy cattle) publishes a yearly report related to the livestock organisation's 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 Sweden (2020), 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 treatment of clinical mastitis in dairy cows has decreased from 14.2 recorded treatments per 100 completed/interrupted lactations in 2011 to 8.5 in 2019. Of all recorded treatments, benzylpenicillin was by far the most common (around 92% of reported systemic treatments for clinical mastitis). Treatment of dairy cows and heifers with fluoroquinolones for any indication has decreased from 10% of recorded treatments 2011 to 1% in 2019.

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.

The year 2010 was chosen for comparisons as in 2011, there was a lack of completeness regarding products sold on special license, and this has a particular influence on sales of antibiotics for pigs. In 2010 and 2020 the sales of antibiotics for pigs were 3 276 and 3 219 kg active substance, respectively, or 12.4 and 13.1 mg/kg per slaughtered pig. Of the total sales in kg active substance in 2020, 80% were products for use in individual animals, and of these 65% were products containing benzylpenicillin.

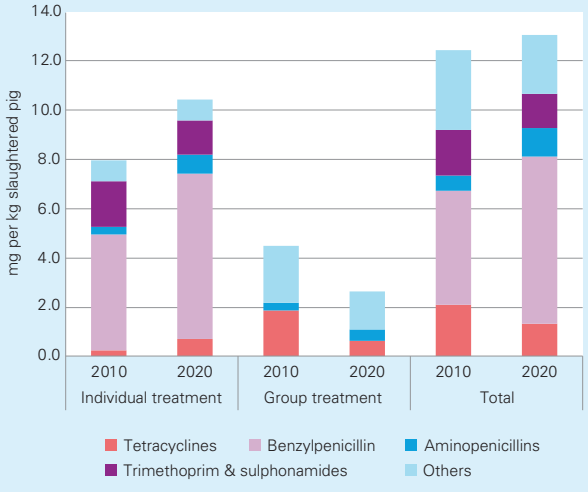
Sales of fluoroquinolones for use in pigs were negligible, and no cephalosporins were sold for pigs in 2020. In Sweden, polymyxins (colistin) are only used for pigs. As noted under Population corrected overall sales, a marked decrease is noted over the past ten years.

The number of pigs has decreased between 2010 and 2020, and therefore the sales are presented as mg/kg pig slaughtered in Figure 2.2. 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, 2012).

Measured in mg/kg slaughtered pig, there is an apparent increase of total sales for pigs. This is partly explained by increased sales of benzylpenicillin (up by 45% from 2010 to 2020). As procaine benzylpenicillin is used at a comparatively high dose, this increase will influence the total sales. A shift towards benzylpenicillin is well in line with national guidance.

Sales of aminopenicillins have also increased, both for individual medication and for oral administration to groups of animals (80% increase in total). The increase mainly occurs between 2019 and 2020. It partly reflects recurrent outbreaks of infections with *Glaesserella parasuis* during 2020 in one larger integrated herd, accounting for almost one third of the difference between 2019 and 2020. Other explanations are outbreaks of infections with *Actinobacillus pleuropneumoniae* during 2020. This illustrates that when sales are comparatively low, localised outbreaks can have a major influence on the sales in a specific year.

Figure 2.2. Sales of antibiotics for pigs in 2010 and 2020 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. Mostly the types of products sold with chickens, hens or turkeys as recorded species are tablets or injectables and quantities very small, indicating that they were not used for treatment of commercially raised chickens. 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 2020 corresponds to 0.14 mg active substance/kg slaughtered chicken. All the flocks were treated for necrotic enteritis with phenoxymethylpenicillin. In addition, parent flocks were treated on five 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.

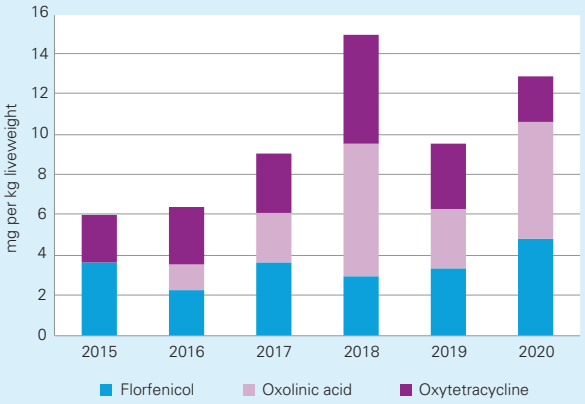
Year	Number of flocks treated	Total number of flocks
2011	6	3 185
2012	1	2 853
2013	4	3 133
2014	4	3 138
2015	28	3 191
2016	14	3 300
2017	1	3 300
2018	4	3 223
2019	54	3 368
2020	11	3 557

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 2020, a total of 123 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 2020 were florfenicol, oxolinic acid and oxytetracycline.

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



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 2.2 do not translate to treatment frequencies or actual exposure of individual fishes.

Horses

Around 70% of the sales of trimethoprim-sulphonamides are products for oral use in horses (paste or powder). Since 2011, there has been a decrease in sales of such products by 11%, 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

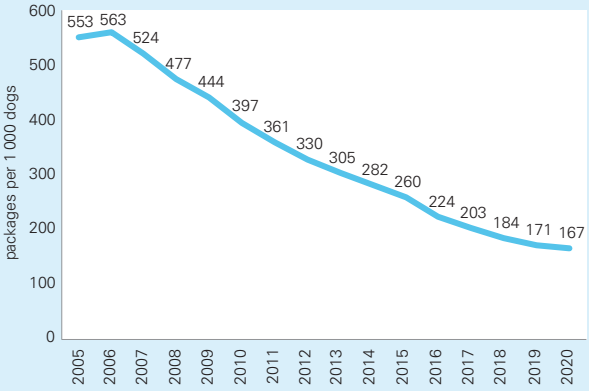
In 2020, the overall sales of veterinary medicinal products for oral medication of dogs was 589 kg compared to 1 200 kg in 2011. As in previous years, aminopenicillins (with and without clavulanic acid), first generation cephalosporins and lincosamides were by far the classes with largest sales in 2020.

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 167 packages per 1000 dogs (-70%) (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 used here does not reflect that, and it is possible that the number of packages per 1000 individuals for 2020 in figure 2.4 is an overestimate.

The most prominent changes relative to 2006 are noted for first generation cephalosporins (-89%), fluoroquinolones (-92%) and aminopenicillins with clavulanic acid (-78%).

As described in Svarm 2008, the emergence of infections with multiresistant methicillin-resistant *Staphylococcus pseudintermedius* and methicillin-resistant *S. aureus* 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 microbiological 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.

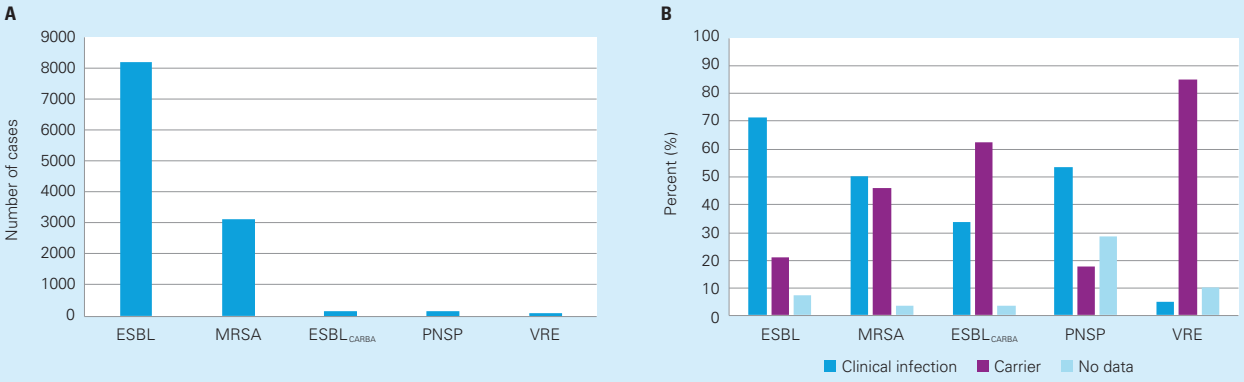
Species, group or type	Sampling
Mandatory reporting (SmiNet)	
Enterobacterales (previously Enterobacteriaceae) with ESBL Enterobacterales (previously Enterobacteriaceae) with $ESBL_{CARBA}$ *Staphylococcus aureus* resistant to methicillin *Streptococcus pneumoniae* non-susceptible to penicillin *Enterococcus faecium* or *Enterococcus faecalis* resistant to vancomycin *Mycobacterium tuberculosis*[a] *Neisseria gonorrhoeae*[a]	Samples of all types for clinical, screening or case finding purposes.
Neisseria meningitidis[a]	Invasive disease (blood, CSF, or other normally sterile sample).
Voluntary surveillance (Svebar)	
Escherichia coli	Clinical sampling from blood and urine.
Klebsiella 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 and nasopharynx.
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 2020 (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 2020.

	ESBL	$ESBL_{CARBA}$	MRSA	PNSP	VRE
Number of cases (inc)	8 230 (79)	128 (1.2)	3 112 (30)	112 (1.1)	79 (0.8)
Proportion clinical infection	71%	34%	50%	54%	5%
Gender	65% women	54% men	53% women	65% men	54% men
Median-age (range)	58 years (0-100+)	59 years (0-100)	32 years (0-100+)	52 years (0-99)	66 years (20-92)
Proportion of domestic cases	no information	37% (10% no data)	67% (8% no data)	63% (32% no data)	43% (10% no data)
Short epidemiological information	Community and health-care	Hospital abroad	Community	Community	Hospital, domestic spread
Bloodstream infections	727 (535 new cases 2020, 192 cases known from previous years)	11 (10 new cases 2020, 1 case known from previous year)	98 (78 new cases 2020, 20 cases known from previous years)	4	4

Table 3.3. Number of laboratories used for antibiotic resistance calculations during 2015- 2020.

	2015	2016	2017	2018	2019	2020
Resistance data based on number (n) of clinical laboratories	n=12	n=14	n=11	n=10	n=19	n=20
Coverage of population (%)	70	72	67	65	85	86

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. For unusual resistance types this can result in overestimation of the resistance, especially if these patients are sampled frequently. Large differences in resistance trends for these types of resistance should be interpreted with caution. Data analysed from the voluntary surveillance system (Svebar) are collected from laboratories with validated data (Table 3.3). All antibiotic resistance levels presented in this report are based on primary susceptibility testing, thus avoiding the bias from hierarchical testing. Data are excluded when not all isolates are tested routinely. 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 are 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 and 2020. Twelve clinical laboratories covering around 60% of the population in Sweden were included. Complete data for 2019 and 2020 from these twelve laboratories are given in table 3.4 A and B. In Figure 3.2 A and E the annual numbers of requested analyses together with number by age group and divided per 100 000 inhabitants 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 decreased by 12% between 2019 and 2020. For blood cultures the decrease was 2%, for urine cultures 6%, for nasopharyngeal cultures 28% and for throat cultures 34%. This corresponds with data on antibiotic use, where antibiotics for respiratory infections decreased more than other groups. The number of isolated *E. coli*, *S. aureus*, *S. pneumoniae* and *S. pyogenes*, regardless of specimen type, were also decreasing with 9%, 13%, 48% and 51% respectively.

For most types of culture, and for the total number of cultures, the age-group with the largest decrease was children 1-4 years old. For nasopharyngeal cultures the group with the largest decrease was children <1 years old, Figure 3.2.

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, as well as the number of blood cultures taken, is shown in Figure 3.3.

Figure 3.2 A to E. Number of requested analyses together with number by age group and divided per 100 000 inhabitants are presented for: total number of cultures (A), blood cultures (B), urine cultures (C), nasopharyngeal cultures (D) and throat cultures (E).

Source: The Public Health Agency of Sweden

Table 3.4 A and B. Denominator data from twelve laboratories, number of analysis, positive samples and number of cultures (*S. aureus, S. pneumoniae, S. pyogenes* and *E. coli*), A) year 2019 and B) year 2020. NP, not performed.

A

Laboratory	Blood	Cerebro-spinal fluid (CFS)	Nasopharynx	Throat	Urine	Faeces SSYC	Blood (positive samples)	*Staphylococcus aureus*	*Streptococcus pneumoniae*	*Streptococcus pyogenes*	*Escherichia coli*
Stockholm, Karolinska Universitets-sjukhuset	100 831	2 230	32 508	7 546	157 235	18 968	13 454	33 060	2 775	2 966	40 769
Kronoberg, Centrallasarettet Växjö	15 317	104	4 564	1 859	24 846	2 617	1 706	2 932	504	492	6 216
Region Skåne, Lund	82 468	1 141	23 851	10 635	164 115	21 637	9 864	22 789	1 673	2 903	40 703
Blekinge, Blekingesjukhuset Karlskrona	11 516	84	4 109	900	16 888	1 686	1 230	2 251	243	268	4 544
Kalmar, Länssjukhuset Kalmar	15 525	132	4 364	1 681	27 454	3 580	1 975	4 809	552	729	9 594
Västra Götalandsregionen, Norra Älvsborgs länssjukhus Trollhättan	20 113	193	3 045	889	26 253	NP	2 429	3 775	274	403	7 054
Västra Götalandsregionen, Södra Älvsborgs sjukhus Borås[a]	22 598	416	4 344	1 125	21 219	NP	2 989	3 929	279	416	6 261
Östergötland, Universitetssjukhuset Linköping	58 258	1 279	8 519	2 350	53 806	591	5 035	9 356	649	991	14 072
Örebro, Universitetssjukhuset Örebro	21 530	150	9 880	1 707	31 905	4 650	2 345	6 586	676	768	8 708
Värmland, Centralsjukhuset Karlstad	49 644	192	7 192	2 895	40 952	5 134	4 276	7 510	637	1 051	11 317
Gotland, Visby lasarett	2 948	16	2 148	375	7 673	886	488	1 473	177	184	2 147
Västerbotten, Norrlands Universitets-sjukhus Umeå	35 226	446	5 220	1 642	34 279	3 109	3 513	6 123	624	443	10 305

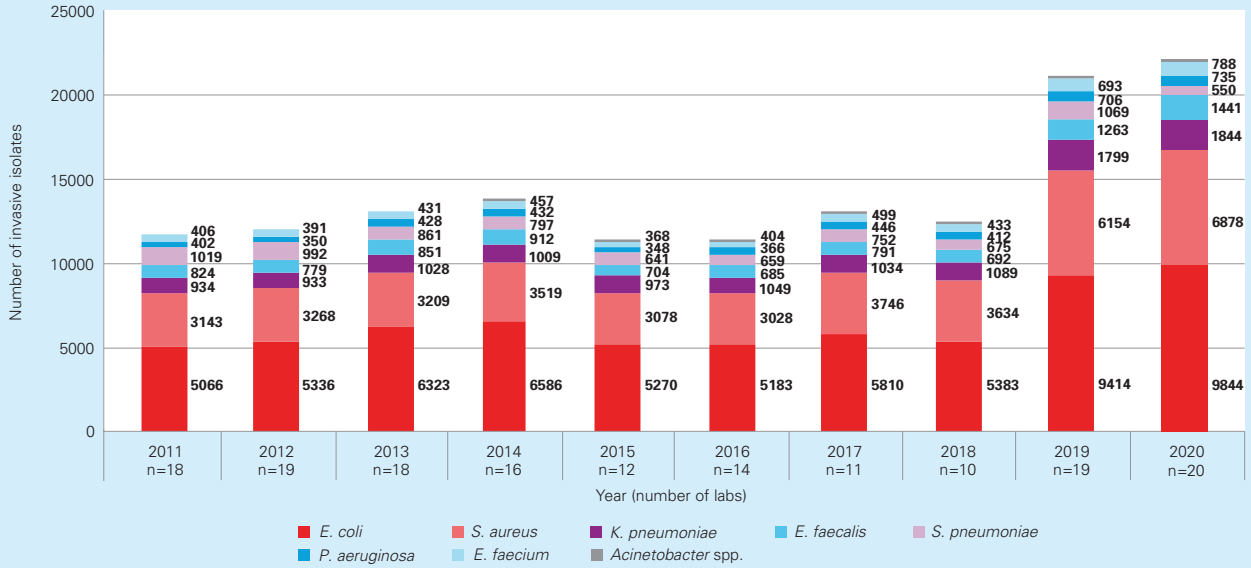
[a]Svebardata and data from local laboratory.

B

Laboratory	Blood	Cerebro-spinal fluid (CFS)	Nasopharynx	Throat	Urine	Faeces SSYC	Blood (positive samples)	*Staphylococcus aureus*	*Streptococcus pneumoniae*	*Streptococcus pyogenes*	*Escherichia coli*
Stockholm, Karolinska Universitets-sjukhuset	103 790	1 957	22 402	5 017	154 001	14 085	14 159	28 758	1 592	1 565	37 827
Kronoberg, Centrallasarettet Växjö	14 472	90	3 369	1 268	23 818	1 851	1 613	2 727	241	263	5 802
Region Skåne, Lund	76 777	847	14 786	6 559	140 480	3 085	9276	17 958	810	1 414	32 240
Blekinge, Blekingesjukhuset Karlskrona	10 510	65	3 224	609	16 131	1 250	1 233	2 127	122	153	4 242
Kalmar, Länssjukhuset Kalmar	15 468	130	3 468	1 039	27 278	2 591	2 255	4 538	257	266	9 270
Västra Götalandsregionen, Norra Älvsborgs länssjukhus Trollhättan	18 708	160	2 001	666	24 897	NP	2 117	3 345	138	208	6 834
Västra Götalandsregionen, Södra Älvsborgs sjukhus Borås[a]	21 057	362	3 262	836	20 691	NP	2 779	3 466	127	246	5 818
Östergötland, Universitetssjukhuset Linköping	61 532	1 511	6 941	1 738	52 757	1 591	4 751	8 313	412	489	13 308
Örebro, Universitetssjukhuset Örebro	21 072	95	7 818	1 138	32 715	3 688	2 354	6 062	337	345	8 467
Värmland, Centralsjukhuset Karlstad	45 847	151	5 261	1 703	38 829	4 289	4 139	6 711	280	436	10 730
Gotland, Visby lasarett	2 571	13	1 678	204	7 339	614	474	1 345	96	66	2 116
Västerbotten, Norrlands Universitets-sjukhus Umeå	33 794	442	4 158	1 253	31 695	2 426	3 127	5 256	308	283	9 743

[a]Svebardata and data from local laboratory.

Figure 3.3. Number of isolates, collected from blood during 2011-2020, reported to EARS-Net.



Source: The Public Health Agency of Sweden

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

Mandatory reporting of ESBL-producing Enterobacterales (previously Enterobacteriaceae)

Results from 2020

- Number of reported cases: 8 230 (previous year 10 717), relative change -23%
- Number of bloodstream infections: 727 (previous year 835), relative change -13%

Trends

The incidence for ESBL has steadily increased over several years. A slight decrease was noted 2017. In 2020 the incidence was 79 new cases per 100 000 inhabitants, see Figure 3.4. A decrease with 24% compared with 2019 (incidence 104). 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 in 2020 the number of BSI decreased with 13% (Figure 3.5). *E. coli* was the most common cause of BSI, 81% followed by *K. pneumoniae* 14%.

All 21 regions in Sweden reported ESBL-cases and a nearly threefold difference in incidence was noted, from 48 to 125 cases per 100 000 inhabitants. The large variation could partly be explained by different local practices in sampling.

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=819, incidence 312) followed by children under one year (n=324 incidence 285 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 87% 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 3.4).

Outbreaks

In 2020, twelve clusters of ESBL$_A$ and/or ESBL$_M$ were confirmed based on SNP-analysis (n=2-12 cases per cluster). Eight clusters were of ESBL-producing *E. coli* and four clusters were of ESBL-producing *K. pneumoniae* (Table 3.5). Nine of these clusters were healthcare related. However, outbreaks with ESBL-producing Enterobacterales (previously Enterobacteriaceae) are not consistently reported.

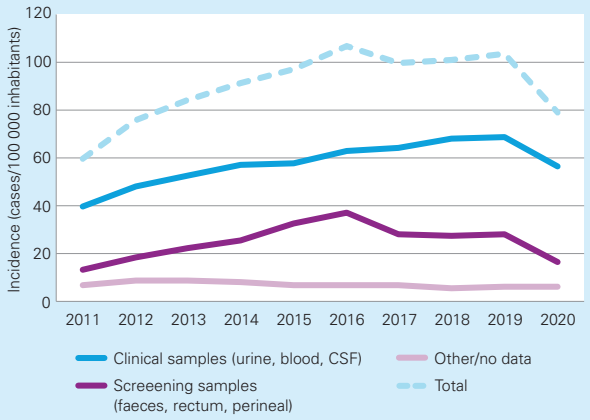
Table 3.5. Clusters of ESBL-producing *E. coli* and *K. pneumoniae* 2020.

Species	ESBL gene	Number of clusters	Number of cases/cluster
E. coli	CTX-M	5	2, 3, 3, 4, 10
E. coli	CTX-M and CIT	1	12
E. coli	CIT	1	2
E. coli	DHA	1	2
K. pneumoniae	CTX-M	4	2, 3, 10, 12

Comments

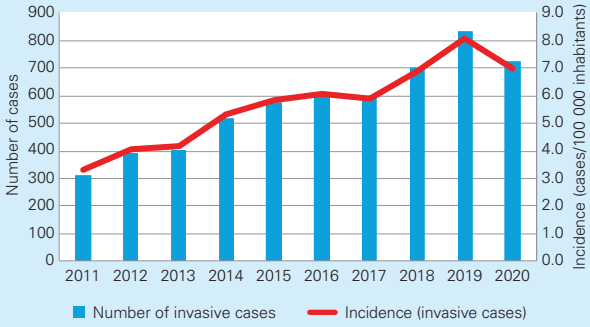
In 2020, the number of cases with ESBL-producing Enterobacterales (previously Enterobacteriaceae) decreased sharply. The decrease is largely due to reduced international travel and screening for inpatient care due to the COVID-19 pandemic. Differences in sampling, screening and contact tracing in the regions have a significant impact on incidence.

Figure 3.4. The incidence (cases/100 000 inhabitants) of cases with ESBL-producing Enterobacterales (previously Enterobacteriaceae) in relation to type of infection, year 2011–2020.



Source: The Public Health Agency of Sweden

Figure 3.5. Number and incidence (cases/100 000 inhabitants) of invasive cases with ESBL-producing Enterobacterales (previously Enterobacteriaceae), reported during year 2011–2020.



Source: The Public Health Agency of Sweden

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

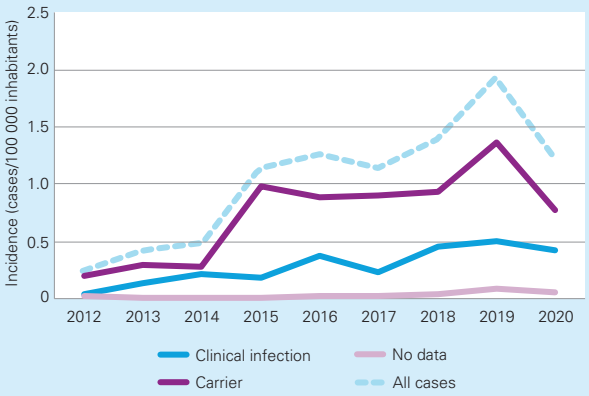
Results from 2020

- Number of reported cases: 128 (previous year 201), relative change -36%
- Number of bloodstream infections: 11 (previous year 6)
- An increasing number of health care related, smaller clusters of $ESBL_{CARBA}$, three 2020 compared to one in 2019.

Trends

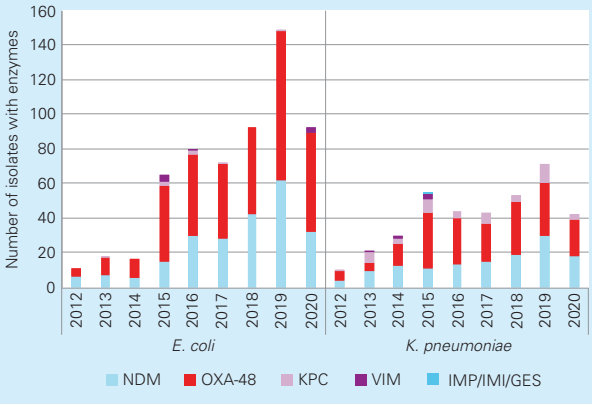
In 2020, the incidence for $ESBL_{CARBA}$ producing Enterobacterales (previously Enterobacteriaceae) was 1.2 cases per 100 000 inhabitants, a decrease with 36% (73 cases) compared to 2019. The decrease was seen in cases with $ESBL_{CARBA}$ acuired abroad (n=143, 2019 and n=68, 2020). A majority, 63% of the cases, were carriers (Figure 3.6). Cases were reported from 17 of 21 regions in Sweden. The majority of cases were reported as acquired abroad (53%) and identified in targeted screening after hospitalisation abroad. Out of the 47 domestic cases, 30 were identified by investigation of clinical infection. The proportion of domestic cases with health care acquired $ESBL_{CARBA}$ remained at the same level as previous year (30%, n=14). For 23 domestic cases information of acquisition was missing. The $ESBL_{CARBA}$ cases were unequally distributed between women and men (46% women, 54% men) with median ages of 47 and 63 years for women and men respectively.

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 2012-2020.



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 2012-2020.



Source: The Public Health Agency of Sweden

Epidemiological typing of ESBL$_{CARBA}$

ESBL$_{CARBA}$ isolates from notified cases in 2020 have been characterised using whole genome sequencing (WGS). The most common carbapenemase-producing Enterobacterales (previously Enterobacteriaceae) was *E. coli*, accounting for 61% of all cases, followed by *K. pneumoniae* (26%). Genes encoding for carbapenem resistance have also been detected in several other species of Enterobacterales (previously Enterobacteriaceae). The dominating enzyme type in 2020 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. Apart from the genotypic analysis, isolates have been tested for antibiotic susceptibility using broth microdilution (BMD) (since June 2020) see Table 3.6. Of the 125 isolates of *E. coli* and *K. pneumoniae* tested for colistin, 12 isolates were resistant (10 *K. pneumoniae* and 2 *E. coli*).

Outbreaks

In 2020, ten smaller clusters of ESBL$_{CARBA}$ in Sweden were confirmed based on SNP analysis (n=2-3 cases per cluster) compared to 2019 when a smaller transmission of ESBL$_{CARBA}$ was identified (n=3). Nine clusters were ESBL$_{CARBA}$-producing *E. coli* and one cluster was ESBL$_{CARBA}$-producing *K. pneumoniae* (see table 3.7). Of the ten clusters, three were spreads of infection in the healthcare system and for one cluster the source of the infection is likely to be attributed to another country.

Comments

The number of ESBL$_{CARBA}$ cases is still low in Sweden. The decrease during 2020 is largely due to reduced international travel and screening for inpatient care due to the COVID-19 pandemic. The number of cases infected in Sweden remains at the same level as previous year. 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.

Table 3.7. Number of clusters with ESBL$_{CARBA}$ in Sweden identified by "single nucleotide polymorphism" SNPs based analysis, year 2020.

Type	*E. coli*	*K. pneumoniae*
NDM-5	4	
OXA-48	2	
OXA-232		1
OXA-244	3	

Table 3.6. Antibiotic resistance in ESBL$_{CARBA}$ producing *E. coli* (n=90) and *K. pneumoniae* (n=36), year 2020. Breakpoints for tigercycline and nitrofurantoin are only provided for *E. coli*.

Antibiotic	*E. coli*, %S	*E. coli*, %R	*K. pneumoniae*, %S	*K. pneumoniae*, %R
Amoxicillin-clavulanic acid	0	100	0	100
Piperacillin-tazobactam	0	100	0	100
Ceftazidime	19	67	11	86
Cefotaxime	14	78	8	86
Ceftolozane-tazobactam	32	68	11	89
Ceftazidime-avibactam	60	40	44	56
Tigecycline	98	2	-	-
Trimethoprim-sulphamethoxazole	27	73	39	56
Nitrofurantoin	99	1	-	-
Colistin	98	2	72	28
Tobramycin	69	31	19	81
Amikacin	94	6	47	53
Gentamicin	81	19	39	61
Ciprofloxacin	34	53	8	92
Imipenem	57	37	8	86
Ertapenem	17	83	0	100
Meropenem	62	34	14	83

Escherichia coli, from blood and urine cultures

Results from 2020

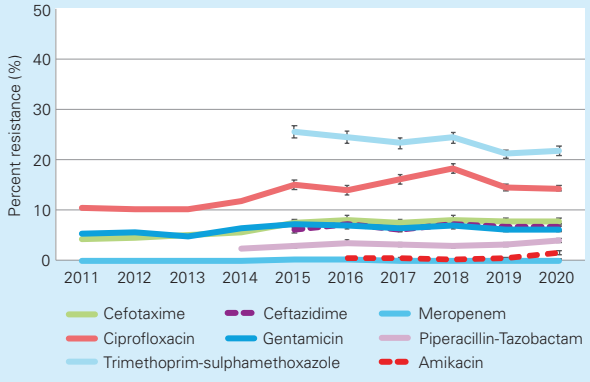
- Number of reported cases with $ESBL_{CARBA}$-producing *E. coli*: 88
- Number of reported cases with bloodstream infections caused by $ESBL_{CARBA}$-producing *E. coli*: 3
- Number of reported cases with ESBL-producing *E. coli*: 7 297
- Number of reported cases with bloodstream infections caused by ESBL-producing *E. coli*: 601

Table 3.8. Proportion (%) of antibiotic resistant *E. coli* from blood or urine 2020. Resistance to Piperacillin-tazobactam in urine is based on selective testing.

Antibiotic	Blood isolates, % R (n=9 844)	Urine isolates, % R (n=199 172)
Ampicillin	NA	29.2
Cefadroxil	NA	6.1
Cefotaxime	7.7	3.9
Ceftazidime	6.4	2.8
Ciprofloxacin	14.2	10.7
Gentamicin	6.1	NA
Mecillinam	NA	4.8
Meropenem	0.0	NA
Nitrofurantoin	NA	1.2
Piperacillin-tazobactam	3.8	4.0
Trimethoprim	NA	19.9
Trimethoprim-sulphamethoxazole	21.6	NA
Combined resistance to Cefotaxime/ceftazidime + Gentamicin/tobramycin	2.6	NA
Combined resistance to both Piperacillin-tazobactam + Gentamicin/tobramycin	1.2	NA

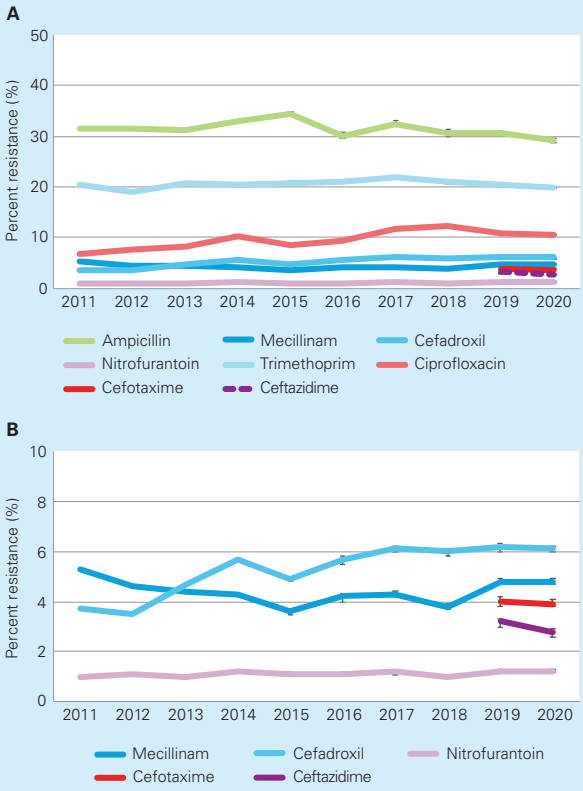
Trends

Figure 3.8. Antibiotic resistance in *E. coli* isolated from blood during the years 2011-2020. The numbers of AST isolates for all years and antibiotics ranges from 3 983 to 9 884. The exact numbers are given in the attached file.



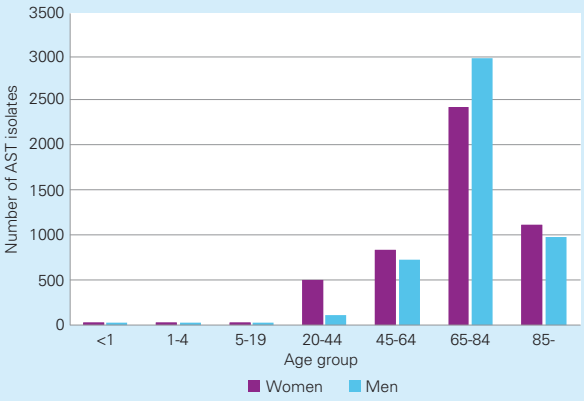
Source: The Public Health Agency of Sweden

Figure 3.9 A and B. Antibiotic resistance in *E. coli* isolates from urine during the years 2011-2020. 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 5 892 to 204 386. The exact numbers are given in the attached file.



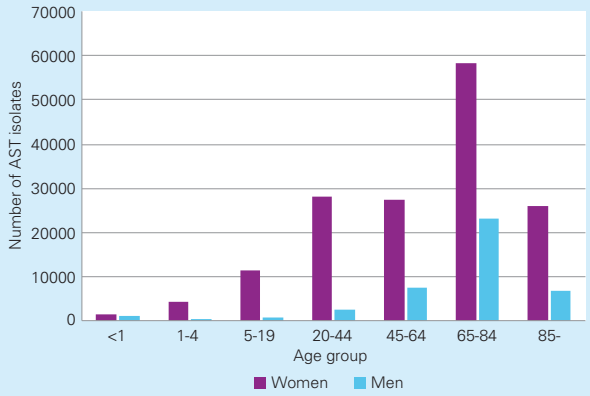
Source: The Public Health Agency of Sweden

Figure 3.10. Age distribution among patients with *E. coli* isolated from blood. The number of isolates is based on cefotaxime AST.



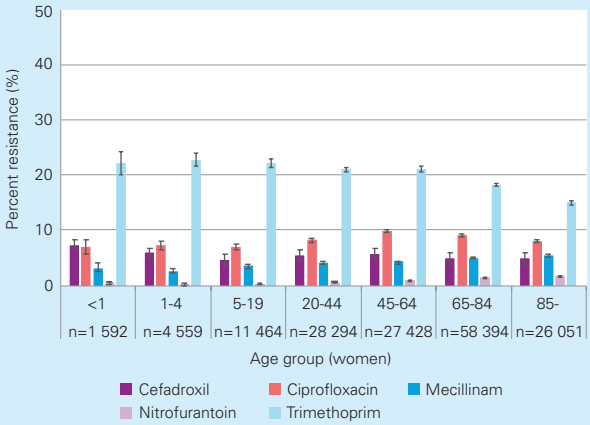
Source: The Public Health Agency of Sweden

Figure 3.11. Age distribution among patients with *E. coli* isolated from urine. The number of isolates is based on ciprofloxacin AST.



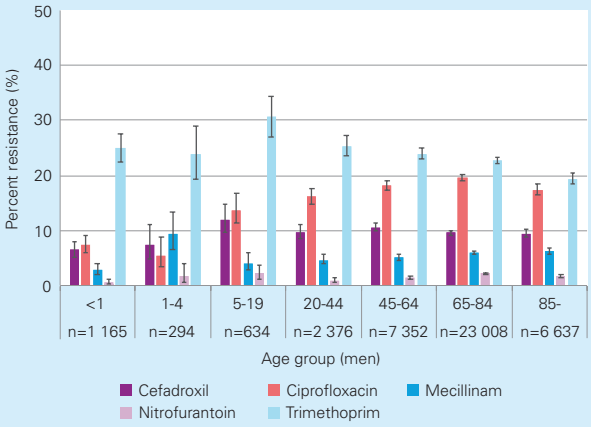
Source: The Public Health Agency of Sweden

Figure 3.12. Antibiotic resistance in *E. coli* from urine in women divided in age groups, year 2020.



Source: The Public Health Agency of Sweden

Figure 3.13. Antibiotic resistance in *E. coli* from urine in men divided in age groups, year 2020.



Source: The Public Health Agency of Sweden

The age and gender distributions (Figure 3.10 and 3.11) among patients with *E. coli* isolated from urine and blood 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 are shown in figures 3.12 and 3.13. 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 7.7%. The carbapenem resistance is still very low. Combined resistance to cefotaxime/ceftazidime and gentamicin/tobramycin or the combination piperacillin-tazobactam and gentamicin/tobramycin was 2.6% and 1.2% respectively (Table 3.8 and Figure 3.8).

Resistance to commonly prescribed oral antibiotics for treatment of urinary tract infections (UTI) caused by *E. coli* remained stable (Figure 3.9). Cefadroxil resistance, which can be used as an indicator for production of ESBL, remained at 6%.

Resistance to ciprofloxacin is still high, but decreased slightly during 2019, and is now at approximately 14% and 11% for blood and urine isolates respectively (Table 3.8, Figure 3.8 and 3.9). 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 3.12 and 3.13).

Colistin resistance is occasionally seen in *E. coli* as well as in *K. pneumoniae*, *P. aeruginosa* and *Acinetobacter*. This occurs only in multiresistant isolates and basically only in isolates where there is a connection with healthcare abroad. In multiresistant isolates, it is important to determine colistin susceptibility and only broth microdilution is recommended for AST (MIC determination).

Klebsiella pneumoniae, from blood and urine cultures

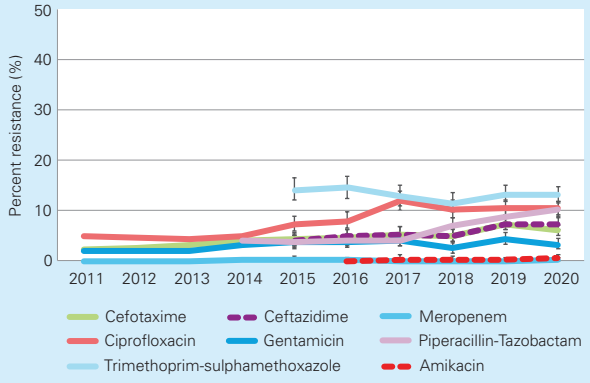
Results from 2020

- Number of reported cases with $ESBL_{CARBA}$-producing *K. pneumoniae*: 38
- Number of reported cases with bloodstream infections caused by $ESBL_{CARBA}$-producing *K. pneumoniae*: 4
- Number of reported cases with ESBL-producing *K. pneumoniae*: 785
- Number of reported cases with bloodstream infections caused by ESBL-producing *K. pneumoniae*: 104

Table 3.9. Proportion (%) of antibiotic resistant *K. pneumoniae* from blood or urine 2020. Resistance to piperacillin-tazobactam in urine is based on selective testing.

Antibiotic	Blood isolates, % R (n = 1 844)	Urine isolates, % R (n=20 492)
Ampicillin	Intrinsic resistance	Intrinsic resistance
Cefadroxil	NA	5.6
Cefotaxime	6.1	3.7
Ceftazidime	7.3	4.3
Ciprofloxacin	10.4	7.8
Gentamicin	3.3	NA
Mecillinam	NA	10.1
Meropenem	0.4	NA
Nitrofurantoin	Intrinsic resistance	Intrinsic resistance
Piperacillin-tazobactam	10.3	12.6
Trimethoprim	NA	17.4
Trimethoprim-sulphamethoxazole	13.1	NA
Combined resistance to Cefotaxime/ceftazidime + Gentamicin/tobramycin	2.6	NA
Combined resistance to Piperacillin-tazobactam + Gentamicin/tobramycin	2.1	NA

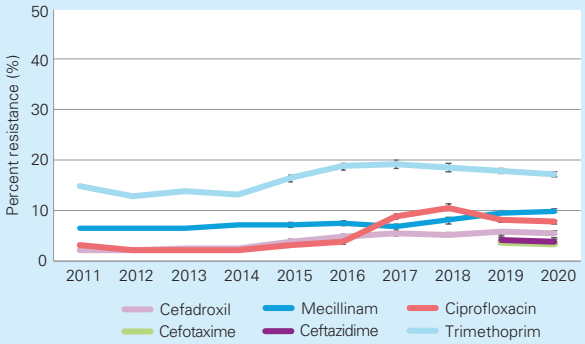
Figure 3.14. Antibiotic resistance in *K. pneumoniae* isolated from blood during the years 2011-2020. The numbers of AST isolates for all years and antibiotics ranges from 751 to 1 844. The exact numbers are given in the attached file.



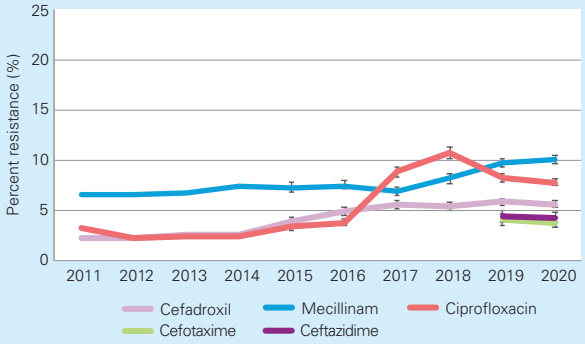
Source: The Public Health Agency of Sweden

Figure 3.15 A and B. Antibiotic resistance in *K. pneumoniae* isolates from urine during the years 2011-2020. Figure A shows all tested antibiotics and figure B shows more detailed data (below 25% resistance) for some antibiotics. The numbers of AST isolates for all years and antibiotics ranges from 2 241 to 21 089. The exact numbers are given in the attached file.

A



B



Source: The Public Health Agency of Sweden

Comments

Among invasive isolates, the resistance levels remained stable for all antibiotics tested as well as for carbapenems where the resistance remains low. The resistance to cefotaxime was 6.1%. Combined resistance to cefotaxime/ceftazidime and gentamicin/tobramycin or the combination piperacillin-tazobactam and gentamicin/tobramycin was 2.6% and 2.1% respectively (Table 3.9 and Figure 3.14).

Resistance to commonly prescribed oral antibiotics for treatment of urinary tract infections caused by *K. pneumoniae* remained stable (Figure 3.15). Cefadroxil resistance, which can be used as an indicator for production of ESBL, was 5.6%. The high increase in ciprofloxacin resistance seen during 2016-2017 can mostly be explained by a breakpoint change for ciprofloxacin. As for *E. coli*, the high levels of resistance to ciprofloxacin must be taken into account when choosing empiric treatment for febrile UTI.

Colistin resistance is occasionally seen in *K. pneumoniae* as well as in *E. coli*, *P. aeruginosa* and *Acinetobacter*. This occurs only in multiresistant isolates and basically only in isolates where there is a connection with healthcare abroad. In multiresistant isolates, it is important to determine colistin susceptibility and only broth microdilution is recommended for AST (MIC determination).

Staphylococcus aureus including MRSA

Mandatory reporting of methicillin-resistant *Staphylococcus aureus*

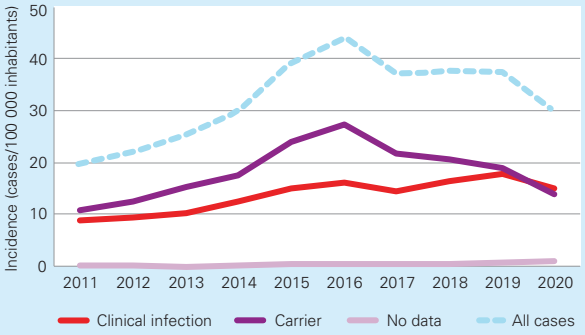
Results from 2020

- Number of reported cases: 3 112 (previous year 3 858), relative change -19%
- Number of bloodstream infections: 98 (previous year 72), relative change +36%

Trends

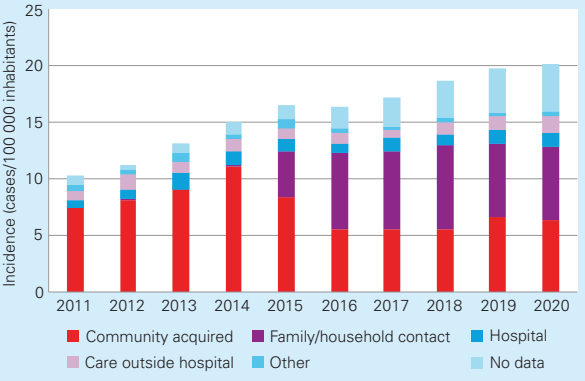
In 2020, a total of 3 112 cases of MRSA were notified. The incidence was 30 cases per 100 000 inhabitants compared to 37 cases per 100 000 inhabitants in 2019 (Figure 3.16). The decrease was 51% for cases with MRSA acquired abroad (n=773, 2020 and n=1572, 2019, respectively) while the number of domestically acquired cases remained largely unchanged. The number of cases reported with clinical infections were 1 561 (50%) while 1 436 cases (46%) were listed as carriers. MRSA-cases were reported from all 21 regions in Sweden with incidences varying from 18 to 55 cases per 100 000 inhabitants. These differences could likely be explained by differences in screening and contact tracing practices between the regions.

Figure 3.16. The incidence (cases/100 000 inhabitants) of cases with MRSA in relation to type of infection, year 2011–2020.



Source: The Public Health Agency of Sweden

Figure 3.17. Epidemiological classification of notified cases with MRSA acquired in Sweden, year 2011-2020. Presented as incidence (cases/100 000 inhabitants).

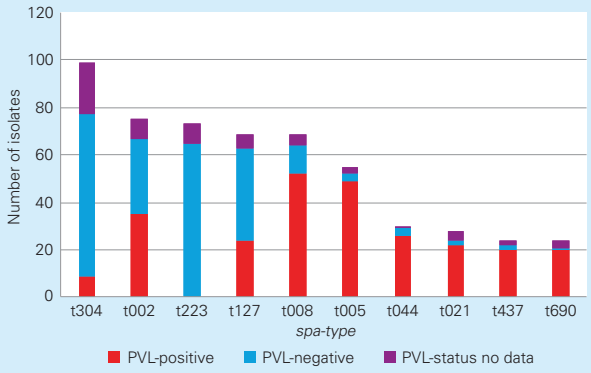


Source: The Public Health Agency of Sweden

There was almost equal distribution between women and men, as 53% (n=1 653) were women and 47% (n=1 459) men, with a median age of 30 and 34 years respectively. Among the domestic MRSA cases (n=2 084, 67%), the incidence was highest for children below one year of age (n=204, 180 cases/100 000 inhabitants) followed by the elderly, 85 years or older (n=151, 57 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 most prominent route of acquiring MRSA (Figure 3.17). A change in the clinical notification form was made in 2015, where community-acquired infections were divided into family/household-acquired or community-acquired. Among MRSA cases acquired in Sweden, 32% each were reported as community-acquired (n=664) and as acquired from family/household contacts (n=667). The proportion of domestic cases with MRSA acquired in hospital as well as healthcare/care outside hospital was six and eight percent respectively (n=129 and n=159). Twentyone percent (n=434) of the domestic cases, lacked information on acquisition.

Figure 3.18. The ten most common *spa*-types (with PVL status) among cases with MRSA with clinical infections, 2020.



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 are also obtained from regional microbiological laboratories. Typing data were available for isolates from 1 185 (76%) of the clinical cases and for 581 isolates (40%) sampled from asymptomatic carriers. Among the isolates from clinical cases, a total of 251 *spa*-types were identified. The ten most common *spa*-types were seen in 46% of the clinical cases (Figure 3.18).

Outbreaks

Several minor healthcare associated transmissions of MRSA were reported from the regions during 2020 most within care homes for the elderly.

Comments

The number of reported cases decreased with 19% between 2019 and 2020. The decrease during 2020 is largely due to reduced international travel and screening for inpatient care due to the COVID-19 pandemic. However, for healthcare acquired cases in Sweden, there is a small increase. It is worrying that the proportion of domestic cases with missing information on where the infection was aquired has increased from 6 to 21% since 2012.

Antibiotic resistance in voluntary reported clinical isolates of MRSA

AST results for *S. aureus* from clinical isolates are presented in Table 3.10 and Figure 3.19. Here, isolates from screening and case finding have been excluded.

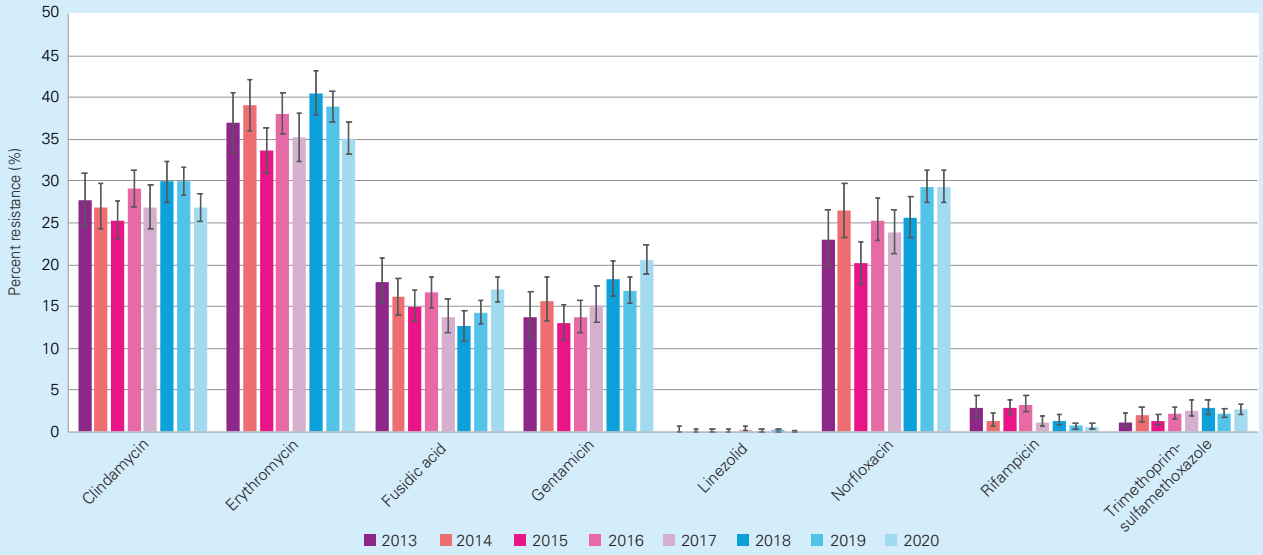
Comments

The proportion of MRSA among clinical *S. aureus* isolates were 2.4% in 2020. The proportion of MRSA has increased almost every year since 2013 (Table 3.10). The resistance in MRSA to other antibiotics remained stable (Figure 3.19).

Table 3.10. Number of *S. aureus* and MRSA from clinical isolates and proportion of MRSA 2013-2020.

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

Figure 3.19. Antibiotic resistance in clinical MRSA isolates 2013-2020. 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

Staphylococcus aureus from blood and skin and soft tissue cultures

Results from 2020

- Number of cases of MRSA reported: 3 112
- Number of cases with bloodstream infections caused by MRSA: 98
- The proportion of MRSA among S. aureus isolated from blood has increased to 2.3%, compared to 1.8% 2019.

Table 3.11. Proportion (%) of antibiotic resistant isolates in *S. aureus* from blood and skin and soft tissue infections 2020.

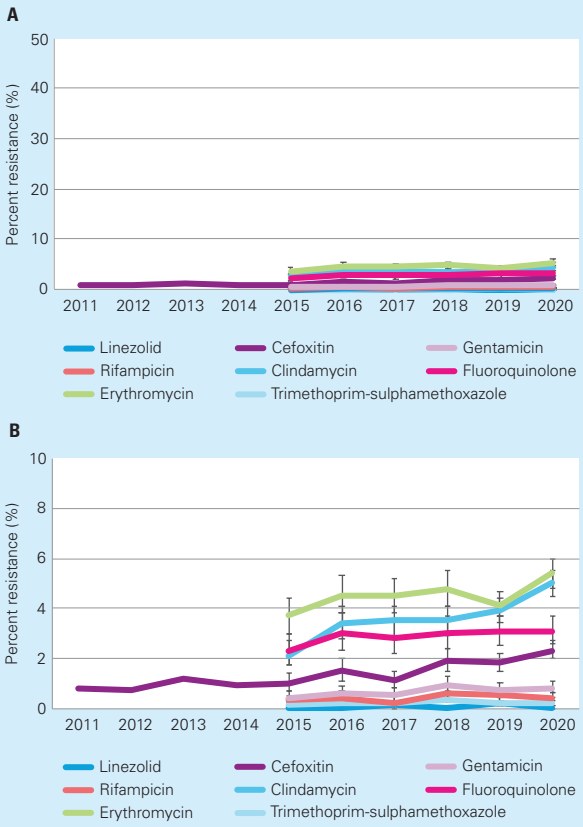
Antibiotic	Blood isolates, % R (n=6 878)	Skin and soft tissue isolates, % R (n=73 519)
Cefoxitin	2.3	2.2
Clindamycin	5.0	5.2
Erythromycin	5.4	5.1
Gentamicin	0.8	0.5[b]
Fluoroquinolone[a]	3.1	2.5[b]
Fucidic acid	NA	2.9
Linezolid	0.0	NA
Rifampicin	0.4	NA
Trimethoprim-sulphamethoxazole	0.2	NA

[a]Based on norfloxacin, [b]Number based on results from less than five laboratories

Comments

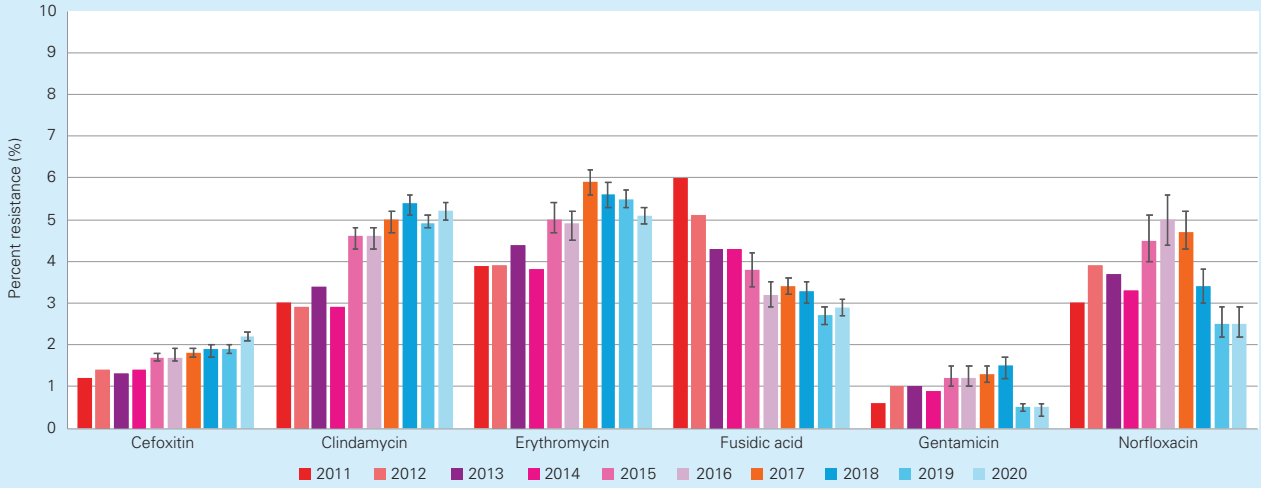
MRSA isolated from blood has slowly increased and is now 2.3% of isolated *S. aureus* (indicated by cefoxitin resistance) and the same proportion is seen for skin and soft tissue infections (Figure 3.20 and 3.21, Table 3.11). Susceptibility testing to vancomycin is not routinely performed on cefoxitin-susceptible *S. aureus*. In 2020, 800 out of 6 878 (12%) isolates were tested for vancomycin resistance with no resistance detected.

Figure 3.20 A and B. Antibiotic resistance in *S. aureus* from blood during the years 2011-2020. 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 2 387 to 6 878. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Figure 3.21. Antibiotic resistance for *S. aureus* from skin and soft tissue samples 2011-2020. The resistance for norfloxacin is based on results from less than five laboratories in 2018-2020 and for gentamicin in 2020. 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 2020

- Total number of reported cases: 79 (previous year: 232), relative change -66%.
- Number of reported cases of *E. faecium* with vancomycin resistance: 77 (previous year: 221), relative change -65%
- Number of reported cases of *E. faecalis* with vancomycin resistance: 4 (previous year: 11)
- There were two cases infected with both *E. faecium* and *E. faecalis*.
- Number of bloodstream infections: 4 (previous year: 10)

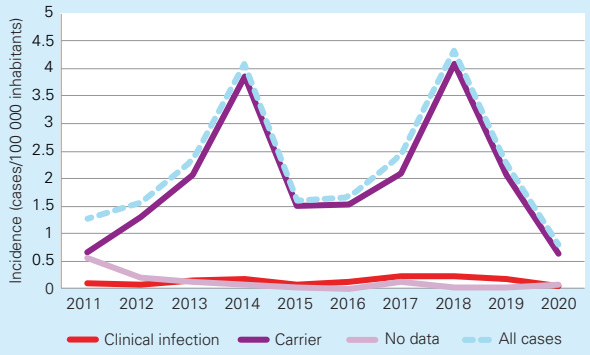
Trends

The national incidence decreased from 2.2 to 0.8 cases per 100 000 inhabitants between 2019 and 2020. Sixteen out of twenty-one regions reported cases of VRE during 2020. Out of these cases, 53 (67%) were healthcare related. A majority of the isolates (n=63, 80%) were from faeces, and only 16% from urine, wound or other clinical samples (Figure 3.22). Four invasive VRE infections were reported in 2020.

In 2020, nearly half of the cases were reported as acquired abroad. Most domestic cases were found through contact tracing (59%) in contrast to cases acquired abroad, which were detected through screening (95%).

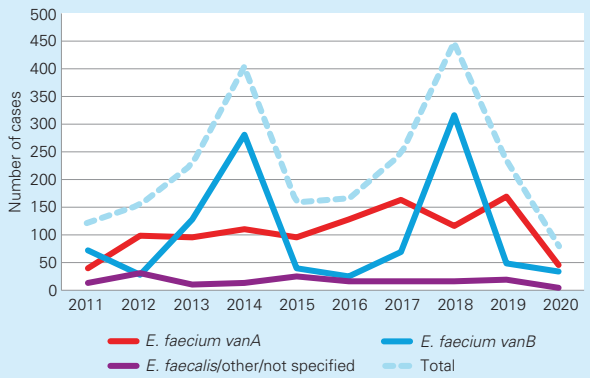
The median age for VRE was 66 years and it is still most common among men, 54%. In 2020, 77 *E. faecium* cases and 4 *E. faecalis* cases were reported. The *vanA* genotype was most commonly found (n=48) (Figure 3.23). In some cases, different genotypes of VRE were detected in the same patient and therefore slightly more isolates than cases were epidemiologically typed.

Figure 3.22. The incidence (cases/100 000 inhabitants) of cases with VRE in relation to type of infection, year 2011-2020.



Source: The Public Health Agency of Sweden

Figure 3.23. Number of VRE cases and their corresponding *van*-type.



Source: The Public Health Agency of Sweden

Epidemiological typing

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

In 2020, eight hospital-related clusters of *E. faecium* were reported with 2-7 cases each. Three cases belonged to the large national outbreak seen in 2018 with totally 279 cases, denoted SE-EfmB-1707.

During 2020, four isolates of *E. faecium vanA* with vancomycin variable phenotype were identified, all belonging to an earlier spread of ST1421. Vancomycin-variable enterococci (VVE) are *E. faecium* harbouring the *vanA*-gene, but are phenotypically vancomycin susceptible, which makes diagnostics of VVE challenging. Of concern is the spread of ST1421 associated with a vancomycin variable phenotype reported in Denmark and the risk of cross-border spread. This scenario was seen, in the south of Sweden, in the fall of 2019 with a small cluster including four patients of which one had connection with Denmark. This strain is difficult to detect and can therefore be underdiagnosed and facilitate further spread.

All four invasive cases had *E. faecium* harbouring *vanB*. Three of the invasive cases were part of clusters and only one case were unique (Table 3.12).

Comments

The number of VRE cases decreased with over 66% during 2020. As for other notifiable antibiotic resistance this is largely due to the changed spectrum of inpatient care due to the COVID-19 pandemic. A decrease was also seen in the number of hospital-related clusters and patients included in these clusters. Following the same trend the number of invasive cases decreased to 4 compared to 10 cases last year. Like previous year, a majority of the invasive cases were part of hospital clusters. This stresses the importance of preventing spread of VRE in hospitals. 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 3.12. Epidemiological typing of VRE 2020.

Epidemiological typing *E. faecium*	Sequence type (ST)	Number of typed VRE
EfmA unique	16 different sequence types	39
EfmB unique	9 different sequence types	14
SE-EfmB-1707	80	3 (total 282 isolates)
SE-EfmA-1904	80	1 (total 7 isolates)
SE-EfmB-2001	17	1 (total 2 isolates)
SE-EfmB-2002	80	7
SE-EfmB-2003	80	2
SE-EfmB-2004	117	3
SE-EfmB-2005	117	2
VVE[b]	1421	4
Total number of typed VRE	20 different sequence types	**76[a]**
Epidemiological typing *E. faecalis*	**Sequence type (ST)**	**Number of typed VRE**
EfsA unique	6	4
Total number of typed VRE	1 sequence type	4

[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 and not all cases are sent to the Public Health Agency of Sweden for epidemiological typing. [b]Vancomycin-variable enterococci (VVE), phenotypically vancomycin susceptible *E. faecium* with the *vanA*-gene.

Enterococcus faecalis and *Enterococcus faecium*, from blood cultures

Results from 2020

- Total number of VRE cases reported: 79 (previous year: 232), relative change -66%. There were two cases with double infection.
- Number of reported cases of *E. faecium* with vancomycin resistance: 77 (previous year: 221), relative change -65%
- Number of reported cases of *E. faecalis* with vancomycin resistance: 4 (previous year: 11)
- Number of bloodstream infections caused by VRE: 4 (previous year: 10)

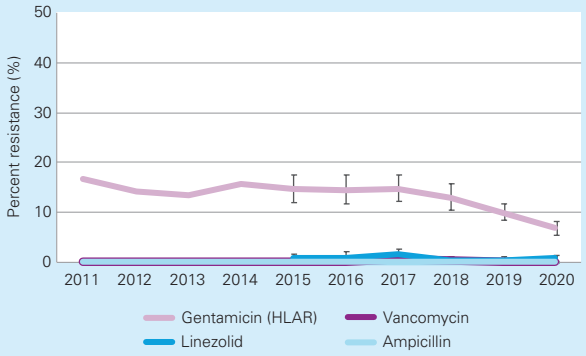
Table 3.13. Proportion (%) of antibiotic resistant *E. faecalis* and *E. faecium* isolated from blood 2020.

Antibiotic	Blood isolates *E. faecalis*, % R (n=1 441)	Blood isolates *E. faecium*, % R (n=788)
Ampicillin	0.0	82.0
Gentamicin (HLAR)	6.8	7.7
Linezolid	0.7	0.7
Piperacillin-tazobactam	0.0	88.4
Vancomycin	0.0	0.3

Comments

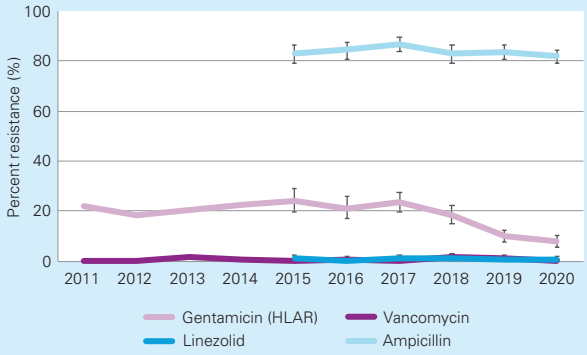
The vancomycin resistance among invasive isolates remains low and was 0.0% for *E. faecalis* and 0.3% for *E. faecium* in 2020. The continued decrease in high-level aminoglycoside resistance (HLAR) could possibly be explained by the reduced use of aminoglycosides and difference in the clonality of the enterococci that resides within hospitals (Table 3.13 and Figures 3.24 and 3.25).

Figure 3.24. Antibiotic resistance in *E. faecalis* isolated from blood during the years 2011-2020. The numbers of AST isolates for all years and antibiotics ranges from 685 to 1 441. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Figure 3.25. Antibiotic resistance in *E. faecium* isolated from blood during the years 2011-2020. The numbers of AST isolates for all years and antibiotics ranges from 368 to 788. 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 2020

- Number of reported cases: 112 (previous year 118), relative change -5%
- Number of bloodstream infections: 4 (previous year 9)

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.

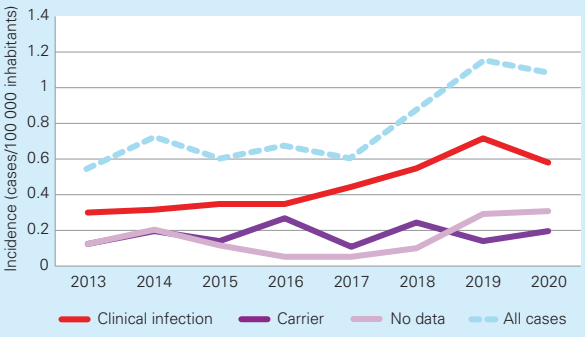
Trends

The national incidence of PNSP in 2020 was 1.1 cases per 100 000 and remained unchanged from 2019. The incidence for PNSP acquisition was highest among children under five years of age (2.9 cases per 100 000 inhabitants) representing 15% of all cases. Most cases were found in the age group 65 years and older (37%). Of all cases, 65% were men and 35% women.

PNSP was most often found in cultures from the nasopharynx (48%). Thirty-four isolates were found in sputum/bronchoalveolar lavage (30%). Half of the PNSP cases were reported with clinical infetions (54%, n=60, incidence 0.6) and 18% (n=20, incidence 0.2) as carriers (Figure 3.26).

A majority of the cases had been acquired in Sweden (63%, n=71) and four percent of the cases abroad. For the remaining cases, no country of acquisition was given (32%).

Figure 3.26. The incidence (cases/100 000 inhabitants) of cases with PNSP in relation to type of infection, year 2013-2020.



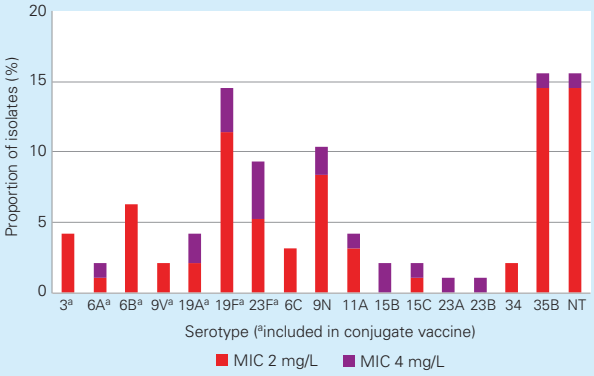
Source: The Public Health Agency of Sweden

Epidemiological typing

A total of 96 isolates with PcG MIC > 1 mg/L were sent to PHAS for serotyping during 2020 (89% of notified cases). Of these isolates 44% (n=42) belonged to serotypes included in the conjugate vaccines (PCV10 and/or PCV13; Figure 3.27). The corresponding figures for 2019 and 2018 were 60 and 63% respectively. Two of the four invasive cases typed in 2020 were of vaccine type (serotypes 6A and 19F).

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 2020, 224 isolates were collected (including the 96 isolates from cases of PNSP). The serotype distribution were, in decending order: NT (21%), 19F (13%), 35B (12%), 19A (9%), 9N (6%), 23F (6%) and 11A (4%). Of the 224 isolates, 38% constituted of types included in the conjugate vaccines (PCV10 and/or PCV13).

Figure 3.27. Distribution of MICs among PNSP with PcG MIC > 1 mg/L (n=96).



Source: The Public Health Agency of Sweden

Outbreaks

No clusters were reported during 2020.

Comments

Overall, the incidence of PNSP has remained fairly stable up to 2017 after the case definition was changed in May 2012 (Figure 3.26). The increase in 2019 and 2020 could partly be due to changes in diagnostics, as more laboratories have switched to reporting data from the broth microdilution method.

Streptococcus pneumoniae, from blood and nasopharynx

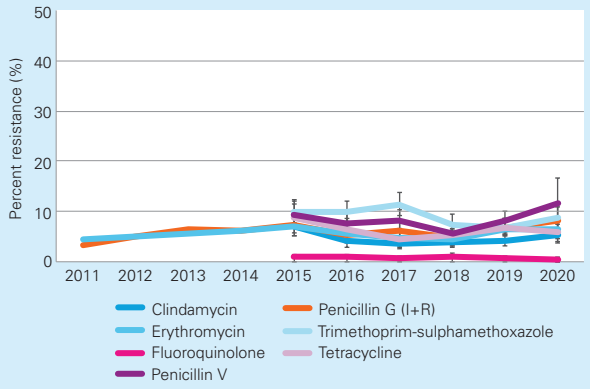
Results from 2020

- Number of reported cases of PNSP: 112 cases
- Cases with bloodstream infections caused by PNSP: 4
- Cases of invasive pneumococcal disease: 648

Table 3.14. Proportion (%) of antibiotic resistant *S. pneumoniae* isolated from blood and nasopharynx 2020.

Antibiotic	Blood isolates, % R (n=552)	Nasopharynx isolates, % R (n=2 359)
Clindamycin	5.3	6.4
Erythromycin	6.5	8.5
Fluoroquinolone	0.6	1.5
Penicillin G (I+R)	8.3	12.6
Penicilln V	11.7	14.7
Tetracycline	6.1	8.3
Trimethoprim-sulphamethoxazole	8.9	9.9

Figure 3.28. Antibiotic resistance in *S. pneumoniae* isolated from blood during the years 2011-2020. 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.



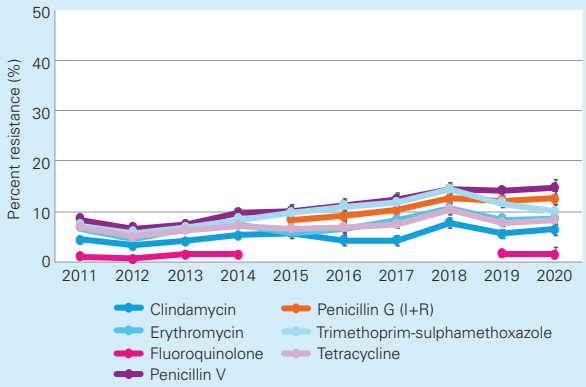
Source: The Public Health Agency of Sweden

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.

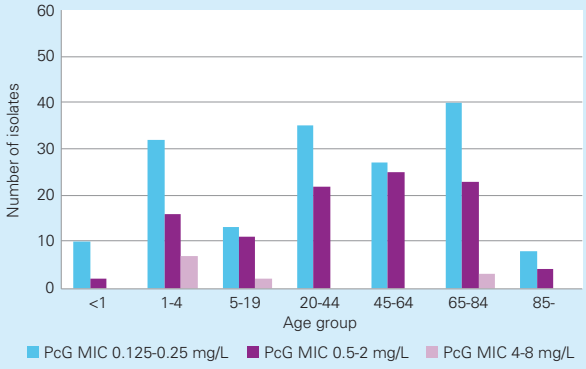
Among invasive infections, the proportion of PcG non-susceptible isolates was 8.3% in 2020 (Table 3.14 and Figure 3.28). Since 2012, there has been a slow increase in resistance for almost all tested antibiotics for respiratory tract infections (Figure 3.29). The methodological problems regarding gradient tests results in difficulties when interpreting MIC. Some isolates interpreted as I (purple bars) are probably incorrect and would be interpreted as R if BMD was used (Figure 3.30). In the current Svebar data, both methods are reported, making the proportion of R hard to follow. The total resistance proportion (I+R) is not influenced.

Figure 3.29. Antibiotic resistance in *S. pneumoniae* isolated from nasopharynx during the years 2011-2020. Penicillin V resistance is based on susceptibility testing using oxacillin. The numbers of AST isolates for all years and antibiotics ranges from 2 081 to 5 904. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Figure 3.30. Distribution of *S. pneumoniae* with reduced susceptibility to penicillin G from nasopharynx 2020. Benzylpenicillin MIC values above 0.06 mg/L are categorised as susceptible, increased exposure (I) or resistant (R>2 mg/L).



Source: The Public Health Agency of Sweden

Recently published, ongoing, and planned development of EUCAST criteria for antimicrobial susceptibility testing of organisms

EUCAST and the EUCAST Development Laboratory (EDL) are currently developing clinical breakpoints and methodology for several species which are hitherto lacking criteria for antimicrobial susceptibility testing (AST). Some new criteria have recently been finalised and published. These will be of great importance in the management of patients with serious infections caused by uncommon species.

The projects require the assistance of international institutions with special interest and know-how. The EDL, after many years of coordinating such projects now have the contacts needed to bring the strains, agents and data together.

Recently published criteria

EUCAST and EDL have recently published criteria for

- *Burkholdera pseudomallei*
- *Bacillus* spp.
- *Achromobacter* spp.

For all of these we recommend the use of standard Muller-Hinton media (broth and plates) and that susceptibility testing is only performed and reported for agents with breakpoints in the EUCAST breakpoint table.

For anyone interested in the EUCAST and ADL work, publications can be found here: https://www.eucast.org/publications_and_documents/publications_in_journals/ and more general information on how data on new agents or species is validated an calibrated, here: https://www.eucast.org/ast_of_bacteria/calibration_and_validation/.

Ongoing and planned development

- *Vibrio* spp. (*V. cholerae*, *V. parahaemolyticus*, *V. vulnificus*, *V. alginolyticus*, *V. fluvialis*)
  A large collection of isolates has been gathered from many countries across the world. Broth microdilution and disk diffusion are being performed on 400 – 500 strains. The relevant antibiotics have been identified by EUCAST and clinical MIC breakpoints and disk diffusion criteria are under development. In Scandinavia, the need for breakpoints in *Vibrio* spp. is primarily with *V. parahemolyticus* and *V. vulnificus*, both responsible for serious infections.
- *Corynebacterium diphtheriae* and *Corynebacterium ulcerans*
  In collaboration with French and German reference laboratories a material of altogether 200 isolates each of these species are being tested. On this material, MIC and zone diameter distributions, EUCAST can determine clinical breakpoints and disk diffusion correlates.
- *Nocardia* spp.
  Approximately 125 isolates have been subjected to MIC agar dilution and disk diffusion, following two years of EDL development work, to find the most suitable methods for choosing media, preparing inocula and investigating the most appropriate incubation time. Currently the whole collection is being subjected to sequencing to ascertain the species of each isolate. This is in collaboration with Australian and French colleagues, experts on Nocardiae. The MIC distributions and zone diameter correlates will be generated once all *Nocardia* species are known. This will form the basis for breakpoint discussions in EUCAST.
- Anaerobic bacteria
  There is currently no EUCAST disk diffusion method for anaerobic bacteria. This is now being developed for fast growing anaerobes, namely *Bacteroides* spp., *Prevotella* spp., *Fusobacterium necrophorum*, *Clostridium perfringens* and *Cutibacterium acnes*. A medium, available from several manufacturers, has been identified for reference purposes and for development of the disk diffusion method. Zone diameter breakpoints are for 16 – 20h incubation, with no extension following poor growth. Meanwhile clinical breakpoints for these anaerobic bacteria are being reviewed for a possible revision.
- Other organisms
  Stenotrophomonas maltophilia and *Burkholderia cepacia* complex, as well as *Neisseria* spp. are in need of methodological development and review of breakpoints. These will be next.

The use of standardised criteria is a basis for collecting and reporting reliable data on antibiotic resistance. With a wider implementation of common criteria for the more unusual species surveillance of their resistance can be accomplished.

Haemophilus influenzae, from blood and nasopharynx cultures

Results from 2020

- Number of reported cases of invasive *H. influenzae*: 89

Table 3.15. Proportion (%) of antibiotic resistant *H. influenzae* from blood or nasopharynx 2020..

Antibiotic	Blood isolates, % R (n = 60)	Nasopharynx isolates, % R (n = 5 655)
Ampicillin/ Amoxicillin	43.8	32.4
Amoxicillin-Clavulanic acid	NA	NA
Cefotaxime	3.0	NA
Fluoroquinolone[a]	2.3	1.6
Penicillin G	50.0	40.7
Tetracycline	3.4	0.7
Trimethoprim-sulphamethoxazole	12.2	25.6
Cefaclor	28.6	NA

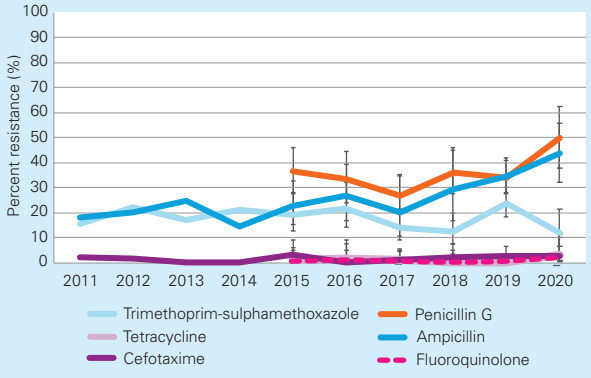
[a]Nalidixic acid was used for detection of fluoroquinolone resistance.

Trends

During 2020, 36 isolates were received within the microbiological characterisation program for cephalosporin resistance in *H. influenzae* at PHAS. The majority of these, 33 isolates, showed high-level resistance to extended-spectrum cephalosporins, caused by alterations in penicillin-binding protein 3 (PBP3). Seven of these isolates also carried the betalactamase $bla_{\text{TEM-1}}$ gene which is the most prevalent gene of the acquired betalactamases. The remaining three isolates showed lower level resistance to cephalosporins.

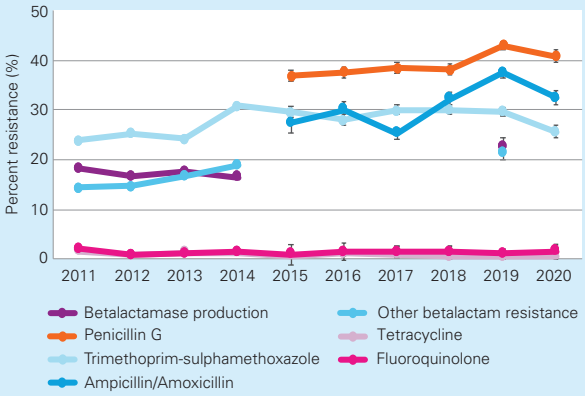
One large cluster with high-level cephalosporin resistant *H. influenzae* from 2019 continued in 2020 with 12 cases, and four small clusters with two to three cases each were seen during 2020.

Figure 3.31. Antibiotic resistance in *H. influenzae* isolated from blood during the years 2011-2020. The numbers of AST isolates for all years and antibiotics ranges from 60 to 209. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Figure 3.32. Antibiotic resistance in *H. influenzae* isolated from nasopharynx during the years 2011-2020. 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

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 3.15 and Figure 3.31). The variation in resistance should be interpreted with caution since there is a small number of tested isolates. Among respiratory isolates, the resistance levels are relatively stable (Figure 3.32).

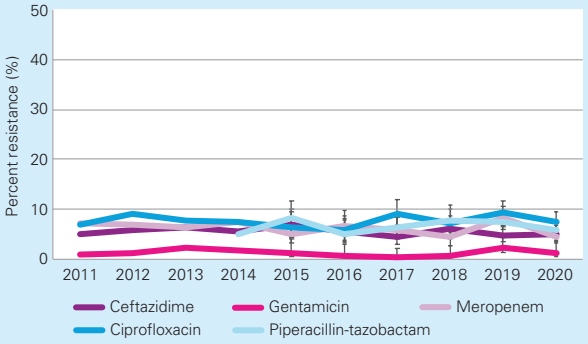
Pseudomonas aeruginosa, from blood and non-respiratory cultures

Results from 2020

Table 3.16. Proportion (%) of antibiotic resistant *P. aeruginosa* isolated from blood and non-respiratory specimens 2020.

Antibiotic	Blood isolates, % R (n = 735)	Non-respiratory isolates, % R (n=17 014)
Ceftazidime	5.0	4.6
Ciprofloxacin	7.5	10.4
Gentamicin	1.3	4.0
Tobramycin	0.7	0.8
Meropenem	4.5	4.6
Piperacillin-tazobactam	6.0	6.4

Figure 3.33. Antibiotic resistance in *P. aeruginosa* isolated from blood during the years 2011-2020. The numbers of AST isolates for all years and antibiotics ranges from 337 to 735. The exact numbers are given in the attached file.

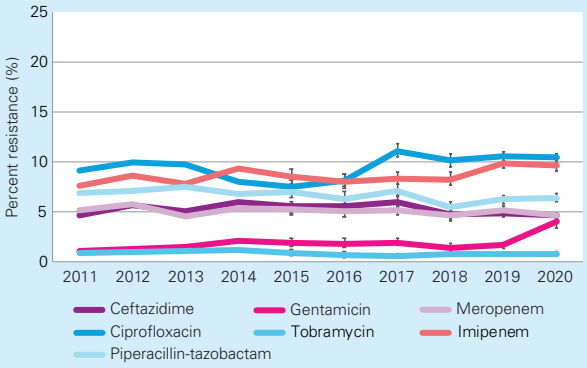


Source: The Public Health Agency of Sweden

Comments

Resistance to ceftazidime is most often due to efflux pumps and porin loss, not ESBL production. The resistance for most antibiotics is stable for both blood isolates and non-respiratory isolates (Table 3.16, Figure 3.33 and 3.34). An increase in gentamicin resistance is noted for *P. aeruginosa* from non-respiratory isolates, from 1.7% to 4.0%. It should be noted that this year's result is based on half as many isolates, from half as many laboratories. Instead, AST with tobramycin has increased and no change in resistance rates can be noted for tobramycin. Colistin resistance is occasionally seen in *P. aeruginosa* as well as in *E. coli*, *K. pneumoniae*, and *Acinetobacter* spp. This occurs only in multiresistant isolates and basically only in isolates where there is a connection with healthcare abroad. In multiresistant isolates, it is important to determine colistin susceptibility and only broth microdilution is recommended for AST (MIC determination).

Figure 3.34. Antibiotic resistance in *P. aeruginosa* from non-respiratory isolates 2011-2020. The numbers of AST isolates for all years and antibiotics ranges from 1 980 to 17 014. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Acinetobacter spp., from blood cultures

Results from 2020

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

Species		Antibiotic	2014		2015		2016		2017		2018		2019		2020	
	Sample		n	% R	n	% R	n	% R	n	% R	n	% R	n	% R	n	% R
Acinetobacter species	Blood	**Number of AST isolates**	**59**		**84**		**54**		**54**		**55**		**113**		**126**	
		Meropenem		3.4	85	2.4	53	1.9	53	0.0	54	3.7	113	3.5	125	7.2
		Ciprofloxacin			84	4.8	54	5.6	54	0.0	55	7.3	113	8.0	126	7.1
		Trimethoprim-sulfamethoxazole			83	6.0	53	5.7	54	0.0	55	3.6	112	4.5	126	9.5
		Gentamicin			66	3.0	43	7.0	51	0.0	49	6.1	72	6.9	90	11.1

Comments

During 2020, a total of 126 isolates of *Acinetobacter* spp. from blood was reported to Svebar. The carbapenem resistance was 7.2% (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 *Acinetobacter* spp. as well as in *E. coli*, *K. pneumoniae* and *P. aeruginosa*. This occurs only in multiresistant isolates and basically only in isolates where there is a connection with healthcare abroad. In multiresistant isolates, it is important to determine colistin susceptibility and only broth microdilution is recommended for AST (MIC determination).

Streptococcus pyogenes, from blood cultures

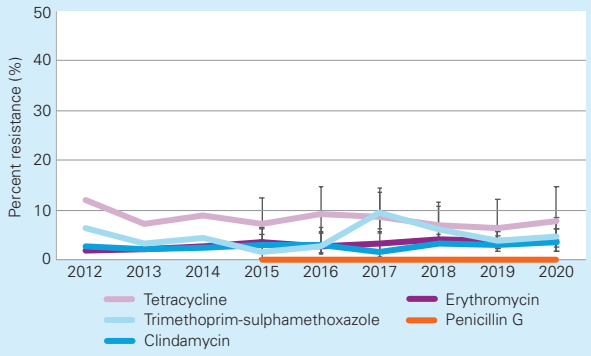
Results from 2020

- Number of reported cases of invasive *S. pyogenes*: 376

Table 3.18. Antibiotic resistance in *S. pyogenes* isolated from blood 2020.

Antibiotic	Blood isolates, % R (n=298)
Penicillin G	0.0
Erythromycin	3.4
Clindamycin	3.4
Tetracycline	7.8
Trimethoprim-sulphamethoxazole	4.7

Figure 3.35. Antibiotic resistance in *S. pyogenes* isolated from blood during the years 2012-2020. The numbers of AST isolates for all years and antibiotics ranges from 103 to 539. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Comments

Invasive cases of *S. pyogenes* are notifiable according to the Communicable Disease Act and in 2020 a total of 376 cases were reported. This is a decrease with 51% compared with previous year (n=768) and in line with most respiratory infections during the COVID-19 pandemic. AST results from 298 isolates were available from Svebar (Table 3.18). Some laboratories did not test susceptibility for trimethoprim-sulphamethoxazole and tetracycline. Resistance to both erythromycin and clindamycin remained stable (Figure 3.35).

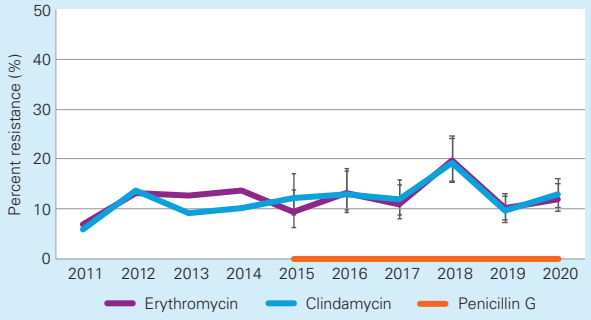
Streptococcus agalactiae, from blood cultures

Results from 2020

Table 3.19. Proportion of resistant *S. agalactiae* isolated from blood 2020.

Antibiotic	Blood isolates, % R (n=531)
Penicillin G	0.0
Erythromycin	12.0
Clindamycin	12.9

Figure 3.36. Antibiotic resistance in *S. agalactiae* (GBS) from blood- during the years 2011-2020. The numbers of AST isolates for all years and antibiotics ranges from 184 to 531.The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Comments

S. agalactiae is not included in the Communicable Disease Act. It is an important pathogen in the context of pregnancy and child birth and can cause serious infections among others as well, mainly elderly with predisposing disease. Resistance to erythromycin and clindamycinis is now approximately 12% and 13% (Table 3.19 and Figure 3.36).

Shigella species

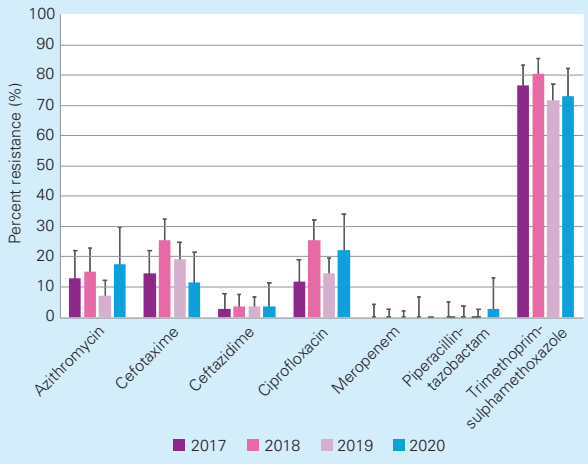
Mandatory reporting of *Shigella*

A total of 161 cases with shigellosis were notified in 2020, as compared to 524 cases in 2019. The decrease in notified cases is a result of the pandemic and, most likely, the change in international travel. The number of 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 almost three quarters of all cases the infection was acquired abroad. Species identification were available for 98 of the cases. *S. flexneri* were identified in 52% of the isolats, followed by *S. sonnei* (42%). *S. boydii* and *S. dysenteriae* were reported in three or less cases.

In 2020, 12 cases with *Shigella* were also mandatory notified as ESBL-producing Enterobacterales (previously Enterobacteriaceae). All six cases with known ESBL-type had $ESBL_A$. No cases with *Shigella* carrying $ESBL_{CARBA}$ have been reported.

Figure 3.37. Antibiotic resistance in *Shigella* spp. from faecal samples 2017-2020. The numbers of AST isolates for all years and antibiotics ranges from 40 to 242. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Shigella spp., from faecal samples

In 2020, 67 isolates of *Shigella* were reported and AST results were available from 63 isolates. The majority of isolates were *S. flexneri and S. sonnei*, with 45% and 44%, of isolates respectively. *S. boydii* and *S. dysenteriae* were reported for a few isolates. None of the isolates were carbapenem resistant (Figure 3.37). The difference in resistance to cefotaxime (11%) and ceftazidime (3%) indicates carriage of $ESBL_A$.

Comments

In 2020, very few isolates with an AST were available for analysis. Hence, results should be interpreted with some caution. According to the mandatory reporting of shigellosis three out of four cases in 2020 were acquired abroad.

Mycobacterium tuberculosis, mandatory reporting

During 2020 a total of 335 cases of tuberculosis (TB) were reported compared to 491 cases during 2019 which is a decrease of 32%. Out of the 335 cases 7 were already on TB treatment when arriving in Sweden.

The number and proportion of culture confirmed cases were 264 (79%) compared to 396 (81%) in 2019. *Mycobacterium bovis* was identified in six cases, *Mycobacterium africanum* in three cases and *Mycobacterium tuberculosis* in 255 cases. The proportions of cases diagnosed with MDR-TB was 2.4% (6/255) compared to 1.8% (7/388) in 2019. None of the MDR-cases was classified as XDR-TB.

Isolates of *M. tuberculosis* resistant to at least one of the four first line drugs (isoniazid, rifampicin, ethambutol or pyrazinamid) were identified in 28 patients corresponding to 11% of the 255 with culture confirmed *M. tuberculosis*, see Figure 3.38. As always the most common resistance found was against isoniazid.

Among the cases born in Sweden one of 35 with culture confirmed diagnosis had multidrug resistant TB and two had TB monoresistant to isoniazid.

Of all the TB cases reported in Sweden 2020, 87% were born in another country. In total 220 in this group had a culture confirmed infection with *M. tuberculosis* and 25 (11%) had some kind of resistance out of which five had MDR-TB.

Genetic typing of TB isolates has been performed in Sweden since the late 1990's. This is done to identify clusters of cases as clustering indicates possible recent transmission and helps to identify missed opportunities of infection control. Of all the cases 17% (58/335) were considered as infected in Sweden and of 262 (including *M. africanum* and *M. bovis*) cases analysed with whole genome sequencing 83% were unique isolates not belonging to any cluster.

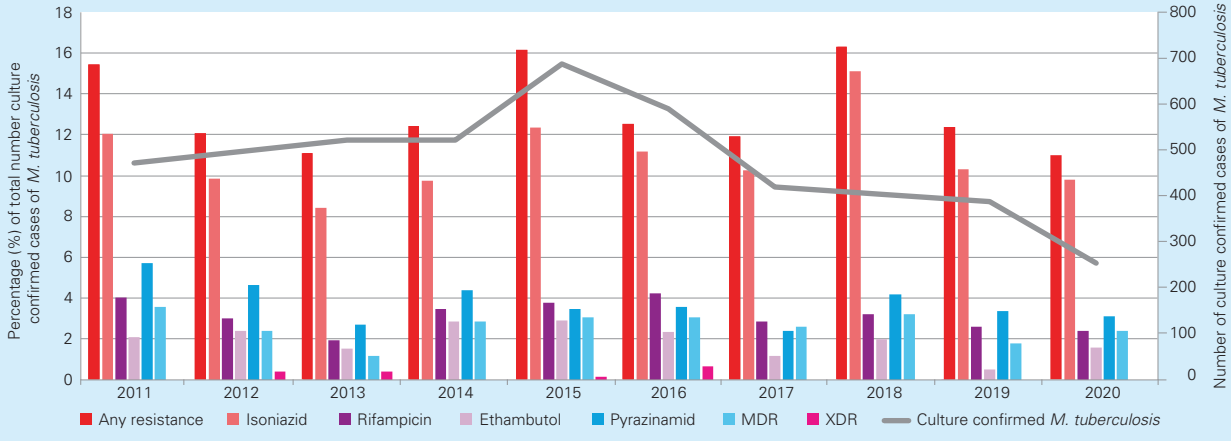
The number of reported cases of TB has decreased considerably during 2020 which in part can be attributed to the COVID-19 pandemic. As the majority of cases in Sweden are diagnosed in migrants from high burden countries, the reduced migration during the pandemic affects the number.

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 2020, 2 689 cases (26 cases per 100 000 inhabitants) of gonococcal infections were reported to the Public Health Agency of Sweden. This is a decrease with approximately 17% compared to 2019 (3 244 cases), however, the decreased gonorrhoea incidence in 2020 was most likely significantly affected by the COVID-19 pandemic, i.e. 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. Most of the gonorrhoea cases in 2020 were identified in the three largest counties of Sweden: the cities Stockholm, Göteborg, and Malmö. 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 2020,

Figure 3.38. Drug resistance and number of culture confirmed *M. tuberculosis* in Sweden 2011-2020.



1713 clinical *N. gonorrhoeae* isolates (multiple isolates from some patients) were fully characterised at the Swedish Reference Laboratory for Sexually Transmitted Infections.

Antimicrobial susceptibility testing was performed according to standardized and quality assured methodology using Etest for MIC determination of ceftriaxone, cefixime, azithromycin, spectinomycin, and ciprofloxacin. The used clinical resistance breakpoints have been determined by The European Committee on Antimicrobial Susceptibility Testing (EUCAST). 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 3.20, the antibiotic resistance in clinical gonococcal isolates cultured in 2020 are compared with those from 2011 to 2019. Briefly, the level of resistance to ciprofloxacin, which previously was used as first-line treatment for gonorrhoea, remains very high, i.e. 58% in 2020. The proportion of isolates above the azithromycin ECOFF was 19%, which represents a substantial increase since 2019 (12%). However, this increase was due to the higher level of azithromycin resistance among gonococcal isolates in Stockholm (23% resistance), which was not included in the 2019 report, compared to isolates at the Reference Laboratory in Örebro and Göteborg (12% resistance). The resistance to cefixime slightly increased from approximately 1% (observed from 2016 to 2019) to around 2%. As in 2015-2019 no resistance to ceftriaxone was identified in 2020. 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 (500-1 000 mg) plus azithromycin (2 g) OR ceftriaxone 1 000 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.

Neisseria meningitidis, mandatory reporting

Invasive meningococcal disease is a notifiable disease, and in 2020 a total of 28 cases (0.3 cases per 100 000 inhabitants) of the disease were reported, which is a decrease with approximately 58% compared to 2019 (66 cases). In total, 23 clinical invasive isolates from blood, cerebrospinal fluid and/or joint fluid (one isolate per patient) 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 2020 is most likely associated with the COVID-19 pandemic restrictions, e.g. social distancing and travel restrictions.

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

Five (22%) isolates had an intermediate susceptibility to penicillin G (MIC>0.064 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: 0.5-2 mg/L), ciprofloxacin (0.002-0.008 mg/L), and rifampicin (MICs: 0.002-0.25 mg/L). None of the isolates obtained in 2020 produced β-lactamase, and in fact no β-lactamase-producing meningococcal isolate has ever been identified in Sweden.

Table 3.20. Antibiotic resistance rates (%) of Swedish clinical *Neisseria gonorrhoeae* isolates 2011-2020.

	2011 (n=805)	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)
Cefixime	8	10	4	2	2	1	1 (0.6)	1 (1.2)	1 (0.8)	2[b]
Ceftriaxone	2	1	<1 (0.3)	<1 (0.3)	0	0	0	0	0	0
Azithromycin	11	10	13	9	10	3	5	5[a]	12[a]	19[a]
Ciprofloxacin	55	62	53	60	53	53	47	57	60	58
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]1 519 isolates examined

Clostridioides difficile

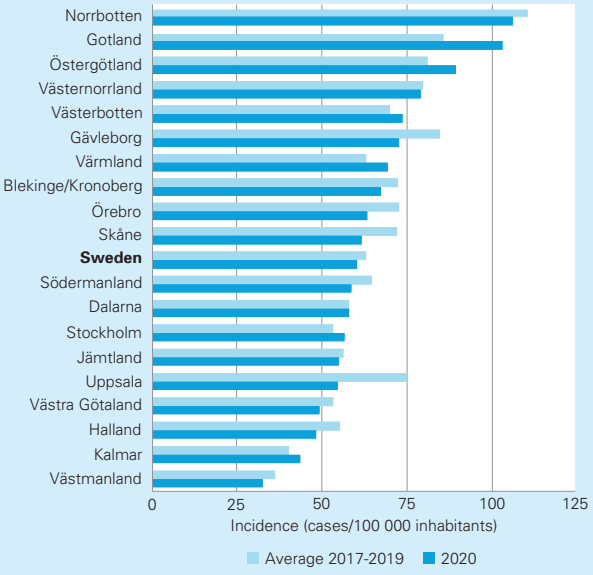
Incidence of CDI

In 2020, 6 036 new CDI cases were reported corresponding to an incidence of 60 cases per 100 000 inhabitants (corrected for region Jönköping). The laboratory in Jönköping made several changes to the diagnostics for *C. difficile* during the year, which is why data are missing for this region in the national statistics. As in previous years, there are major differences between regions (spread 32-106 cases per 100 000 inhabitants; Figure 3.39). The incidence has decreased by 9% between 2016 and 2020.

The ribotype distribution changed in 2020, with ribotype 001 accounting for 9.4% of typed isolates whereas in previous years ribotype 014 has been the most prevalent. An in depth analysis of isolates of ribotype 001 was performed by whole genome sequencing and the results showed that the increase of prevalence of ribotype 001 was not due to local or nation wide outbreaks. The diversity of ribotype was also reduced compared to previous years, this could be caused by fewer laboratories sending isolates for typing. The 20 most common ribotypes accounted for 78% of typed isolates compared to 72 to 73% for the years 2018-2019.

Since the resistance situation has been stable in recent years, no testing of isolates for antibiotic susceptibility was done in 2020.

Figure 3.39. The incidence of new cases with *C. difficile* (cases/100 000 inhabitants) by region in 2020 and average for the years 2017-2019. The regions are ranked from lowest to highest incidence in 2020. 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*

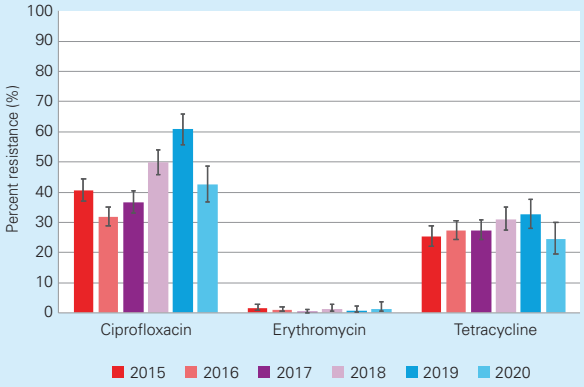
Mandatory reporting of *Campylobacter*

A total of 3 434 cases were reported in 2020, half as many reported cases as in 2019. The decrease in number of reported cases is a result of the COVID-19 pandemic and, most likely, the decrease in international travel. Twenty-six percent of cases were considered to be infected abroad, as compared to 55% in 2019. In the national surveillance program, isolates from domestic cases were collected during four weeks in 2020 (week 34-37). The focus of the epidemiological typing using whole-genome sequencing, is species identification and cluster analysis to identify potential outbreaks.

Campylobacter jejuni, from faecal samples

A total of 1 906 *Campylobacter* species were found in faecal sampling, less than half of the isolates reported in 2019. More than half of the 1 906 isolates were reported as *C. jejuni* (53%), 35% as *C. jejuni/C. coli* and 11% were another species. The presence of AST data, and in a sufficient number of isolates, were highest for *C. jejuni* (27% of all isolates).

Figure 3.40. Antibiotic resistance in *Campylobacter jejuni* from faecal samples 2015-2020. 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 43% and 24% for tetracycline in 2020. Just above one percent were resistant to erythromycin (Figure 3.40). The proportion of isolates fully susceptible to erythromycin, ciprofloxacin and tetracycline were 56% and fully resistant were 1.2% (Table 3.21). It should be noted that the number of isolates with combined AST are the lowest since 2015, and that the fully resistant isolates are only three in total.

During 2018-2019, the majority of notifiable *Campylobacter* infections were acquired abroad. In 2016 and 2017, there was a large outbreak of *Campylobacter* in humans, linked to domestic poultry production. During these two years the proportions of isolates with Swedish origin were higher. It can be noted

that the resistance to ciprofloxacin were lower 2016-2017 (Figure 3.40) and a higher percentage of isolates were fully suscepible as well (Table 3.21).

Table 3.21. Combined suceptibility and resistance to erythromycin, ciprofloxacin and tetracycline in *Campylobacter jejuni* from faecal samples 2015-2020.

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

Salmonella

Mandatory reporting of *Salmonella*

Infection with *Salmonella* species is 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 2020, a total of 826 cases were notified with *Salmonella* infections (*S.* Typhi and *S.* Paratyphi excluded), 11 cases with typhoid fever and 6 cases with paratyphoid fever For *Salmonella* infections, the number of notified cases in 2020, compared with 2019, decreased with 59% as a result of the COVID-19 pandemic. The decrease in international travel could be one explanatory factor for the lower number of cases. Of the *Salmonella* infections, 46% of the cases were infected abroad, 51% were domestic cases and information about country of infection was lacking for 3% of the cases. In 2019 this proportion were 61%, 38% and 1%, respectively.

The national surveillance program using whole-genome sequencing, focus on epidemiological typing of domestic isolates in order to identify potential outbreaks. During 2020, isolates from 413 cases were analysed in the program (83% of the domestic cases). The three most prevalent serotypes in the domestic cases, of the 56 identified, were *S.* Typhimurium (21%), *S.* Enteritidis (16%) and monophasic *S.* Typhimurium (14%). Among the 13% of investigated isolates from cases infected abroad, *S.* Enteritidis was the most prevalent serotype (28%). The majority of cases with typhoid fever and paratyphoid fever were infected abroad and epidemiologically linked to South Asia.

A total of 11 cases in 2020 were reported having *Salmonella* with ESBL. All eight cases with known ESBL-type had $ESBL_A$. No cases with *Salmonella* species have been reported with $ESBL_{CARBA}$.

Invasive infections were reported for 67 cases in the mandatory reporting, 55 cases with *Salmonella* infection (*S.* Typhi and *S.* Paratyphi excluded), in 7 with typhoid fever and 5 of the cases with parathyphoid fever.

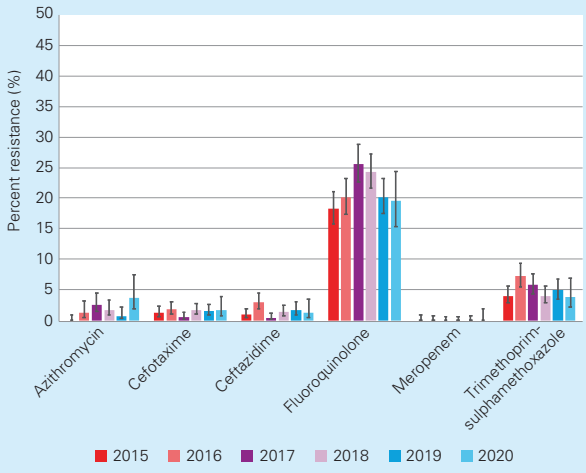
Salmonella spp., from faecal and urine samples

A total of 724 *Salmonella enterica* isolates were reported in Svebar, 73% were from faecal samples, 15% from blood and 10% from urine. In approximately half of the faecal and urine isolates an AST were reported.

Table 3.22. Antibiotic resistance in *Salmonella enterica* (*S.* Typhi and *S.* Paratyphi excluded) isolated from blood or from faeces and urine samples in 2020.

Antibiotic	Blood isolates, % R (n = 59)	Faeces/urine isolates, % R (n= 298)
Azithromycin	3.1	3.7
Cefotaxime	10.2	1.7
Ceftazidime	10.5	1.2
Fluoroquinolone	32.2	19.5
Meropenem	0.0	0.0
Piperacillin-tazobactam	3.6	0.6
Trimethoprim-sulfamethoxazole	15.3	3.8

Figure 3.41. Antibiotic resistance in *Salmonella enterica* from faecal and urine samples 2015-2020. 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

Comments

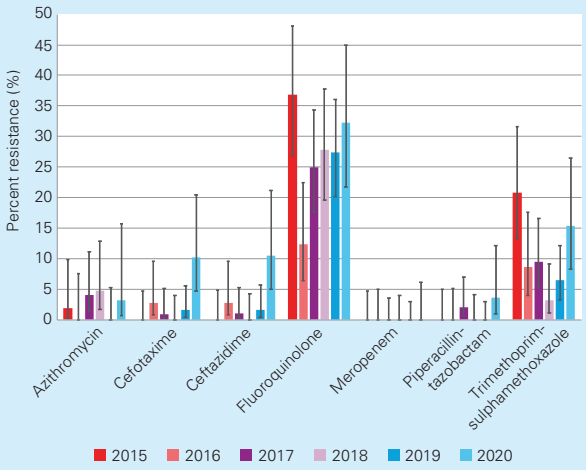
No significant changes in antibiotic resistance is seen between 2015- 2020 (Figure 3.41). During this period no carbapenem-resistent *Salmonella* have been reported. The highest resistance was against fluoroquinolones in isolates from faeces and urine, 20% in 2020. Almost 80% of the *Salmonella* from faecal and urine samples are fully susceptible to azithromycin, cefotaxime and ciprofloxacin (Table 3.23).

Table 3.23. Combined susceptibility and resistance to azithromycin, cefotaxime and ciprofloxacin in *Salmonella enterica* from faecal and urine samples 2015-2020. Results from *S.* Typhi and *S.* Paratyphi have been excluded.

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

Salmonella from blood

Figure 3.42. Antibiotic resistance in *Salmonella enterica* from blood samples 2015-2020. Results from *S.* Typhi and *S.* Paratyphi are excluded. The numbers of AST isolates for all years and antibiotics ranges from 32 to 125. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Comments

In 2020, there were 59 isolates of *Salmonella* reported in blood with an AST (Figure 3.42). 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. In 2020, the resistance proportions are higher for several antibiotics in isolates from blood, compared with isolates from faeces and urine. The noted differences should be interpreted with caution considering the low number of isolates. (Table 3.22). No carbapenem resistance was detected.

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)

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 and 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 healthy animals and meat of Swedish origin are shown in Table 4.1.

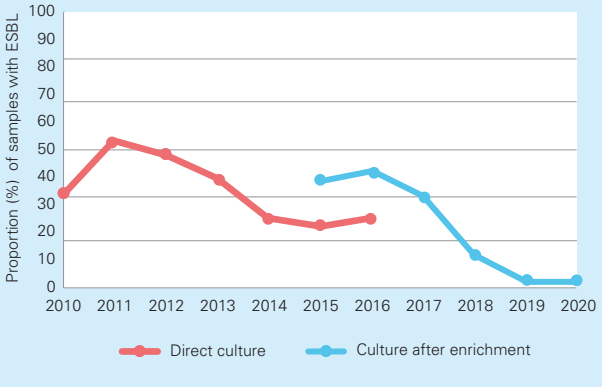
During 2020, samples of intestinal contents from healthy broilers (n=300) and turkeys (n=45) collected at slaughter as well as samples of broiler meat (n=306) collected at retail were screened for *E. coli* resistant to ESCs and carbapenems using selective media. Isolates with reduced susceptibility 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).

When investigating samples of intestinal contents from broilers, *E. coli* with ESC-resistance was isolated from 34 (11%) of 300 samples and a transferable gene coding for ESC resistance was detected in 10 isolates, i.e. 3% of the samples. All of these were $ESBL_A$ and carried $bla_{CTX\text{-}M\text{-}1}$. The remaining 24 isolates had an AmpC phenotype and genome sequencing of these isolates revealed mutations causing hyperproduction of AmpC beta-lactamases in 23 of them. All but one of the 23 isolates had a shift from C to T at position 42, whereas the remaining isolate had a shift from T to A at position 32. The last isolate carried $bla_{TEM\text{-}1}$, but apart from that no known mechanisms explaining the ESC resistance were detected in this isolate. Carbapenem resistant *E. coli* was not isolated from any sample.

Seven of the ten isolates with transferable ESC-resistance were also resistant to sulphonamides and tetracycline. This was also the only resistance apart from resistance to beta-lactams, including ESCs detected among the 34 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 the current method and the one used from 2010 (i.e. by direct culturing on MacConkey agar with cefotaxime, for details on methodology see Material and methods, resistance in bacteria from animals). 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 recently described (Nilsson et al., 2020), see also In focus: ESBL in broiler breeding animals 2010-2020.

Figure 4.1. Proportion (%) of samples from broilers positive for *Escherichia coli* with $ESBL_A$ or $ESBL_M$ from 2010 to 2020. The number of samples each year varies (n=100-302, 2020 n=300).



The 306 samples of broiler meat comprised of fresh meat originating both from Sweden (n=284) and other EU countries (n=22). In total, *E. coli* with ESC-resistance was isolated from 29 (9%) of the samples. Separated by the origin of the meat, *E. coli* with ESC-resistance was isolated from 22 (8%) of the samples of Swedish origin (Table 4.1) and 7 (32%) of the samples originating from other countries within EU.

A transferable gene coding for ESC resistance was detected in 14 of the isolates, which equals 5% of the samples. Out of the 22 isolates from samples of Swedish origin, 7 isolates (which equals 2% of the samples) carried a transferable gene. Six of the isolates were $ESBL_A$ and carried the gene $bla_{CTX\text{-}M\text{-}1}$ whereas the last isolate was $ESBL_M$ and carried the genes $bla_{CMY\text{-}2}$ (Table 4.1). Out of the 7 isolates from samples originating from other countries within EU, all (which equals 32% of the samples) carried a transferable gene. Two isolates were $ESBL_A$ and carried the gene $bla_{SHV\text{-}12}$, four isolates were $ESBL_M$ and carried the gene $bla_{CMY\text{-}2}$, and one isolate had an $ESBL_A$+$ESBL_M$-phenotype and carried both the genes $bla_{SHV\text{-}12}$ and $bla_{CMY\text{-}2}$. Carbapenem resistant *E. coli* was not isolated from any sample of broiler meat.

Among the 29 isolates with resistance to ESCs, 10 isolates were resistant also to other substances besides beta-lactams. All of these carried transferable genes responsible for the ESC resistance. Of the ten isolates, nine were resistant to tetracycline, seven to sulphonamides, four to quinolones and two were resistant to trimethoprim. All but one of the ten isolates were resistant to at least two antibiotics besides beta-lactams, i.e. multiresistant.

Escherichia coli with ESC-resistance was not isolated from any of the 45 samples of caecal content from healthy turkeys. Carbapenem resistant *E. coli* was also not isolated from any sample.

Companion animals and horses

In Svarm, there are no recurring active screenings for ESBL-producing Enterobacterales (previously Enterobacteriaceae) in healthy companion animals or horses. However, the occurrence of such bacteria in healthy dogs was investigated in a project in 2017 and 2018 and 3 out of 325 dogs were positive for *E. coli* with $ESBL_A$. See In focus: Screening of healthy dogs for carriage of ESBL producing Enterobacterales (previously Enterobacteriaceae) and methicillin-resistant coagulase positive staphylococci for further details. The results of this and other 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 (previously Enterobacteriaceae) free of charge for referring laboratories. During 2020, 57 submitted isolates of Enterobacterales (previously Enterobacteriaceae) 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=8), dogs (n=25) 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 (59%) and gentamicin (53%). Resistance to quinolones and tetracycline were also common traits.

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	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	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	2019	300	39	8	3			4	3		1			
Pigs	Meat	2019	254	1	1	<1								1	
Pigs	Intestine	2017	241	29	9	4			6	2		1			
Pigs	Meat	2017	228	0	0	0									
Pigs	Intestine	2015	303	35	4	1				1		2			1
Pigs	Meat	2015	286	1	1	<1						1			
Pigs	Intestine	2011	184	9	3	2		1		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 $bla_{CTX\text{-}M\text{-}1}$. [b]CIT-group, five caecal and three meat isolates were sequenced and possessed the gene $bla_{CMY\text{-}2}$. [c]One isolate carried both an $ESBL_A$ and an $ESBL_M$ gene. [d]CIT-group, all isolates from broilers or broiler meat with a CIT-group enzyme in other years possessed the gene $bla_{CMY\text{-}2}$. [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, 2008-2020.

Animal species	Beta-lactamase group	Beta-lactamase gene	Bacterial species	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
CATS	**All**	**All**	**Enterobacterales**		**1**	**3**	**3**			**1**	**2**	**2**	**5**	**3**	**4**	**8**
	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-16	*Escherichia coli*							1						
		CMY-2 + CTX-M-65	*Escherichia coli*										1	1		
		CMY-2 + SHV-28	*Klebsiella pneumoniae*													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
			Klebsiella pneumoniae			1	1									
	CTX-M-9	CTX-M-14	*Escherichia coli*											1	1	
			Kluyvera sp.				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**	**25**
	CIT	CMY-2	*Escherichia coli*			1	9	4	5	5	6	5	4	9	5	5
			Klebsiella pneumoniae								1					
			Proteus mirabillis				1				2	2				
		CMY-2 + CTX-M-27	*Escherichia coli*										1			
		CMY-2 + CTX-M-15 + SHV-67	*Klebsiella pneumoniae*													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	1	2
		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
			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									
	CTX-M-9	CTX-M-9	*Escherichia coli*				1	2	1	1						
		CTX-M-14	*Escherichia coli*								5	5	2	1		
			Klebsiella pneumoniae								1			1		
		CTX-M-27	*Escherichia coli*				3		1	1	1	1	3		2	4
		CTX-M-65	*Escherichia coli*													1
			Proteus mirabillis													1
	DHA	DHA-1	*Escherichia coli*											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									3	
HORSES	**All**	**All**	**Enterobacterales**	**2**	**5**	**24**	**16**	**6**	**9**	**8**	**14**	**18**	**32**	**22**	**14**	**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			
			Enterobacter spp.						1							
			Escherichia coli		2	9	8	3	3	2	3	5	13	6		2
			Klebsiella oxytoca							1						
			Serratia odorifera			1										
		CTX-M-15	*Escherichia coli*		1	1						1			3	
			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	2	18
			Enterobacter spp.		1	3	5	3	3							
			Escherichia coli	2		2	2					3	6	6	1	1
			Escherichia hermannii			1										
			Escherichia species												1	
			Klebsiella oxytoca						2		1	1	3			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									4	
			Klebsiella pneumoniae			5										

ESBL in broiler breeding animals 2010-2020

The first time that broilers were screened for carriage of *Escherichia coli* with resistance to extended spectrum cephalosporins was in 2010. It was then discovered that a large proportion of broilers in Sweden were colonized with ESBL-producing *E. coli* (Figure 1).

Following this finding, the National Veterinary Institute (SVA), in cooperation with the Swedish Poultry Meat Association and the two broiler breeding companies in Sweden started to investigate the sources and reasons for the high prevalence. Extended spectrum cephalosporins are not used at all for broilers or broiler breeders in Sweden, and the use of other antibiotics for broilers is low, with generally less than 1% of raised flocks being treated each year. Selection by use of antibiotics was not considered a likely cause. Instead, it was hypothesised that the high occurrence was due to transfer from higher levels in the production pyramid.

As of August 2010, samples of paper linings from all shipments of breeders imported into Sweden by the companies associated to the Swedish Poultry Meat Association have been cultured for ESBL-producing *E. coli* using selective methods. Initially all samples were cultured on MacConkey agar with cefotaxime (1 mg/L) after pre-enrichment in MacConkey broth with cefotaxime (1 mg/L), but from late June 2015, the pre-enrichment was changed to buffered peptone water without antibiotics. The investigations were funded by the Swedish Board of Agriculture and SVA.

From August 2010 to December 2020, 1 430 samples of paper linings from breeders originating from 134 shipments were cultured. At least one sample per breeder line and source farm was sampled, which resulted in 4 to 26 samples per shipment. In total, ESBL-producing *E. coli* was isolated from 195 samples (14%) from 43 (32%) of the shipments. The proportion of positive samples and shipments has varied between the years (Figure 2), but as of 2017 to 2020 only one shipment has been positive for ESBL-producing *E. coli*. In general, there has been a decreasing trend since 2010 except for a large increase in positive shipments and samples in 2015. The reason for this temporary increase remains unknown but it was not due to the shift in methodology in June 2015 as the increase was noticed already at the end of 2014, i.e. before the change in methodology. Most of the isolates carried genes belonging to the bla_{CMY}-group (n=146). The remaining isolates carried a gene in the $bla_{CTX\text{-}M\text{-}1}$ -group (n=36), or bla_{SHV} -group (n=7). Six isolates from two shipments were lost and not available for confirmation. However, the occurrence of $ESBL_M$-producing *E. coli* carrying genes belonging to the bla_{CMY}-group in the birds from these shipments has been confirmed in subsequent sampling in these flocks.

The exact reasons for the decrease of ESBL-producing *E. coli* in imported breeding stocks remain unsolved. However, since 2010, the situation regarding ESBL-producing *E. coli* in the broiler production and potential measures to improve the situation have been discussed regularly between experts from SVA and the Swedish stakeholders, and with the international breeding companies. Possibly, this dialogue that included requests by the Swedish companies that acquired breeders should be free from ESBL-producing *E. coli* and feedback on results have contributed to motivate and encourage the international companies to work towards reducing the occurrence among breeders.

Figure 1. Proportion (%) of caecal samples from broilers positive for ESBL-producing *E. coli* from 2010 to 2020.

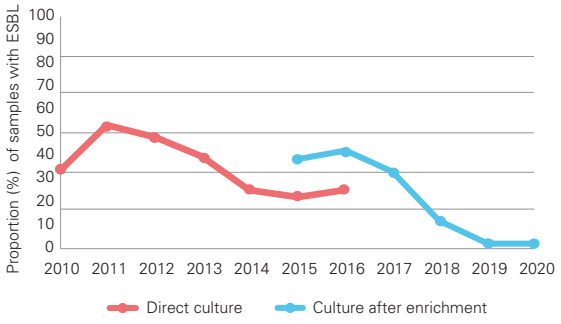
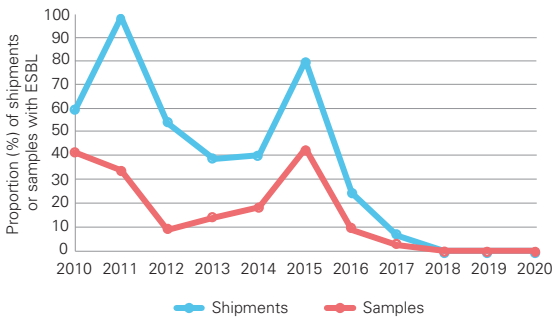


Figure 2. Proportion (%) of shipments and paper lining samples from imported breeders positive for ESBL-producing *E. coli* from August 2010 to December 2020.



This In focus is a summary of Nilsson et al. (2020), updated with data for 2020. Further description of the study and a list of references can be found in the paper.

Reference

Nilsson O, Börjesson S, et al. 2020, Decreased detection of ESBL- or pAmpC-producing *Escherichia coli* in broiler breeders imported into Sweden. *Acta Vet Scand*, 62:33.

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 and horses) and Table 4.4 (companion animals).

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 just over 1300 isolates have been tested up to and including 2020. 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 2020 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, using bulk-milk samples and pooled swabs, were screened for occurrence of MRSA with no positive samples found (Persson et al., 2021).

Companion animals and horses

Up to and including 2020, a total of 162 cases of MRSA in companion animals and horses have been confirmed. These include 59 dogs, 26 cats, 2 rabbits and 75 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. In 2017-2018 a study on 325 healthy dogs showed no detection of MRSA (see In focus: Screening of healthy dogs for carriage of ESBL producing Enterobacterales (previously Enterobacteriaceae) and methicillin-resistant coagulase positive staphylococci). Screening studies in horses have been performed twice, in 2007 and 2010, with one positive sample in 2007.

In 2020, MRSA was detected in clinical samples, mainly from wound infections, from five dogs and four cats. Since the first finding of MRSA in companion animals, *spa*-type t032 has been most common, but during the most recent years the identified *spa*-types have varied (Table 4.4).

In 2020 MRSA was isolated from 27 horses, an increase compared to previous years (2007-2019) when between one and nine cases were notified per year (Table 4.3). The rise could partly be explained by two separate outbreaks including 18 horses (11 and 7, respectively) at two equine hospitals. Historically has MRSA *spa*-type t011, CC398, been dominating among horses in Sweden. However, in 2020 14 of the 27 isolates were of *spa*-type t1971, ten were of *spa*-type t011, one t1257, one t088, and one t843. All the mentioned *spa*-types have also been detected more or less frequently in samples from humans and the *spa*-type t843 with *mecC* also in hedgehogs and cows in Sweden. For details of the *spa*-types and the outbreaks, see In focus: Methicillin resistant *Staphylococcus aureus* (MRSA) in horses.

Wild animals

High occurrence of *mecC*-MRSA has been described in hedgehogs both in Sweden, 64%, and Denmark, 61% (Bengtsson et al., 2017 and Rasmussen et al., 2019). It has been suggested that *mecC*-MRSA could have its origin from wildlife (Becker et al., 2014), and the high occurrence in European hedgehogs could indicate that hedgehogs could be this potential reservoir. During 2019 five additional hedgehogs were described to carry *mecC*-MRSA in an ongoing research project.

Table 4.3. Farm animals and horses. Isolates of methicillin-resistant *Staphylococcus aureus* (MRSA) in Swedish horses, pigs, cows, goats, and sheep up to and including 2020. 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**	**Ery**	**Tet**	**Fus**	**Gen**	**Cip**	**Tmp**	**Chl**	**Lin**	***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	2	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	2013	1	R	≤0.25	1	64	1	>64	1	>32	16		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	2	R	≤0.25	>32	32	≤0.25	>16	>4	>8	8	≤1-2	t1257	*A*
Horse	2018	2	R	0.25	0.5	>16	≤0.5	>16	≤0.25-0.5	>32	8	2	t011	*A*
Horse	2018	5	R	≤0.12-0.25	≤0.25-0.5	>16	≤0.5	>16	8->8	>32	≤4-8	2	t011	*A*
Horse	2019	1	R	0.25	>8	>16	≤0.5	>16	>8	>32	8	2	t1971	*A*
Horse	2019	1	R	≤0.12	>8	>16	≤0.5	>16	>8	>32	8	2	t1257	*A*
Horse	2020	13	R	≤0.12-0.25	0.5-1	>16	≤0.5	>16	>8	>32	≤4-16	≤1-4	t1971	*A*
Horse	2020	1	R	≤0.12	>8	>16	≤0.5	>16	>8	>32	8	≤1	t1971	*A*
Horse	2020	10	R	≤0.12-0.25	0.5-1	>16	≤0.5	>16	8->8	>32	≤4-16	2-4	t011	*A*
Horse	2020	1	R	≤0.12	>8	>16	≤0.5	>16	>8	>32	16	4	t1257	*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*
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	3	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	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. Companion animals. Isolates of methicillin-resistant *Staphylococcus aureus* (MRSA) in Swedish dogs, cats, and rabbits up to and including 2020. All isolates were positive for the *mecA* or *mecC* and *nuc* genes, *mec*-gene showed in bold indicates PVL-positivity. Shaded areas indicate MIC above EUCAST ECOFF. One isolate from a cat, in 2013 and four from dogs in 2017, 2018 and 2019 respectively were not available for further testing and are 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**
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	>32	≤0.5	0.5	≤0.5	>4	8	4		t020	*A*
Dog	2010	1	R	≤0.25	≤0.25	≤0.5	8	1	0.5	2	8		t002	*A*
Dog	2013	1	R	≤0.25	>32	16	0.25	2	0.25	2	8		t127	*A*
Dog	2013	1	R	≤0.25	1	≤0.5	0.5	≤0.5	0.5	4	8		t304	*A*
Dog	2013	1	R	≤0.25	1	≤0.5	0.25	≤0.5	0.5	2	8		t127	*A*
Dog	2013	1	R	0.5	1	1	1	1	>4	4	8		t032	*A*
Dog	2013	1	R	≤0.25	0.5	≤0.5	0.5	≤0.5	0.5	>32	8		t223	*A*
Dog	2014	1	R	≤0.25	1	16	0.5	1	0.5	4	8		t325	*A*
Dog	2014	1	R	≤0.25	>32	≤0.5	≤0.06	≤0.5	0.25	1	8		t002	***A***
Dog	2015	1	R	0.5	≤0.25	≤0.5	0.5	≤0.5	0.25	≤0.5	8		t373	*C*
Dog	2015	3	R	≤0.25	>32	16-32	≤0.06-0.5	≤0.5	0.12-0.25	1-2	4-8		t127	*A*
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	1	R	≤0.25	>32	16	0.12	≤0.5	0.25	1	4		t177	*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	≤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	≤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	>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	>4	0.5	4	2	t022	*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	8	>4	>8	8	2	t891	***A***
Dog	2018	2	R	≤0.12-0.25	>8	>16	≤0.5	≤1	≤0.25-0.5	≤2	≤4-8	≤1-2	t127	*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	≤0.5	≤0.5	≤1	>8	≤2	16	2	t003	*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	>8	>16	≤0.5	≤1	≤0.25	≤2	8	2	t127	*A*
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	2020	1	R	>4	>8	≤0.5	≤0.5	≤1	>8	≤2	8	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*
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	>4	≤1	≤0.25	≤2	8	2	t132	*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	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	16	2	t843	*C*
Cat	2020	1	R	≤0.12	0.5	≤0.5	≤0.5	≤1	0.5	≤2	8	2	t359	*A*
Cat	2020	1	R	0.25	0.5	≤0.5	≤0.5	≤1	≤0.25	≤2	8	2	t843	*C*
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 aureus* (MRSA) in horses

Methicillin resistant *Staphylococcus aureus* (MRSA) in animals became notifiable in Sweden in 2008 (SJVFS 2021:10 and previously SJVFS 2012:24 with amendments). The monitoring of MRSA in horses has since then primarily been passive with clinical sampling of infected horses. In addition, two screening studies of non-infected horses (active monitoring) has been performed. One study in 2007, the year before MRSA became notifiable, with one positive sample and another study in 2010 with no findings of MRSA. Additionally, some cases have been notified after tracing in connection to outbreaks. The nostrils have been sampled in the screening studies and the tracing.

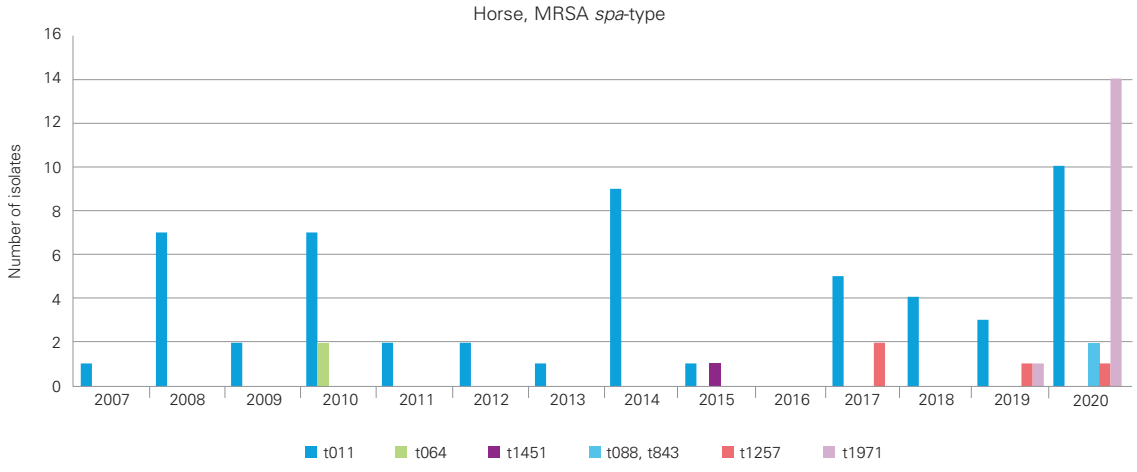
In 2020 the number of MRSA isolated from horses in Sweden increased. Twenty-seven MRSA cases were verified, compared to 1-9 cases per year (or 48 cases in total) between 2007 and 2019. The high number of MRSA cases in 2020 was partly explained by an outbreak of *spa*-type t1971 at one equine hospital (11 cases), and an outbreak of *spa*-type t011 at another equine hospital (7 cases).

Between 2007 and 2019 MRSA *spa*-type t011, clonal complex (CC) 398, has dominated with a total of 41 isolates compared to seven isolates of other *spa*-types (Figure 1). However, in 2020 the most common *spa*-type was t1971, in 14 of 27 cases (Figure 1), although *spa*-type t011 was still common (10/27). Three single cases of other *spa*-types were also noticed, one *spa*-type t1257 (previously also found in humans in Sweden), one t088 (previously also found in humans in Sweden), and one t843 (with the *mecC* gene, previously found also in humans, hedgehogs and cows in Sweden).

In the outbreak with *spa*-type t1971 eight horses suffered from post-operative wound infections or thrombophlebitis. Three more horses visiting the hospital during the outbreak period, were sampled in their nostrils at home and found positive, but without clinical infection, with the same *spa*-type. A fourth horse found positive with the same *spa*-type was sampled due to a long lasting, non-healing pressure sore. This horse had visited the outbreak hospital one year earlier (2019). The outbreak hospital also had a single case of *spa*-type t1971 in 2019 (Figure 1), i.e., there might have been a small outbreak already in 2019. In addition, at an equine clinic in another part of the country two horses suffering from traumatic wounds in need of surgery were sampled and found positive for MRSA *spa*-type t1971. No obvious epidemiological link was noticed between the two cases and the outbreak. However, as tracing is not required by the authorities no thorough tracing was carried out. *Spa*-type t1971 has not been found in any other animal species in Sweden, but there have been rare notifications in humans, in total three cases of which two cases were reported as domestic (data from the Public Health Agency of Sweden).

Spa-type t1971 belongs to the multilocus sequence type 612 (ST612). The *spa*-type t1257, detected as single cases in horses in Sweden (four cases, Figure 1), is also included in the ST612 complex. From South Africa, the ST612 complex and mainly *spa*-type t1257 has been reported as a common cause of bacteriaemia in humans (Jansen van Rensburg et al., 2012). According to figures from the Public Health Agency of Sweden, ten cases of

Figure 1. The number of isolates and *spa*-type of notified cases of methicillin-resistant *Staphylococcus aureus* in horses in Sweden since the first finding in 2007.



t1257, of which eight domestic, have been reported between 2009 and 2019. In Australia ST612 has been sporadically isolated from humans, as well as from horses and veterinarians working in equine practice (Murphy et al., 2019). In the study from Australia was *spa*-type t1257 detected, but not t1971. The authors claim that in Australia there might be one equine-associated lineage and another lineage related to South Africa. ST612 belongs to the CC8, where also ST8 USA300 MRSA and related USA500 could be found. USA300 is considered a pandemic clonal lineage of MRSA (Strauß et al., 2017). Both humans and horses travel a lot and bacteria mutates, so the emergence of new MRSA-variants would not be surprising.

Of interest is that ST612 has a particular phenotype, resistance to rifampicin (Jansen van Rensburg et al., 2012), as did the Swedish t1971 and t1257 equine isolates. According to Jansen et al. (2012) rifampicin is frequently used to treat tuberculosis in humans in South Africa. The authors suggest that this use has driven the resistance to rifampicin. The theory is supported by a study of Sekiguchi et al. (2006) in two Japanese hospitals, where the measured prevalence of rifampicin-resistant MRSA was significantly higher in tuberculosis wards compared to non-tuberculosis wards. In equine medicine rifampicin is primarily used for treatment of foals with pneumonia caused by *Rhodococcus hoagii* (previously *R. equi*).

The outbreak of MRSA *spa*-type t011 in 2020 included seven horses with post-operative infections or thrombophlebitis. A substantial proportion of MRSA in horses in Europe is of this specific *spa*-type. Reports of outbreaks and sporadic cases as well as screening studies has pointed out t011 as dominating *spa*-type in horses (Cuny et al., 2008; Van den Eede et al., 2009; van Duijkeren et al., 2010; Van den Eede et al., 2013; Vincze et al., 2014; Cuny et al., 2016). The *spa*-type has up to 2020, as mentioned above, dominated also in the Swedish passive surveillance of infected cases (41 of 48 cases) (see previous Swedres-Svarm reports). Genetic analyses of t011 isolates in Denmark and Germany have shown that the isolates of MRSA t011 from horses differs from MRSA t011 isolated from pigs (Islam et al., 2017, Cuny et al., 2015), and it is suggested that horses have their own variant of MRSA *spa*-type t011. This could be important knowledge for the evaluation of transmission risks between animal species and further on to humans.

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Methicillin-resistant *Staphylococcus pseudintermedius* (MRSP)

In 2020, there were 49 MRSP cases reported to the Swedish Board of Agriculture (Figure 4.2). This number is around the same level as in previous years. Isolates from 47 cases from dogs were available for further susceptibility testing and genome sequencing. Information on the sampling site was available for 43 cases; skin (including external ear canal) 14 cases, wounds (including surgical wounds) 22 cases and the remaining seven were isolated from various other sites. Forty-five isolates were defined as multi-resistant. For resistance phenotypes, see Table 4.5.

The results of the genome sequencing divided the isolates into 22 different multi-locus sequence types, of which ST551 was the most common type with 18 isolates. The ST551 was first detected in 2016 and was also the most common ST 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 2020 there were no isolates of this type. The other sequence types occurring in 2020: ST265 (5 isolates), ST258 (3 isolates), ST2119 (3 isolates) and single isolates of ST1296, ST121, ST181, ST282, ST413, ST730, ST742, ST826, ST934, ST1194, ST1627, ST2116-2118 and ST2120-2123.

Figure 4.2. Number of cases of methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) in Sweden 2006-2020. In 2006-2007 the numbers represent the isolates that were sent to SVA and confirmed as *mecA*-positive and from 2008 number of cases notified to the Swedish Board of Agriculture.

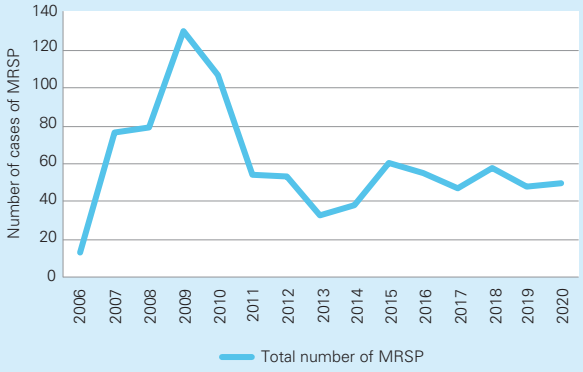


Table 4.5. Resistance phenotypes (beta-lactams excluded) of isolates of methicillin resistant *Staphylococcus pseudintermedius* (MRSP) in 2020. All isolates were positive for the *mecA* gene. Shaded areas indicate resistance.

	Antibiotic MIC (mg/L)								
Beta-lactams	Ery	Cli	Tsu[a]	Tet	Enr	Fus	Gen	Nit	Number of isolates
R	>2	>2	>4	>4	>1	>2	4->4	≤16	1
R	>2	>2	>4	>4	>1	≤0.5	4->4	≤16	25
R	>2	>2	>4	>4	>1	≤0.5	≤1	≤16	1
R	>2	>2	>4	>4	0.5	≤0.5	>4	≤16	1
R	>2	>2	>4	>4	≤0.25	1	≤1	≤16	1
R	>2	>2	>4	>4	≤0.25	≤0.5	>4	≤16	6
R	>2	>2	>4	>4	≤0.25	≤0.5	≤1	≤16	1
R	>2	>2	>4	≤0.25	≤0.25	≤0.5	>4	≤16	1
R	>2	>2	1	>4	0.5	≤0.5	>4	≤16	1
R	>2	>2	1	>4	≤0.25	>2	≤1	≤16	1
R	>2	>2	1	≤0.25	≤0.25	≤0.5	≤1	≤16	1
R	>2	>2	0.5	>4	0.5	>2	≤1	≤16	1
R	>2	>2	0.5	>4	≤0.25	2	≤1	≤16	1
R	≤0.5	≤0.5	>4	>4	≤0.25	1	≤1	≤16	1
R	≤0.5	≤0.5	>4	>4	≤0.25	≤0.5	2	≤16	1
R	≤0.5	≤0.5	0.5	>4	>1	≤0.5	4	≤16	1
R	≤0.5	≤0.5	0.5	>4	≤0.25	≤0.5	≤1	≤16	1
R	≤0.5	≤0.5	0.5	≤0.25	≤0.25	≤0.5	≤1	≤16	1
								Sum	47

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

Screening of healthy dogs for carriage of ESBL-producing Enterobacterales (previously Enterobacteriaceae) and methicillin-resistant coagulase-positive staphylococci

Background

The most recent screening for ESBL producing Enterobacterales (previously Enterobacteriaceae) and methicillin-resistant coagulase positive staphylococci (MR-CoPS) in dogs was conducted in 2012 and included 84 dogs. That study showed that one dog (1%) carried an *E. coli* with bla_{CMY-2} and that no MR-CoPS could be identified. However, later studies from other countries have shown higher prevalence of ESBL producing Enterobacterales (previously Enterobacteriaceae), but that there also appears to be a great variation in prevalence between countries and settings. Studies focusing on $ESBL_A$-producing *E. coli* have shown carriage in 2–82% of dogs, while other studies searching for ESBL -producing Enterobacterales (previously Enterobacteriaceae), including *E. coli*, have shown carriage rates of 9–22%. In the case for MR-CoPS occurrence appears to be generally lower with 0–3% positive dogs being reported.

Objective

The National Veterinary Institute (SVA), in collaboration with AniCura, Sweden wanted to establish the prevalence and types of ESBL producing Enterobacterales (previously Enterobacteriaceae) and MR-CoPS among healthy dogs in Sweden.

Material and Methods

The study was conducted from May 2017 to May 2018, with samples collected from 325 dogs of >1 year of age at eight AniCura animal hospitals. Sampling was conducted during visits for vaccinations or other standard procedures for healthy dogs e.g., x-rays of hips or elbows, blood donations. From each dog, one rectal swab for ESBL producing Enterobacterales (previously Enterobacteriaceae) isolation, and one pooled swab from labial commissure, pharynx, perineum, and wounds (if present) for MR-CoPS, were collected. Both swabs were sent to one of five participating AniCura laboratories for cultivation and identification of ESBL-producing Enterobacterales (previously Enterobacteriaceae) and MR-CoPS. Suspected isolates were sent to SVA for confirmation of species using MALDI-TOF. Presumptive ESBL-producing Enterobacterales (previously Enterobacteriaceae) isolates were then confirmed phenotypically and tested for antibiotic susceptibility, while MR-CoPS were confirmed by PCR. Verified isolates, were subjected to genome-sequencing and bioinformatic analyses.

Results and comments

Of the 325 dogs screened, 3 were identified to carry ESBL-producing *E. coli*, 0.9% (0.3–2.7%, 95% confident interval). The *E. coli* isolates carried $bla_{CTX-M-1}$, $bla_{CTX-M-27}$, and $bla_{CTX-M-55}$, and belonged to three different MLSTs, ST4496, ST354 and ST131. The ST131- $bla_{CTX-M-27}$ was shown to belong to serotype O25:H4, which is a pandemic strain in humans. The three isolates were also multi-resistant, i.e., resistant to >2 antibiotic classes, and carried multiple genes encoding antibiotic resistance. Had these strains been the causative agent of an infection, there would have been non or only a limited number of treatment options available due to legalisation and antibiotic treatment policies in Sweden.

MR-CoPS could not be isolated from any of the dogs. However, the lack of MR-CoPS was not unforeseen as earlier studies has described no or low occurrence of MR-CoPS in healthy dogs.

Conclusions

Occurrence of ESBL-producing Enterobacterales (previously Enterobacteriaceae) and MR-CoPS remains rare among healthy dogs in Sweden. In addition, based on molecular typing the results indicates that the three ESBL-producing *E. coli* isolates identified in the current study could have a human origin.

This In focus is a summary of Börjesson et al. (2020). Further description of the study and a list of references can be found in the paper.

Reference

Börjesson S, Gunnarsson L, et al. 2020, Low occurrence of extended-spectrum cephalosporinase producing Enterobacteriaceae and no detection of methicillin-resistant coagulase-positive staphylococci in healthy dogs in Sweden. *Acta Vet Scand*, 62:18.

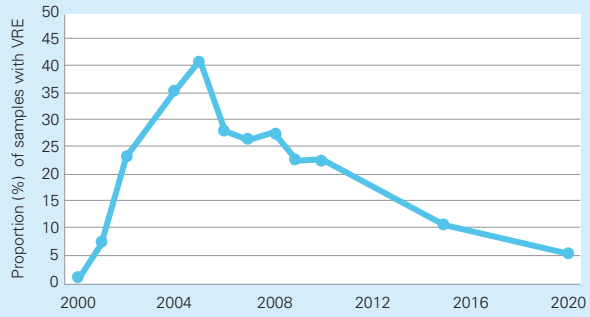
Vancomycin-resistant enterococci (VRE)

Broilers

During 2020, samples of intestinal contents from healthy broilers (n=300) were screened for vancomycin resistant enterococci (VRE) by culture on vancomycin supplemented media (16 mg/L). Presumed enterococci were species identified with MALDI-TOF MS and subsequently typed with genome sequencing (for details see Material and methods, resistance in bacteria from animals).

Vancomycin resistant *E. faecium* with the *vanA* gene was isolated from 17 (6%) of the samples (Figure 4.3). This is the lowest occurrence observed since 2000. The difference between 2015 and 2020 is however not statistically significant (X^2, p=0.07). The reason(s) for this decrease in occurrence is not known.

Figure 4.3. Proportion (%) of samples of intestinal content from healthy broilers positive for VRE from 2000 to 2002, 2004 to 2010, 2015, and 2020 when cultured on vancomycin supplemented media (16 mg/L). The number of samples cultured each year varies (n=99-351, 2020 n=300).



All VRE isolates in 2020 were resistant to vancomycin (MIC >128 mg/L), teicoplanin (MIC 64 mg/L), narasin (MIC 4-8 mg/L) and erythromycin (MIC 8-16 mg/L) but susceptible to all other substances tested (i.e. ampicillin, ciprofloxacin, daptomycin, gentamicin, chloramphenicol, linezolid, tetracycline, and tigecycline). Typing using genome sequencing showed that all the isolates belonged to ST310 which has previously been described to dominate among broilers in Sweden (Nilsson et al., 2009).

Historically, vancomycin resistant *E. faecium* with the *vanA* gene has been isolated from intestinal content of healthy broilers but not from other farm animals studied in Svarm. For further information regarding VRE in broilers see Svarm 2011; Vancomycin resistant enterococci (VRE) in Swedish broiler production – a summary.

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 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 almost invariably *S.* Typhimurium and susceptible to all tested antibiotics. Therefore, only the first 5 and 25 index cases of *Salmonella* from wild birds and cats, respectively, and thereafter every eighth case is serotyped. For details on methodology, see Materials and methods, resistance in bacteria from animals.

All animals 2020

A total of 135 *Salmonella* isolates were tested in 2020, all belonging to the species *S. enterica* and with two subspecies represented, subsp. *enterica* (114 isolates) and subsp. *diarizonae* (21 isolates). The isolates were shared into 22 different serovars with *S.* Typhimurium as the most dominant serovar with 67 isolates, including two isolates belonging to the monophasic *S.* Typhimurium variant type 4,[5],12:i:- (Table 4.6). Some isolates belonged to exotic and unusual serovars, such as *S.* Lomita, *S.* Umbilo and *S.* Volkmarsdorf.

The highest number of isolates were from pigs, 30 isolates, which is more than usual, belonging to 10 different serovars. A reason for this is that in 2020 there were several outbreaks of *Salmonella* in pig herds, dominated by *S.* Typhimurium. It is notable that two cases of *S.* Choleraesuis occurred. This serovar, which is host adapted to pigs and often causes severe disease outbreaks in infected farms, has not been found in Swedish pig production for many years. It is notable that the same serovar was also found in 12 wild boars. A possible

epidemiological connection between the cases in pig farms and the wild boar population is currently under investigation. However, it emphasizes wildlife as a reservoir of zoonotic pathogens.

Among the isolates from wild birds, the *S.* Typhimurium isolates were from siskins, sea gulls, a finch, and a bullfinch, whereas the exotic serovar *S.* 4,5:-:1,5 was from a woodpecker. All *S.* Choleraesuis isolates from wild mammals were from wild boar, and so was the *S.* Coeln, two *S. enterica* subsp. *diarizonae* 38:r:-, the *S.* 4:-:1,5, one *S.* Enteritidis, two *S.* Newport, and two *S.* Typhimurium. Thus, with 21 isolates of seven different serovars, wild boar was the dominant host for *Salmonella* in wildlife animals in 2020 and emphasizes the significance of wild boars as reservoir for *Salmonella*. The three other wild mammals were a squirrel, a wolverine and a porpoise.

From cattle, 21 isolates were found, shared into eight serovars. As for pigs, *S.* Typhimurium including the monophasic variant dominated followed by the host adapted serovar *S.* Dublin (Table 4.6).

The subspecies *diarizonae* is usually associated with reptiles, but none of the subspecies *diarizonae* isolates in 2020 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. Fourteen isolates from sheep and one from a goat belonged to this serovar. The six other subsp. *diarizonae* isolates were from a sqirrel, two wild boars, a pig and two cattle. All subsp. *diarizonae* isolates were susceptible to all antibiotics tested.

Distributions of MICs and resistance for all isolates are presented in Table 4.7 and for the subset *S.* Typhimurium in Table 4.8. No interpretation was done for colistin. In previous years, an ECOFF of 2 mg/L has been used, but it has been realized that there are differences in MIC distributions between serovars, and EUCAST does no longer indicate an ECOFF for *Salmonella*. However, all 22 isolates (Table 4.7) that had an MIC of 4 or 8 mg/L 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. On the other hand, an ECOFF of 16 mg/L has been defined for azithromycin and using this ECOFF, a single isolate, a *S.* Agona, was found resistant (Table 4.9).

The majority of the isolates (123 of 135; 91%) were susceptible to all antibiotics tested, only 12 isolates being resistant to one or more compounds. Of these, the two *S.* Enteritidis isolates were resistant to just ampicillin and quinolones, respectively.

Table 4.6. Serovar distribution and number of *Salmonella* isolates (n=135) tested for antimicrobial susceptibility, 2020.

Serovar	Cattle	Pig	Poultry	Sheep	Goat	Horse	Cat	Dog	Wild birds	Wild mammals	Total
S. Agona		1						1			**2**
S. Bovismorbificans								1			**1**
S. Choleraesuis	1	2								12	**15**
S. Coeln										1	**1**
S. Derby	1	3									**4**
S. Dublin	5										**5**
S. enterica subsp. *diarizonae* 38:r:-		1								3	**4**
S. enterica subsp. *diarizonae* 38:r:z	2										**2**
S. enterica subsp. *diarizonae* 61:-:1,5				14	1						**15**
S. enterica subsp. *enterica* 4:a:-										1	**1**
S. enterica subsp. *enterica* 4,5:-:1,5									1		**1**
S. enterica subsp. *enterica* 4:-:1,5										1	**1**
S. Enteritidis		1	1							2	**4**
S. Livingstone		1									**1**
S. Lomita							1				**1**
S. London		1									**1**
S. Newport		3								2	**5**
S. Reading	1										**1**
S. Stanley		1									**1**
S. Typhimurium	7	16	7			2	14	5	12	2	**65**
S. Typhimurium, monophasic variant	2										**2**
S. Umbilo	1										**1**
S. Volkmarsdorf	1										**1**
Total	**21**	**30**	**8**	**14**	**1**	**2**	**15**	**7**	**13**	**24**	**135**
% of total	**16**	**22**	**6**	**10**	**1**	**1**	**11**	**5**	**10**	**18**	**100**

This *S.* Enteritidis isolate from poultry was the only isolate that was resistant to quinolones. A *S.* Typhimurium isolate was resistant to sulphonamides and another one to sulphonamides and trimethoprim. Remaining isolates – six *S.* Typhimurium, one *S.* Agona and one *S.* Derby were multiresistant, all of them being resistant to sulphonamides and tetracycline, and most of them also to ampicillin and chloramphenicol.

The *S.* Agona isolate from a pig displayed an unusual resistance profile, being resistant to sulphonamides, trimethoprim, tetracyclines, chloramphenicol, gentamicin, and – as the only isolate – to azithromycin. *Salmonella* has been tested against azithromycin since 2018, but hitherto, this isolate is the only one that has demonstrated resistance to this compound.

Table 4.7. Distribution of MICs and resistance (%) in *Salmonella enterica* (n=135) from all animals, 2020.

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	1024	>1024
Ampicillin	6							91.1	3.0						5.9				
Azithromycin	1								9.6	63.7	25.1	0.7			0.7				
Cefotaxime	0					100													
Ceftazidime	0						100												
Chloramphenicol	5										94.1	1.5			0.7	4.4			
Ciprofloxacin	1	80.7	18.5		0.7														
Colistin	NA[a]							69.6	12.6	17.0	0.7								
Gentamicin	1						91.1	8.1						0.7					
Meropenem	0		100																
Nalidixic acid	1									97.8	1.5				0.7				
Sulphamethoxazole	7										28.1	41.5	23.0						7.4
Tetracycline	6								94.1				3.7		2.2				
Tigecycline	0					100													
Trimethoprim	4					86.7	8.9							4.4					

[a]Not applicable as an ECOFF is currently not defined for the genus.

Table 4.8. Distribution of MICs and resistance (%) in *Salmonella* Typhimurium, including monophasic variants (n=67) from all animals, 2020.

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	1024	>1024
Ampicillin	9							88.1	3.0						9.0				
Azithromycin	0								11.9	80.6	7.5								
Cefotaxime	0					100													
Ceftazidime	0						100												
Chloramphenicol	7										91.0	1.5				7.5			
Ciprofloxacin	0	83.6	16.4																
Colistin	NA[a]							55.2	19.4	25.4									
Gentamicin	0						86.6	13.4											
Meropenem	0		100																
Nalidixic acid	0									98.5	1.5								
Sulphamethoxazole	12										1.5	50.7	35.8						11.9
Tetracycline	9								91.0				7.5		1.5				
Tigecycline	0					100													
Trimethoprim	6					88.1	6.1							6.1					

[a]Not applicable as an ECOFF is currently not defined for the genus.

Table 4.9. MICs (mg/L) in the 12 *Salmonella enterica* isolates resistant to one or more antibiotics, 2020. Shaded fields indicate resistance.

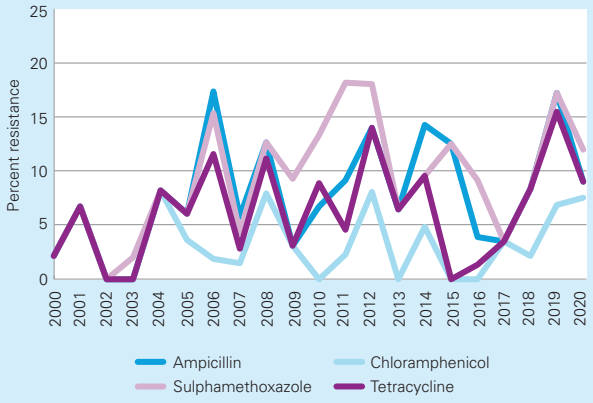
Source	Serovar	Sul	Tmp	Cip	Tet	Mero	Azt	Nal	Ctx	Chl	Tgc	Caz	Col	Amp	Gen
Pig	Agona	>1024	>32	≤0.015	>64	≤0.03	>64	≤4	≤0.25	>128	≤0.25	≤0.5	≤1	≤1	>32
Pig	Derby	>1024	>32	≤0.015	>64	≤0.03	4	≤4	≤0.25	≤8	≤0.25	≤0.5	≤1	>64	≤0.5
Pig	Enteritidis	16	≤0.25	≤0.015	≤2	≤0.03	4	≤4	≤0.25	≤8	≤0.25	≤0.5	8	>64	≤0.5
Poultry	Enteritidis	≤ 8	≤0.25	0.12	≤2	≤0.03	4	>128	≤0.25	≤8	≤0.25	≤0.5	≤1	≤1	≤0.5
Cattle	Typhimurium[a]	>1024	>32	≤0.015	>64	≤0.03	4	≤4	≤0.25	≤8	≤0.25	≤0.5	≤1	>64	≤0.5
Pig	Typhimurium	>1024	≤0.25	≤0.015	32	≤0.03	8	≤4	≤0.25	>128	≤0.25	≤0.5	≤1	>64	≤0.5
Pig	Typhimurium	>1024	≤0.25	≤0.015	32	≤0.03	8	≤4	≤0.25	>128	≤0.25	≤0.5	≤1	>64	≤0.5
Pig	Typhimurium	>1024	≤0.25	≤0.015	32	≤0.03	4	≤4	≤0.25	>128	≤0.25	≤0.5	≤1	>64	≤0.5
Pig	Typhimurium	>1024	≤0.25	≤0.015	32	≤0.03	4	≤4	≤0.25	>128	≤0.25	≤0.5	≤1	>64	≤0.5
Pig	Typhimurium	>1024	>32	0.03	32	≤0.03	4	≤4	≤0.25	128	≤0.25	≤0.5	≤1	>64	≤0.5
Pig	Typhimurium	>1024	>32	≤0.015	≤2	≤0.03	4	≤4	≤0.25	≤8	≤0.25	≤0.5	≤1	≤1	≤0.5
Pig	Typhimurium	>1024	>32	≤0.015	≤2	≤0.03	4	≤4	≤0.25	≤8	≤0.25	≤0.5	≤1	2	≤0.5

[a]monophasic

In the subset of *S.* Typhimurium, resistance has varied over the years (Figure 4.4). The variation is largely due to differences in occurrence of multiresistant strains between the7 years. However, while the resistance to ampicillin, sulphamethoxazole, and tetracycline, decreased compared to 2019, an increase was noted in resistance to isolates with chloramphenicol resistance (DT104 resistance profile).

No isolate was resistant to cefotaxime and ceftazidime (cefalosporins) or to meropenem (carbapenems) indicating that no isolates were ESBL or $ESBL_{CARBA}$.

Figure 4.4. Resistance to ampicillin, chloramphenicol, sulphamethoxazole, and tetracycline in *Salmonella* Typhimurium in all animals, 2000-2020.



Farm animals 2000–2020

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 2000-2020, isolates from the vast majority of notified incidents in major farm animals were tested in Svarm, in total 846 isolates. About half of the isolates, 413 (49%), were *S.* Typhimurium and of these 157 (38%) were from pigs, 135 (33%) from cattle, 116 (28%) from poultry and 5 (1%) from sheep.

In 2020, 32 *S.* Typhimurium were isolated from farm animals. Of these 12 were resistant to one or more compounds (Table 4.9), and 10 of these were multiresistant.

Five isolates from 2020 – all from pigs – were resistant to ampicillin, sulphonamides, tetracycline, and chloramphenicol and one of them also to trimethoprim. 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. 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.

In 2020, two of the notified incidents in farm animals involved monophasic *S.* Typhimurium, both of them from cattle. Since this variant was first found in 2006, only 15 incidents of monophasic *S.* Typhimurium had been confirmed in farm animals in Sweden up till 2019. Eight incidents had involved

only cattle, four only pigs, one only ducks, and one incident involved both cattle and poultry. In 12 of these incidents the isolates were multiresistant, while one of the isolates in 2020 was multiresistant, the other was fully susceptible. However, monophasic *S.* Typhimurium has also been found in other animal species, i.e. from five dogs, two wild birds and a horse. All five isolates from dogs and the horse isolate were multiresistant wheras the isolates from wild birds were susceptible to all antibiotics tested. Monophasic *S.* Typhimurium has spread over the last decade in many European countries and become one of the most prevalent strains. Most of these isolates display resistance to ampicillin, sulfonamides, and tetracycline which was also the case for one of the isolates from 2020, which was additionally resistant to trimethoprim (Table 4.9).

Campylobacter

The isolates of *Campylobacter jejuni* tested are from caecal content of broilers collected at abattoirs and were isolated within the framework of the Swedish Campylobacter control programme 2020. In 2020 approximately 5% of 3594 flocks were culture positive for *C. jejuni*. For details on methodology see Materials and methods, resistance in bacteria from animals. Of the 183 isolates tested, 143 (78%) were susceptible to all six antibiotics. Resistance to fluoroquinolones only (ciprofloxacin and nalidixic acid) was the most common phenotype (17%) (Table 4.10). Seven isolates (4%) were resistant to both fluoroquinolones and tetracycline.

In 2016 resistance to tetracycline was more common than usual (16%) but this year only 5% were resistant to tetracycline (Figure 4.5). The percentage of culture positive flocks was high in 2016 because of an outbreak. The probable explanation for the tetracycline resistance peak and for the increase in fluoroquinolone resistance in 2016 was spread of certain resistant (or susceptible) clones. Selection through use of antibiotics is unlikely since these substances seldom are used in broiler production in Sweden.

Figure 4.5. Ciprofloxacin, nalidixic acid and tetracycline resistance (%) in *Campylobacter jejuni* from broilers years 2001-2020. In years 2001-2002 enrofloxacin was tested instead of ciprofloxacin. The number of isolates per year has varied (n=38-183).

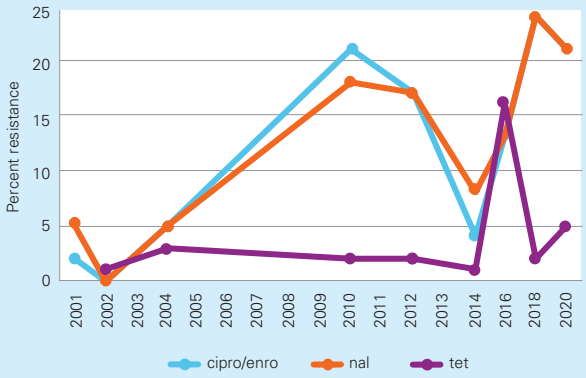


Table 4.10. Distribution of MICs and resistance (%) for *Campylobacter jejuni* from broilers, 2020.

Antibiotic	Resistance (%) n=183	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	32	64	128	>128
Ciprofloxacin	21	77.0	2.2				1.1	15.8	3.8				
Erythromycin	0				98.9	1.1							
Gentamicin	<1	2.2	19.1	60.7	17.5	0.5							
Nalidixic acid	21					45.9	30.1	3.3			6.6	14.2	
Streptomycin	0			4.9	33.9	56.8	4.4						
Tetracycline	5			93.4	1.6				2.2	2.2		0.5	

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 4.11.

As in previous years, resistance to ampicillin, tetracycline and trimethoprim-sulphamethoxazole were the most common resistance traits (Table 4.11). Resistance to ampicillin and to trimethoprim-sulphamethoxazole has increased considerably over the years but the increase levelled off in 2015-2017 (Figure 4.6).

Co-resistance between trimethoprim-sulphonamides and other antibiotics is common.

Projects with randomised (i.e. non-biased) sampling were carried out both in 2016-2017 and 2020. The results showed

Figure 4.6. Resistance (%) in *Escherichia coli* from pigs 1995-2020 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, 2020 n=66). From 2020 only results from isolates with virulence factors are shown.

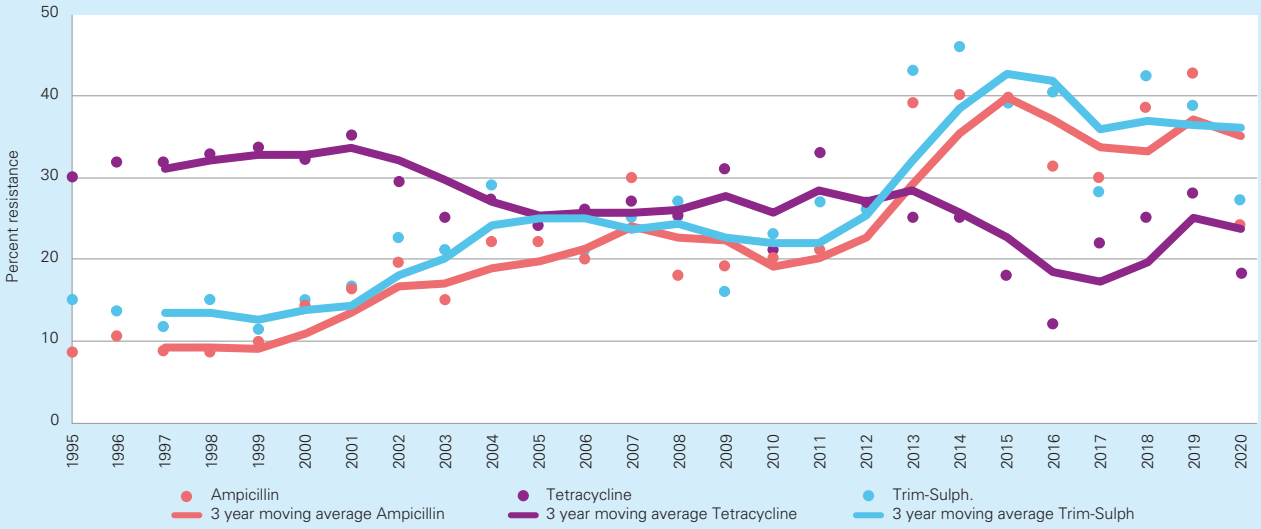


Table 4.11. Distribution of MICs and resistance (%) in enterotoxigenic *Escherichia coli* from pigs 2020. S1 are clinical isolates from faecal samples or from samples taken post-mortem from the gastro-intestinal tract. S2 are isolates from pigs with diarrhoea, sampled in a project.

Antibiotic	Resistance (%) 2020 n=66 S1	Resistance (%) 2020 n=32 S2	Distribution (%) of MICs (mg/L) ≤0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	24	16						65.2	9.1	1.5		24.2		
Cefotaxime	0	0			100									
Colistin	0	0					95.5	4.5						
Enrofloxacin	5	0		95.5	1.5	3.0								
Gentamicin	3	3						97.0	3.0					
Meropenem[a]	0	0	98.5	1.5										
Neomycin	3	0							95.5	1.5		3.0		
Tetracycline	18	28						81.8				18.2		
Trim-Sulph.[b]	27	22				72.7				27.3				

[a]Number of tested isolates n=65, [b]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphamethoxazole)

no major difference in resistance compared to the material from clinical submissions (see table 4.11 and Swedres-Svarm 2017). 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 11% (7/66) of the isolates in 2020 and has varied over the years (33% in 2019, 31% in 2018, 20% in 2017, 25% in 2016 and 2015, 42% in 2014 and 38% in 2013). Fifty-eight percent of the isolates were susceptible to all tested antibiotics. Resistance phenotypes are shown in Table 4.12. For comparison of resistance in *E. coli* from other animal species see Comparison of antibiotic resistance in *E. coli* and *Staphylococcus* spp., Table 4.35.

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 4.13 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 2017-2020.

Table 4.12. Resistance phenotypes of isolates of *Escherichia coli* from pigs 2020. Shaded areas with "R" indicate resistance.

Resistance phenotypes									Number of isolates
Amp	Tsu	Tet	Enr	Neo	Gen	Col	Ctx	Nit	
R	R	R							4
R	R		R	R					1
R	R		R		R				1
R	R								7
R		R		R					1
R									2
	R	R							2
	R								3
		R							5
			R						1
					R				1
									38
								Sum	**66**

Table 4.13. Resistance (%) in *Brachyspira hyodysenteriae* from pigs 2005-2020 and distribution of MICs for isolates from 2017-2020. Clinical isolates from faecal samples. The number of isolates each year varies (n=5-29, 2020 n=12).

	Resistance (%)					Distribution (%) of MICs (mg/L)												
Antibiotic	2005-06	2007-08	2009-11	2012-16	2017-20	≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	>128
	n=54	n=38	n=40	n=40	n=39														
Doxycycline	9	3	5	0	0			18.0	61.5	20.5									
Tiamulin	7	18	8	10[a]	23[a]		30.8	2.6	43.6	10.3	7.7		2.6		2.6				
Tylosin	81	76	60	45	59							10.3	17.9	10.3	2.6				59.0
Tylvalosin		93	55	48	69				2.6	10.3	17.9	10.3	5.1	23.1	25.6		5.1		
Valnemulin	0	18	3	13	28	35.9	33.3	2.6	5.1	7.7	7.7	2.6	2.6	2.6					

[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 tiamulin of >2 mg/L and for tylosin of >16 mg/L are used at SVA. With these breakpoints, 10% of the isolates were resistant to tiamulin and 43% to tylosin (Table 4.14). If the same wild type cut-off value as for *B. hyodysenteriae* is used, 24% of the isolates were resistant to tiamulin.

Actinobacillus pleuropneumoniae

Isolates of *Actinobacillus pleuropneumoniae* are from post-mortem investigations of lungs. The resistance situation is favourable and almost no resistance was detected (Table 4.15). However, compared to the results ten years ago, the MICs for penicillin were higher. 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 substances.

Streptococcus suis

Isolates of *Streptococcus suis* are from post-mortem examination of different organs in diseased pigs from 2013-2017 (n=36) and 2018-2020 (n=27). Resistance to penicillin was detected in 2019 and 2020 (Table 4.16).

Table 4.14. Distribution of MICs for *Brachyspira pilosicoli* from pigs 2010-2020, n=187. Clinical isolates from faecal samples. The number of isolates each year varies (n=7-27, 2020 n=22).

Antibiotic	Distribution (%) of MICs (mg/L)													
	≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	>128
Doxycycline			35.3	54.5	5.3	2.7	1.6	0.5						
Tiamulin		51.9	14.4	10.2	9.6	2.7	1.6	1.6	2.7	5.3				
Tylosin							10.7	17.6	24.6	4.3	5.9	4.8	7.5	24.6
Tylvalosin				0.5	16.6	29.9	23.5	7.5	3.7	3.7	4.8	9.6		
Valnemulin	58.8	8.6	5.9	11.8	9.1	3.2	1.1		1.6					

Table 4.15. Distribution of MICs and resistance (%) in *Actinobacillus pleuropneumoniae* from pigs 2019-2020. Clinical isolates from post-mortem investigations of lungs.

Antibiotic	Resistance (%) 2019-2020 n=31	Distribution (%) of MICs (mg/L)									
		≤0.06	0.12	0.25	0.5	1	2	4	8	16	>16
Ampicillin	0		19.4	80.6							
Enrofloxacin	0	100									
Florfenicol	0			87.1	12.9						
Gentamicin	NR[b]								90.3	9.7	
Oxytetracycline	0				48.4	51.6					
Penicillin	0		6.5	19.4	74.2						
Trim-Sulph[a]	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.

Table 4.16. Resistance (%) in *Streptococcus suis* from pigs 2013-2020. Distribution of MICs from 2018-2020. Clinical isolates from various organs of pigs. The number of isolates each year varies (2013-2017 n=36, 2018-2020 n=27).

Antibiotic	Resistance (%)		Distribution (%) of MICs (mg/L)								
	2013-2017 n=36	2018-2020 n=27	≤0.03	0.06	0.12	0.25	0.5	1	2	4	>4
Cephalothin	3	7						85.2	7.4	3.7	3.7
Enrofloxacin	NR[b]	NR[b]				44.4	55.6				
Erythromycin	8	4					96.3		3.7		
Gentamicin	NR[b]	NR[b]						7.4	33.3	29.6	29.6
Clindamycin	11	15					85.2		3.7	11.1	
Penicillin	0	15	74.1	11.1			7.4	3.7	3.7		
Tetracycline	67	67				25.9	7.4	3.7	48.1	7.4	7.4
Trim-Sulph[a]	11	11				85.2	3.7	11.1			

[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, tetracycline and neomycin (Table 4.17 and Figure 4.7). Multiresistance occurred in 19% (7/37) of the isolates from 2019-2020, compared to 47% in 2017-2018, 32% in 2016, 56% in 2015, 76% in 2014 and 70% in 2013. For resistance phenotypes in isolates in 2019-2020, 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 4.35.

Figure 4.7. Resistance (%) in *Escherichia coli* from calves 2007-2020. 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, 2019-2020=37).

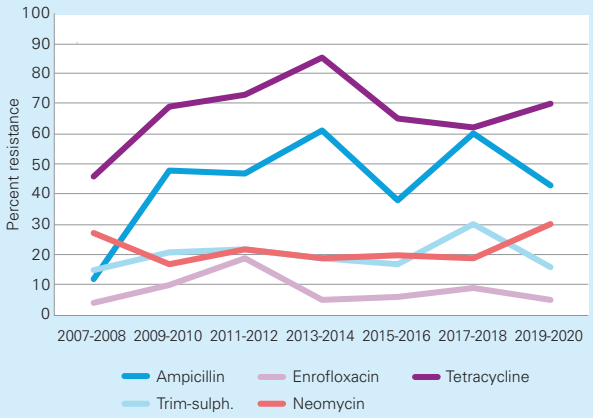


Table 4.17. Distributions of MICs and resistance (%) in *Escherichia coli* from calves 2019-20. Clinical isolates from faecal samples or from samples taken post-mortem from the gastro-intestinal tract.

Antibiotic	Resistance (%) 2019-2020	Distribution (%) of MICs (mg/L)											
	n=37	≤0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	43						56.8				43.2		
Cefotaxime	0			100									
Colistin	0					97.3	2.7						
Enrofloxacin	5		94.6	5.4									
Gentamicin	5						94.6	5.4					
Meropenem[a]	0	100											
Neomycin	30							70.3		2.7	13.5	13.5	
Tetracycline	70						27.0	2.7			70.3		
Trim-Sulph.[b]	16				83.8				16.2				

[a]17 isolates tested. [b]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphamethoxazole).

Table 4.18. Resistance phenotypes of isolates of *Escherichia coli* from calves 2019-20. Shaded areas with "R" indicate resistance.

Resistance phenotypes									Number of isolates
Amp	Tet	Neo	Tsu	Enr	Gen	Ctx	Col	Nit	
R	R		R	R					1
R	R		R						3
R	R			R					1
R	R								6
R			R		R				1
R			R						1
R									3
	R	R							1
	R	R			R				10
	R								4
									6
								Sum	37

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.

The majority of the isolates (82%) was susceptible to all antibiotics tested. Resistance to ampicillin (15%), tetracycline (7%), and trimethoprim-sulphamethoxazole (5%) were the most common traits (Table 4.19). One isolate (2%) was 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). Resistance was uncommon and 84% (38/45) of isolates was susceptible to all tested antibiotics, excluding ampicillin. Multiresistance did not occur in isolates from 2020.

Table 4.19. Resistance (%) in *Escherichia coli* from dairy cows 2016-2020. Distribution of MICs from 2020. Clinical isolates from milk.

Antibiotic	Resistance (%)					Distribution (%) of MICs (mg/L)											
	2016 n=74	2017 n=79	2018 n=100	2019 n=74	2020 n=60	≤0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	27	15	24	24	15						46.7	33.3	5.0		15.0		
Cefotaxime	1[b]	0	0	0	0			100									
Colistin	0	4[c]	0	0	0					98.3	1.7						
Enrofloxacin	4	3	1	3	2		98.3		1.7								
Gentamicin	1	0	1	3	2						98.3	1.7					
Meropenem					0[d]	100											
Neomycin	0	4	5	1	2							95.0	3.3			1.7	
Streptomycin	26	14	20	14	NT[e]												
Tetracycline	16	9	8	18	7						91.7	1.7			6.7		
Trim-Sulph.[a]	22	9	14	11	5				93.3	1.7			5.0				

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphamethoxazole); [b]One isolate with MIC 1 mg/L was further tested and had an AmpC phenotype but no genes conferring transferable ESC resistance were detected with PCR; [c]Three isolates with MIC 4 mg/L were negative for mcr-1, mcr-2, mcr-3, mcr-4 and mcr-5 genes with PCR; [d]Number of tested isolates n=55; [e]NT, not tested.

Table 4.20. Resistance (%) in *Klebsiella pneumoniae* from dairy cows 2016-2020. Distributions of MICs from 2020. Clinical isolates from milk.

Antibiotic	Resistance (%)					Distribution (%) of MICs (mg/L)											
	2016 n=36	2017 n=34	2018 n=52	2019 n=34	2020 n=45	≤0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	NR[b]	NR	NR	NR	NR									11.1	88.9		
Cefotaxime	0	0	0	0	0			100									
Colistin	3[c]	9[d]	0	0	4[e]					93.3	2.2			4.4			
Enrofloxacin	14	3	8	6	4		95.6	2.2			2.2						
Gentamicin	0	0	0	0	2						97.8	2.2					
Meropenem					0[f]	100											
Neomycin	0	4	5	1	0							100					
Streptomycin	26	14	20	14	NT[g]												
Tetracycline	16	9	8	18	11						84.4	4.4			11.1		
Trim-Sulph.[a]	22	9	14	11	13				86.7		2.2		11.1				

[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]One isolate with MIC 16 mg/L was negative for *mcr-1* and *mcr-2* genes with PCR; [d]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; [e]Two isolates with MIC >8 mg/L were negative for *mcr-1*to *mcr-9* genes with PCR; [f]number of isolates tested n=44; [g]NT, not tested.

Staphylococcus aureus from milk samples

Isolates of *Staphylococcus aureus* are from clinical submissions of milk samples from dairy cows with clinical mastitis. In 2020, 527 isolates were analysed for penicillinase production of which 1.5% (n=8) were positive.

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 2013-2020 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.

Table 4.21. Resistance (%) in *Pasteurella* spp. from calves 2005-2020. Distribution of MICs from 2020. 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 n=65	≤0.06	0.12	0.25	0.5	1	2	4	8	16	>16
Ampicillin	0	13	2	5	3	5			93.8	1.5						4.6
Enrofloxacin	0[b]	0	0	0	0	0		100								
Florfenicol						0			27.7	72.3						
Penicillin	0	13	2	5	8	5		87.7	7.7						4.6	
Tetracycline	0	0	0	0	0	0				96.9	3.1					

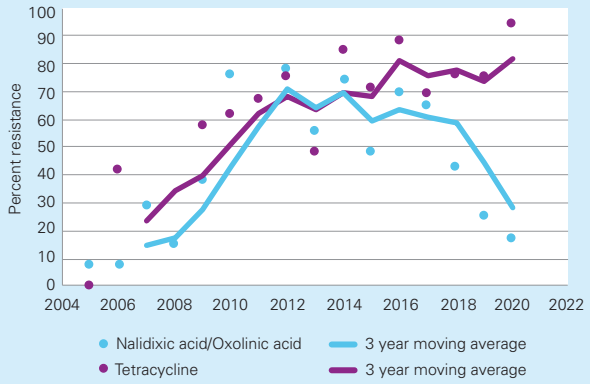
[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphamethoxazole); [b]314 isolates tested.

Farmed fish

Flavobacterium psycrophilum

Isolates of *Flavobacterium psycrophilum* are from clinical submissions of farmed fish. Data from 2015-2020 are compiled and presented as distributions of MICs in Table 4.22. 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 4.8. Resistance (%) in *Flavobacterium psycrophilum* from farmed fish 2005-2020 with a three-year moving average. The number of isolates each year varies (n=8-31, 2020 n=18). No resistance to florfenicol was detected.



In Figure 4.8 resistance to tetracycline and quinolones (nalidixic acid or oxolinic acid) in *F. psycrophilum* 2005-2020 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).

Aeromonas salmonicida var. *salmonicida* and atypical *Aeromonas salmonicida*

Isolates of *Aeromonas salmonicida* var. *salmonicida* and atypical *Aeromonas salmonicida* (2015-2018 *Aeromonas salmonicida* var. *achromogenes*) are from clinical submissions of farmed fish. Data from 2015-2020 are compiled and presented as distributions of MICs in Table 4.23. Most isolates of *Aeromonas salmonicida* var. *salmonicida* are from arctic char and of atypical *Aeromonas salmonicida* from brown trout/sea trout. Epidemiological cut-offs issued by CLSI are being used (CLSI, 2020c).

Table 4.22. Distributions of MICs and resistance (%) in *Flavobacterium psycrophilum* from farmed fish 2015-2020. The number of isolates each year varies (n=8-31, 2020 n=18).

Antibiotic	Resistance (%) 2015-2020 n=124	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					4.8	18.5	45.2	26.6	4.8			
Oxolinic acid	49	0.8			4.0	34.7	11.3	0.8	3.2	45.2			
Oxytetracycline	79			0.8	18.5	1.6	1.6	1.6	10.5	21.8	37.9	5.6	

Table 4.23. Distributions of MICs and resistance (%) in *Aeromonas salmonicida* var *salmonicida* (ASS) and atypical *Aeromonas salmonicida* (ASA) from farmed fish 2014-2020. The total number of isolates are 30 for ASS and ASA respectively.

Antibiotic	Bacterial species	Resistance (%) 2014-2020 n=30 each	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	ASS	0						26.7	73.3					
	ASA	0					10.0	30.0	56.7	3.3				
Oxolinic acid	ASS	10	3.3	60.0	26.7			3.3		6.7				
	ASA	20		30.0	23.3	13.3	13.3			3.3	16.7			
Oxytetracycline	ASS	0					23.3	73.3	3.3					
	ASA	0				16.7	6.7	56.7	20.0					

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. 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

Screening for methicillin resistant *Staphylococcus aureus* (MRSA) in milk samples from dairy cows started in 2010 and is still ongoing. Selected isolates of beta-lactamase producing *Staphylococcus aureus* from routine submissions to SVA are analysed for methicillin resistance. During 2010-2020, about 1300 isolates were tested and MRSA was confirmed in 9 isolates. In addition, about 500 isolates of *S. aureus* without beta-lactamase production were tested in 2013, but MRSA was not detected.

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. Most bacteria causing mastitis in dairy cows in Sweden are susceptible to penicillin and penicillin is the drug of choice if antibiotic treatment is needed. *Staphylococcus aureus* was the most common bacterial species followed by *Streptococcus dysgalactiae*, *Escherichia coli* and *Streptococcus uberis*. Resistance to penicillin in *S. aureus* from cows with clinical mastitis in this monitoring is very uncommon.

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. A sampling of calves in large dairy herds was carried out in 2020. Farmers were also interviewed about herd management, with the aim to investigate correlations to calf health and antibiotic resistance. Preliminary results show that *P. multocida* was the most common isolated bacteria and all susceptibility-tested isolates were sensitive to penicillin.

Efficacy of penicillin treatment of respiratory disease in calves

In a pilot study, benzylpenicillin, oxytetracycline and florfenicol had equal and high efficacy in treatment of undifferentiated respiratory disease in calves (Welling et al., 2020). This supports the Swedish recommendation of benzylpenicillin as a first line antibiotic in treatment of calves with respiratory disease, although this may not be appropriate in countries with a different panorama of infectious agents and antimicrobial resistance.

Umbilical infections in calves

In a study of autopsied calves with umbilical infection, sepsis was more common in calves less than one week old than in older calves (Johansson, 2021). *Escherichia coli* was the most frequently isolated bacteria of which some were resistant to trimethoprim-sulphamethoxazole. Younger calves were to a greater extent infected by bacteria that has inherently low susceptibility to penicillin.

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

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 favorable 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, resistance patterns in field isolates were compared, and a number of isolates with different MICs for tiamulin and tylosin have been selected for whole genome sequencing. The aim is to search for resistance mechanisms.

Escherichia coli

Resistance to ampicillin and trimethoprim-sulphamethoxazole in *Escherichia coli* isolated from pigs 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 post-weaning diarrhoea.

A study with randomized sampling in 2020 showed no clear difference in resistance between enterotoxigenic isolates from the project and isolates from routine clinical submissions. This indicates that the rather high occurrence of resistance in isolates from routine submissions is representative for the situation in Swedish pig herds.

Lameness in Swedish finisher pigs

Legs from finisher pigs euthanized due to clinical lameness were investigated by pathology and in some cases bacteriology (Gripsborn, 2021). Chronic infectious arthritis was the most common finding, many of which had highly degradative changes. Treatment failure was probably due to late treatment rather than antibiotic resistance.

References

Welling V, Lundeheim N, et al. 2020, A pilot study in Sweden on efficacy of benzylpenicillin, oxytetracycline, and florfenicol in treatment of acute undifferentiated respiratory disease in calves. Antibiotics (Basel) 9(11):736.

Johansson J. 2021, Bacteriological diagnosis and risk factors for umbilical infections in calves. Student master exam thesis, Swedish University of Agricultural Sciences. https://stud.epsilon.slu.se/16444/1/johansson_jennifer_210118.pdf

Gripsborn J. 2021, Lameness in Swedish finisher pigs – pathological changes and treatment. Student master exam thesis, Swedish University of Agricultural Sciences. https://stud.epsilon.slu.se/16526/1/gripsborn_j_210122.pdf

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 most common in 2020 (Table 4.24 and Figure 4.9). The resistance to trimethoprim-sulphamethoxazole has gradually increased from 10 to 17% between 2013 and 2018, and in 2019 and 2020 the figure was 15% (Table 4.24 and Figure 4.9). The resistance to gentamicin is continuously low. However, the proportion of resistance in the tested isolates have differed somewhat over the years and trends are difficult to estimate.

Seventy-nine percent (201/253) of the isolates were susceptible to all the tested antibiotics. The proportion of multiresistance for the isolates was 5% (13/253), and comparable to the figures in 2017-2018 (7 and 6% respectively) but has somewhat declined compared to 2019 (9%) (see previous Swedres-Svarm reports). Nine of the thirteen multiresistant isolates were resistant to three antibiotics and four to four antibiotics. The most common phenotype was resistance to ampicillin, tetracycline and trimethoprim-sulphamethoxazole, occurring in ten of the multiresistant isolates. This phenotype was also the most common in *E. coli* isolated from dogs (65%). All isolates resistant to four antibiotics had the common phenotype and all four were in addition resistant to gentamicin. For comparison of resistance in *E. coli* from other animal species see Comparison of antibiotic resistance in *E. coli* and *Staphylococcus* spp., Table 4.35.

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

Figure 4.9. Resistance (%) in clinical isolates of *Escherichia coli* from horses 2004-2020. Isolates are from clinical sampling of the genital tract of mares. The number of isolates each year varies (n=124-324, 2020 n=253).

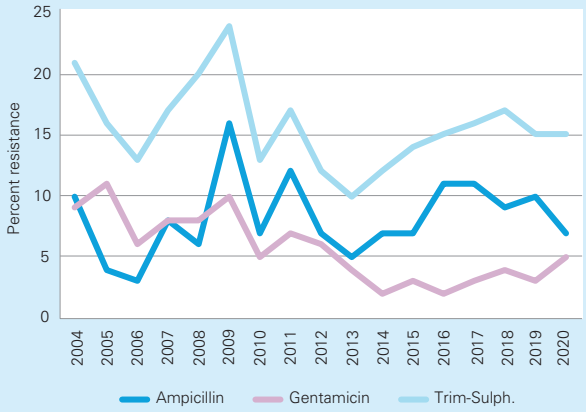


Table 4.24. Distributions of MICs and resistance (%) in *Escherichia coli* from horses, 2020. Clinical isolates from the genital tract of mares.

Antibiotic	Resistance (%) 2020 n=253	≤0.06	0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	7						40.3	50.2	2.4	0.4	6.7	
Cefotaxime	0			100								
Colistin	0					98.4	1.6					
Enrofloxacin	1		98.8	0.8			0.4					
Gentamicin	5						94.9	2.8		0.8	1.6	
Meropenem	0	100										
Neomycin	0							98.8	1.2			
Tetracycline	6						92.9	0.4	0.4		6.3	
Trim-Sulph.[a]	15				85.0	0.4			14.6			

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

Streptococcus equi ssp. *zooepidemicus*

Isolates of *Streptococcus equi* ssp. *zooepidemicus* are from clinical submissions, mainly from the respiratory tract (75%). The tested isolates of *S. equi* ssp. *zooepidemicus* have remained uniformly susceptible over the years studied apart from clindamycin and trimethoprim-sulphamethoxazole. The proportion of resistance has varied, for clindamycin between 4% and 11% in 2015-2020 and for trimethoprim-sulphamethoxazole 2-18% during the same period (Table 4.25 and previous Swedres-Svarm reports).

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

Staphylococcus aureus

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

The proportions of resistance to gentamicin, penicillin, tetracycline and trimethoprim-sulphamethoxazole have differed slightly over the years and therefore trends are difficult to estimate (Figure 4.10). Although the resistance to penicillin due to pencillinase production varies over the years and still is the most common trait, the proportion has overall declined from 36% in 2008-2009 to 21% in 2020 (Figure 4.10 and Table 4.26). Resistance to fusidic acid among the tested isolates has varied between 2017 and 2020 with 9, 17, 5 and 6% resistance respectively (Table 4.26 and previous Swedres-Svarm reports).

Sixty percent (79/131) of the isolates were susceptible to all the tested antibiotics. Three isolates (2%) were resistant to three of the tested antibiotics (i.e., multiresistant), and comparable to the figures in 2015-2019 (0-5%) (see previous Swedres-Svarm reports). No 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 4.36.

No MRSA was detected in this sample collection. Nevertheless, in 2020 the notification of MRSA isolated from horses increased. For more information on MRSA in horses in Sweden, see Notifiable diseases, Methicillin resistant *Staphylococcus aureus* (MRSA) and In Focus: Methicillin resistant *Staphylococcus aureus* (MRSA) in horses.

Figure 4.10. Resistance (%) in clinical isolates of *Staphylococcus aureus* 2008-2020 from skin of horses. The number of isolates each year varies (n=75-145, 2020 n=131).

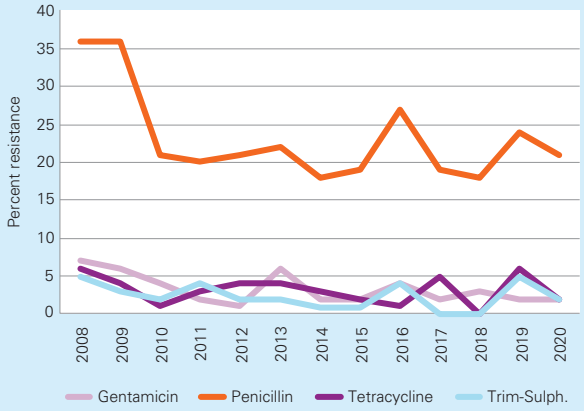


Table 4.25. Distribution of MICs and resistance (%) in *Streptococcus equi* ssp. *zooepidemicus* isolated from horses, 2020. Clinical isolates mainly from the respiratory tract.

Antibiotic	Resistance (%) 2020 n=64	Distribution (%) of MICs (mg/L) ≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Cephalotin	0						98.4	1.6						
Clindamycin	11					89.1	10.9							
Erythromycin	0					100								
Gentamicin	NR[b]							1.6	7.8	90.6				
Nitrofurantoin	0										100			
Penicillin	0	100												
Tetracycline	NR[b]				3.1	1.6	1.6	42.2	42.2	9.4				
Trim-Sulph.[a]	2				96.9	1.6	1.6							

[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.

Table 4.26. Distribution of MICs and resistance (%) in *Staphylococcus aureus* isolated from horses, 2020. Clinical isolates from the skin.

Antibiotic	Resistance (%) 2020 n=131	Distribution (%) of MICs (mg/L) ≤0.25	0.5	1	2	4	8	16	32	64	>64
Cefoxitin	0		0.8	0.8	10.7	87.8					
Cephalotin	5			94.7	5.3						
Clindamycin	5		95.4	3.8	0.8						
Enrofloxacin	4	85.5	10.7	1.5	2.3						
Erythromycin	4		90.1	6.1	3.1	0.8					
Fusidic acid	6		93.9	3.1	1.5	1.5					
Gentamicin	2			95.4	2.3	1.5	0.8				
Nitrofurantoin	<1							95.4	3.8		0.8
Penicillin[a]	21										
Tetracycline	2	48.1	45.0	4.6		0.8	1.5				
Trim-Sulph[b]	2	93.9	4.6	0.8			0.8				

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

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 2020 (Table 4.27 and Figure 4.11), but the proportion of resistance in the tested isolates has differed somewhat throughout the years and trends are difficult to estimate (Figure 4.11).

Eighty-one percent (875/1078) of the isolates were susceptible to all the tested antibiotics. The proportion of multiresistance for the isolates was 3% (35/1078) and has slightly declined compared to 2015-2019 (6-9%) (see previous Swedres-Svarm reports). Forty-six percent (16/35) of the multiresistant isolates were resistant to three antibiotics; 40% (14/35) to four; 9% (3/35) to five and 3% (1/35) to six and seven antibiotics. For comparison of resistance in *E. coli* from

Figure 4.11. Resistance (%) in clinical isolates of *Escherichia coli* from dog urine 2005-2020. The number of isolates each year varies (n=304-1162, 2020 n=1078).

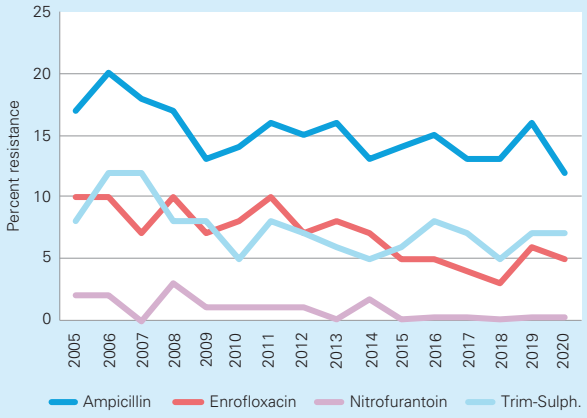


Table 4.27. Distribution of MICs and resistance (%) in *Escherichia coli* from dogs, 2020. Clinical isolates from urine.

Antibiotic	Resistance (%) 2020 n=1078	Distribution (%) of MICs (mg/L) ≤0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	12						53.9	32.3	1.8	0.2	11.9		
Cefalexin	2							8.7	77.7	11.9	0.6	1.1	
Cefotaxime	1[b]			98.8		0.5	0.2	0.6					
Colistin	<1[c]					99.1	0.7			0.2			
Enrofloxacin	5		95.1	1.7	1.9	0.5		0.1	0.8				
Gentamicin	2						97.9	1.5	0.1		0.6		
Meropenem	<1[d]	99.5	0.4	0.1									
Neomycin	1							96.9	2.0	0.2	0.8		
Nitrofurantoin	<1										99.4	0.5	0.2
Tetracycline	5						94.2	0.8		0.1	4.9		
Trim-Sulph.[a]	7				92.6	0.5			7.0				

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphamethoxazole); [b]Twelve of 13 isolates resistant to cefotaxime were available for verification. Genes conferring transferable ESC resistance were detected in eight of the isolates; [c]The two isolates with MIC >8 mg/L were not available for PCR detection of the the *mcr-1* to *mcr-9* genes; [d]The isolate with MIC 0.25 mg/L was not available for further testing.

other animal species see Comparison of antibiotic resistance in *E. coli* and *Staphylococcus* spp., Table 4.35. The most common phenotype, resistance to ampicillin, tetracycline and trimethoprim-sulphamethoxazole, was detected in 65% (22/34) of the multiresistant isolates. Seventeen of the 18 (94%) isolates resistant to four or more antibiotics were of the common phenotype, and commonly also resistant to enrofloxacine (14/18, 78%). For the five isolates resistant to five or more antibiotics no specific phenotype more than already mentioned was noticed.

Thirteen (1%) of the *E. coli* isolates were resistant to cefotaxime (MIC >0.25 mg/L) and twelve were available for further testing. Genes conferring transferable ESC resistance were detected in eight of the isolates. For more information about ESBL-producing Enterobacterales (previously Enterobacteriaceae) isolated from dogs in Sweden, see Notifiable diseases, ESBL-producing Enterobacterales (previously Enterobacteriaceae). The one isolate resistant to meropenem (MIC 0.25 mg/L), but susceptible to cefalexin and cefotaxime, was not available for further testing.

Two of the isolates were resistant to colistin (MIC >2 mg/L). The isolates were not available for PCR detection of the *mcr-1* to *mcr-9* genes.

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 2020 figures of resistance from three different sample collections have been compared, namely skin lesions (S1), wounds (S2) and the external ear canal (S3) (Table 4.28 and previous Swedres-Svarm reports).

Resistance to penicillin due to pencillinase production is high for all sample collections (72-77%, Table 4.28). For isolates from skin lesions, where figures for penicillinase production could be compared before 2017, the figure has declined since 2009 (90%) to 74% in 2020. Resistance to clindamycin, fusidic acid and tetracycline has differed somewhat over the years, but has slightly declined and compared to penicillin, remains at lower levels (Table 4.28 and Figure 4.12).

Compared to other staphylococci isolated from animals, the proportion of susceptibility is low and the proportion of multiresistance is high in the tested isolates. Nineteen percent of the isolates in both sample collection S1, skin (109/567) and S2, wounds (158/826), and 22% (174/792) in S3, ear were susceptible to all the tested antibiotics. The proportion of multiresistance for the S1 isolates was 24% (137/567), for

Figure 4.12. Resistance (%) in *Staphylococcus pseudintermedius* from dogs, 2007-2020. Clinical isolates from skin (S1). The number of isolates each year varies (n=220-567, 2020 n=567).

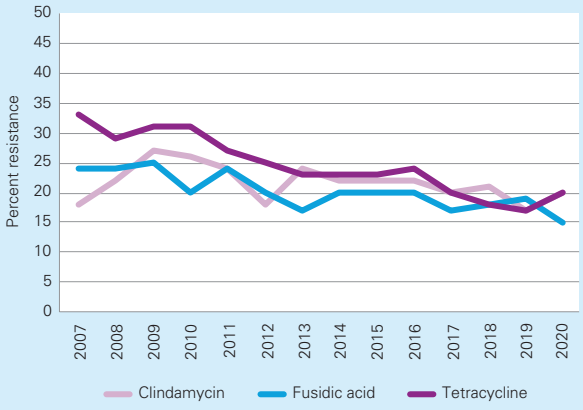


Table 4.28. Distribution of MICs and resistance (%) in *Staphylococcus pseudintermedius* from dogs 2020. Clinical isolates from skin (S1), wounds (S2) and external ear canals (S3).

Antibiotic	Resistance (%)			Distribution (%) of MICs (mg/L), isolates from skin (S1)									
	2020 n=792 S3	2020 n=826 S2	2020 n=567 S1	≤0.25	0.5	1	2	4	8	16	32	64	>64
Cephalothin	1	2	1			98.9	1.1						
Cefoxitin[a]				63.8	33.7	1.2	0.7	0.4	0.2				
Clindamycin	12	13	20		79.7	1.2	0.7	18.3					
Enrofloxacin	2	1	1	94.5	4.2	0.5	0.7						
Erythromycin	15	16	23		76.9	2.1	0.5	20.5					
Fusidic acid	16	13	15		84.3	0.7	1.8	13.2					
Gentamicin	3	3	2			95.4	2.1	0.7	1.8				
Nitrofurantoin	<1	<1	<1							98.2	1.2	0.4	0.2
Oxacillin	0	<1[d]	<1[d]	98.8	1.1		0.2						
Penicillin[b]	72	77	74										
Tetracycline	19	18	20	77.1	1.8	0.9	0.4	0.4	19.6				
Trim-Sulph.[c]	7	7	6	58.7	35.1	3.5	0.7	0.3	1.8				

[a]No cut-off available for *S. pseudintermedius*; [b]Denotes beta-lactamase production; [c]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphamethoxazole); [d]The six isolates with MIC>0.5 for oxacillin were tested with PCR for detection of the *mecA* and *mecC* genes, and all were MRSP.

the S2 isolates 20% (163/826) and for S3 17% (138/792). For comparison of resistance in *Staphylococcus* spp. isolated from other animal species see Comparison of antibiotic resistance in *E. coli* and *Staphylococcus* spp., Table 4.36.

Fifty-five percent (76/137) of the multiresistant S1-isolates were resistant to three antibiotics; 30% (41/137) to four; 9% (13/137) to five; 4% (5/137) to six and <1% (1/137) to seven or eight antibiotics. In 2016 one-third of the multiresistant isolates were resistant to five or more antibiotics, compared to 20-22% in 2017-2019 and 15% (20/137) in 2020. 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 4.12 and previous Swedres-Svarm reports).

Resistance to penicillin, clindamycin and erythromycin was the most common phenotype, for the multiresistant S1-isolates, 77% (106/137), S2 57% (93/163) and S3 63% (88/139). All isolates (100%, 61/61) resistant to four or more antibiotics of sample collection S1 had the common phenotype and combined with resistance to fusidic acid 51% (31/61), tetracyklin 48% (29/61) and/or trimethoprim/sulphamethoxazole 21% (13/61).

One of the S1 isolates and five of the S2 isolates were resistant to oxacillin (MIC >0.5 mg/L). The six isolates were tested with PCR for detection of the *mecA* and *mecC* genes and all six were found to be MRSP. For more information on MRSP isolated from dogs in Sweden, see Notifiable diseases, Methicillin-resistant *Staphylococcus pseudintermedius* (MRSP).

Staphylococcus schleiferi

Isolates of *Staphylococcus schleiferi* are from clinical submissions of samples of various locations, but mainly from the external ear canal (64%) or skin (19%).

The proportion of resistance in isolates of *S. schleiferi* (Table 4.29) was low for most antibiotics compared to isolates of *S. pseudintermedius*, the more common staphylococci isolated from dogs (Table 4.28). Four percent of the tested *S. schleiferi* isolates were penicillinase producing and comparable to figures in 2014-2018 (<1-4%) (see previous Swedres-Svarm reports). The figure was low also compared to other *Staphylococcus* spp. from animals. The proportion of resistance to enrofloxacin has declined between 2016 and 2020, from 20% to 6% in 2020. The proportions of resistance to fusidic acid have differed over the years, between 14% (2016) and 3% (2018). In 2020 the figure was 12%, and trends are difficult to estimate. For the other tested antibiotics there is no major difference between years (see Table 4.29 and previous Swedres-Svarm reports).

Seventy-four percent (175/236) of the *S. schleiferi* isolates were susceptible to all the tested antibiotics. Multiresistance was detected in 4% (9/236) and comparable to figures in 2017-2019 (1-2%). Of the nine multiresistant *S. schleiferi* isolates, seven were resistant to three and two to four of the tested antibiotics. No 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 4.36.

Table 4.29. Distribution of MICs and resistance (%) in *Staphylococcus schleiferi* from dogs, 2020. Clinical isolates from various locations.

Antibiotic	Resistance (%) 2020 n=236	Distribution (%) of MICs (mg/L) ≤0.25	0.5	1	2	4	8	16	32	64	>64
Cephalothin	2			98.3	1.7						
Cefoxitin[a]		24.2	73.7	2.1							
Clindamycin	5		94.9	1.7		3.4					
Enrofloxacin	6	83.5	10.6	5.5	0.4						
Erythromycin	6		94.5	1.7	0.8	3.0					
Fusidic acid	12		77.1	10.6	8.9	3.4					
Gentamicin	0			98.3	1.7						
Nitrofurantoin	0							97.5	2.5		
Oxacillin	0	98.3	1.7								
Penicillin[b]	4										
Tetracycline	3	93.2	2.5	0.8			3.4				
Trim-Sulph.[c]	1	94.5	4.2	0.8			0.4				

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

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 two isolates resistant to colistin (MIC >2mg/L) were not available for PCR detection of the *mcr-1* to *mcr-9* genes.

The proportion of resistance to enrofloxacin has gradually declined from 25% in 2009 to 8% in 2019-2020. The figures for gentamicin have stabilized to about <1-2% over the recent years (Table 4.30 and previous Swedres-Svarm reports). None of the isolates were resistant to more than one of the tested antibiotics.

Pasteurella canis

Isolates of *Pasteurella* spp. are from clinical submissions of samples from various locations, but mainly, 87%, from the external ear canal, wounds, skin, abscesses, and the respiratory tract.

Pasteurella canis was the most common *Pasteurella* sp. isolated in samples from dogs, 81% (248/307). The proportion of resistance to antibiotics was low in the tested isolates (Table 4.31). *Pasteurella* spp. have a low inherent susceptibility to aminoglycosides, e.g., gentamicin.

In 2020 the cut-off for *Pasteurella multocida* were adjusted compared to the years before. For enrofloxacin from MIC 0.25 to 0.06 mg/L and for trimethoprim-sulphamethoxazole from MIC 4 to 0.5 mg/L. The cut-off for *P. multocida* has been applied for all *Pasteurella* spp. isolates tested. The proportion of resistance in *Pasteurella* spp. has been low throughout the years and the change of cut-off had low or no impact on the comparison of the yearly figures. The proportion of resistance to enrofloxacin between 2014 and 2020 has gradually increased, from <1% (2014) to 4% in 2020. Previously (2014-2019) all tested isolates have been susceptible to trimethoprim-sulphamethoxazole. In 2020 one isolate was resistant, but the MIC (>4mg/L) would have been assessed as resistant also before the change of cut-off (Table 4.31 and previous Swedres-Svarm reports). Of the resistant isolates one was resistant to two antibiotics, enrofloxacin and tetracycline, while the rest were resistant to one antibiotic only.

Table 4.30. Distribution of MICs and resistance (%) in *Pseudomonas aeruginosa* from dogs, 2020. Clinical isolates from the external ear canal.

Antibiotic	Resistance (%) 2020 n=324	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	>16
Enrofloxacin	8	2.5	6.2	36.1	38.0	9.0	3.4	4.9		
Colistin[a]	<1				60.2	33.3	5.9	0.6		
Gentamicin	<1					87.3	11.1	1.2	0.3	

[a]Colistin is equivalent to polymyxin B. The two isolates with MIC 8mg/L were not available for PCR detection of the *mcr-1* to *mcr-9* genes.

Table 4.31. Distribution of MICs and resistance (%) in *Pasteurella canis* from dogs, 2020. Clinical isolates from various locations.

Antibiotic	Resistance (%) 2020 n=248	Distribution (%) of MICs (mg/L) ≤0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	>8
Ampicillin	0				98.8	1.2						
Enrofloxacin	4	91.9	4.0		0.4	1.6	1.6	0.4				
Gentamicin	NR[b]			2.0	5.6	41.1	38.3	6.9	4.4	1.2	0.4	
Penicillin	0			95.6	3.6	0.8						
Tetracycline	<1			4.0	39.1	47.2	7.3	2.0				0.4
Trim-Sulph.[a]	<1					99.6				0.4		

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

Cats

Escherichia coli

Isolates are from clinical sampling of urine, submitted either as urine or cultures from dip-slides or other agar plates. As in previous years, and as in *E. coli* isolated from urine in dogs (Table 4.27), resistance to ampicillin was the most common trait in 2020 (Table 4.32 and Figure 4.13). In comparison, in *E. coli* from the genital tract of mares (horses) resistance to trimethoprim-sulphamethoxazole was most common (Table 4.24 and Figure 4.9). The proportions of resistance in the *E. coli* isolated from cats have differed somewhat over the years as shown in Figure 4.13.

Seventy-seven percent (361/470) of the *E. coli* isolates were susceptible to all the tested antibiotics. The proportion of multiresistance was 2% (9/470) of the isolates, and comparable to figures between 2010 and 2019 (2-5%) (see previous Swedres-Svarm reports). Five of the isolates were resistant to three antibiotics, two to four, one to five and one to seven 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 4.35.

Seven of the *E. coli* isolates were resistant to cefotaxime (MIC >0.25 mg/L) and six were available for verification. Genes conferring transferable ESC resistance were detected in one of the isolates. For more information of ESBL isolated from cats in Sweden, see Notifiable diseases, ESBL-producing Enterobacterales (previously Enterobacteriaceae).

Two isolates were resistant to colistin (MIC >2mg/L). One of the isolates was available for PCR detection of the *mcr-1* to *mcr-9* genes and was negative.

Figure 4.13. Resistance (%) in clinical isolates of *Escherichia coli* from urine of cats, 2007-2020. The number of isolates each year varies (n=131-545, 2020 n=470).

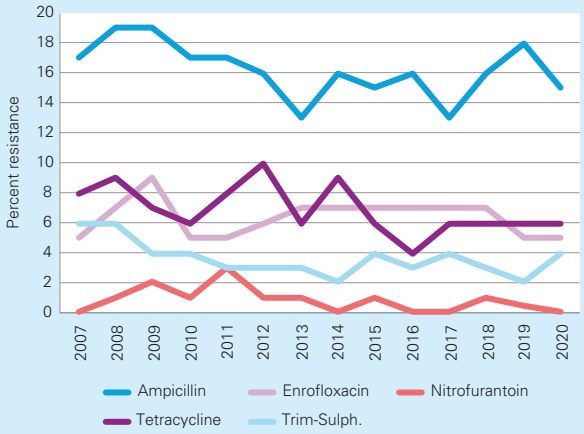


Table 4.32. Distribution of MICs and resistance (%) in *Escherichia coli* isolated from cats, 2020. Clinical isolates from urine.

Antibiotic	Resistance (%) 2020 n=470	Distribution (%) of MICs (mg/L)											
		≤0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	15						63.4	20.2	1.1	0.4	14.9		
Cefalexin	3							9.6	77.4	10.2	1.5	1.3	
Cefotaxime	1[b]			98.5	0.6	0.2	0.2	0.4					
Colistin	<1[c]					98.5	1.1		0.4				
Enrofloxacin	5		95.1	2.8	1.5				0.6				
Gentamicin	3						97.2	2.3			0.4		
Meropenem	0	99.8	0.2										
Neomycin	<1							98.3	0.9			0.9	
Nitrofurantoin	0										99.4	0.6	
Tetracycline	6						92.6	1.5			6.0		
Trim-Sulph.[a]	4				95.7	0.4	0.2		3.6				

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphamethoxazole); [b]Six of seven isolates with MIC >0.25mg/L were available for verification. Genes conferring transferable ESC resistance were detected in one of the isolates; [c]One of the two isolates with MIC 8mg/L was available for PCR detection of the *mcr-1* to *mcr-9* genes and the isolate was negative.

Staphylococcus felis

Isolates of *Staphylococcus felis* are from clinical submissions of samples from various locations, but mainly the external ear canal (39%), abscesses and wounds (27%), and urine (20%).

The proportion of resistance to the tested antibiotics in isolates of *S. felis* (Table 4.33) were less compared to *S. pseudintermedius* in dogs (Table 4.28). For example, resistance to penicillin due to penicillinase production was 19% in *S. felis*, but 70-77% in *S. pseudintermedius*. Seventy-five percent (302/403) of the *S. felis* isolates were susceptible to all the tested antibiotics. Multiresistance was detected in 5% (21/403) of the isolates, and comparable to the figures in 2015-2019 (4-7%). Twenty of the 21 multiresistant isolates were resistant to three of the tested antibiotics and one to four. No 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 4.36.

Pasteurella multocida

Isolates of *Pasteurella* spp. are from clinical submissions of samples from various locations, but mainly from wounds or skin lesions, abscesses, and the external ear canal (85%).

Pasteurella multocida was the most common *Pasteurella* sp. isolated in samples from cats, 89% (382/427). The proportion of resistance to antibiotics was low in the tested isolates (Table 4.34). *Pasteurella* spp. have a low inherent susceptibility to aminoglycosides, e.g., gentamicin.

In 2020 the cut-off for *Pasteurella multocida* were adjusted compared to the years before. For enrofloxacin from MIC 0.25 to 0.06 mg/L and for trimethoprim-sulphamethoxazole from MIC 4 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 low or no impact on the comparison of the yearly figures. In comparison the occurence of resistance in 2020 have not increased from previous years (2014-2019). For enrofloxacin the figures have varied between 0 and 2% and for trimethoprim-sulphamethoxazole <1 to 4%.

Table 4.33. Distribution of MICs and resistance (%) in *Staphylococcus felis* from cats, 2020. Clinical isolates from various locations.

Antibiotic	Resistance (%) 2020 n=403	Distribution (%) of MICs (mg/L) ≤0.25	0.5	1	2	4	8	16	32	64	>64
Cephalothin	1			98.8	1.0	0.2					
Cefoxitin[a]		94.3	3.7	0.5	0.7	0.7					
Clindamycin	5		95.3	1.0	0.7	3.0					
Enrofloxacin	<1	97.8	2.0	0.2							
Erythromycin	7		93.1	1.2	0.5	5.2					
Fusidic acid	2		96.5	1.0	1.0	1.5					
Gentamicin	1			96.8	2.2	0.7	0.2				
Nitrofurantoin	<1							98.8	0.7	0.5	
Oxacillin	0	99.8	0.2								
Penicillin[b]	18										
Tetracycline	1	95.0	2,7	1.0	0.2	0.5	0.5				
Trim-Sulph.[c]	2	95.5	2.0	1.5	0.5	0.5					

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

Table 4.34. Distribution of MICs and resistance (%) in *Pasteurella multocida* from cats, 2020. Clinical isolates from various locations.

Antibiotic	Resistance (%) 2020 n=382	Distribution (%) of MICs (mg/L) ≤0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	>8
Ampicillin	0				42.4	57.1	0.5					
Enrofloxacin	1	72.0	24.6	2.1	0.3	0.3	0.5	0.3				
Gentamicin	NR[b]			0.3			0.3	2.1	40.6	53.4	3.4	
Penicillin	0			54.2	45.0	0.8						
Tetracycline	0			1.3	9.9	83.2	4.5	0.3	0.8			
Trim-Sulph.[a]	<1					99.5	0.3	0.3				

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

Comparison of antibiotic resistance in *E. 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 4.35 and 4.36). Furthermore, for *Staphylococcus* spp. occurrence of pencillinase 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 4.35. Resistance (%) and multiresistance (%) in *Escherichia coli* isolated from different animal species tested with a fixed panel of 10 antibiotics. Isolates from clinical submissions 2020.

Animal species	Multiresistance (%)	Resistance (%) to 0->6 antibiotics							
		0	1	2	3	4	5	6	>6
Cats (urine)	2	77	14	7	<1	<1	<1		
Cattle, calves (faeces)	16	16	19	49	14	3			
Dogs (urine)	3	81	9	6	1	1	<1	<1	<1
Horses (genital tract)	5	80	13	2	4	2			
Pigs (faeces)	11	58	18	14	8	3			

Table 4.36. Resistance (%) and multiresistance (%) in *Staphylococcus* spp. isolated from different animal species tested with a fixed panel of 11 antibiotics. Isolates from clinical submissions 2020.

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	2	21	60	31	7	2						
S. felis – cats	5	18	75	17	2	5	<1					
S. pseudintermedius[b] – dogs	24	74	19	37	20	13	7	2	<1	<1	<1	
S. schleiferi – dogs	4	4	74	18	4	3	<1					

[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.

In 2020, indicator bacteria from broilers and turkeys were studied. Samples of intestinal contents were collected at slaughter and cultured for *E. coli*. 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.

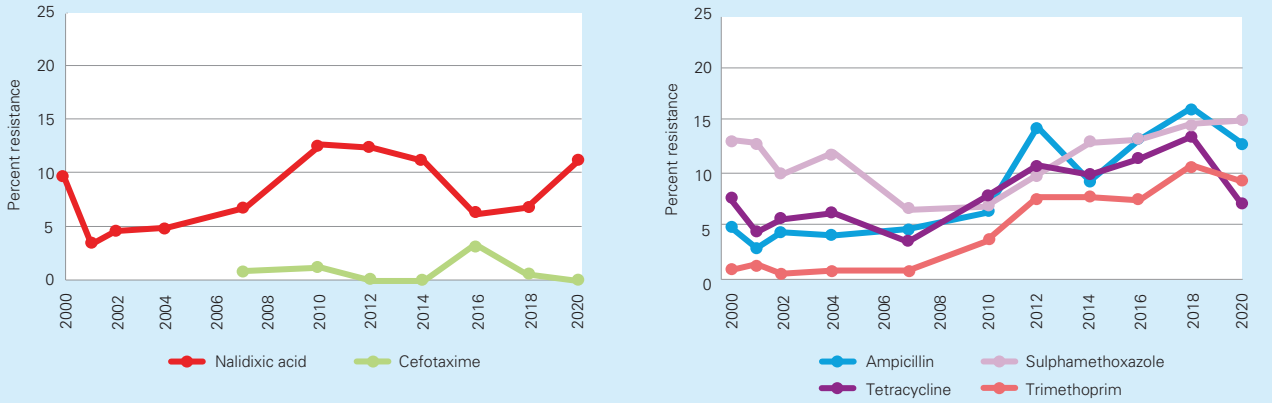
Escherichia coli

Broilers

Escherichia coli was isolated from 172 (98%) of 175 cultured caecal samples from broilers. The majority of the isolates (72%) was susceptible to all antibiotics tested (Table 4.37). Resistance to sulphonamides (15%), ampicillin (12%), and ciprofloxacin (12%) were the most common traits (Table 4.37 and 4.38). Eighteen isolates (10%) were multiresistant, i.e. resistant to three or more antibiotics. All of these had resistance to sulphonamides and ampicillin in their phenotype. Furthermore, all but three of the multiresistant isolates had resistance to trimethoprim in their phenotype.

Levels of resistance in *E. coli* from broilers are low in an international perspective. The proportion of isolates susceptible to all antibiotics tested has been stable in the latest years (75% in 2014, 71% in 2016, 69% in 2018 and 72% in 2020). Yet, for some substances the situation has become less favourable in the latest years (Figure 4.14). More precisely, occurrence of resistance to ampicillin, sulphonamides

Figure 4.14. Resistance (%) in *Escherichia coli* from broilers 2000-2020. The number of isolates each year varies (n=172-307, 2020 n=172).



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 (2010-2020).

and trimethoprim in *E. coli* from broilers has increased considerably since 2007. Likewise, occurrence of resistance to tetracycline has increased during these years even if the occurrence this year dropped considerably since 2018. Regarding substances in the category B (restrict) of the AMEG classification (EMA, 2019a), resistance to ploymyxins (colistin) has been tested since 2010 but has not been detected, and resistance to cefotaxime (tested since 2007) has been stable at a low occurrence (Figure 4.14). However, the occurrence of resistance to quinolones first increased, then decreased again and does now seem to be increasing again. The reason(s) for these changes is not known.

None of the isolates were resistant to cefotaxime or ceftazidime. However, using selective culture, ESC resistant *E. coli* was isolated from 34 (11%) of 300 samples. In ten isolates (3%), transferable genes for resistance to ESC were found and all of these had the $bla_{\text{CTX-M-1}}$ gene. The remaining 24 isolates had an AmpC phenotype and genome sequencing of these isolates revealed mutations causing hyperproduction of AmpC beta-lactamases. For more details and comments on occurrence of resistance to ESC, see section Antibiotic resistance in animals, Notifiable disease.

Turkeys

Escherichia coli was isolated from 44 (98%) of 45 cultured caecal samples from turkeys. The majority of the isolates (80%) was susceptible to all antibiotics tested (Table 4.37). Resistance to ampicillin (9%), sulphonamides (9%), and tetracycline (9%) were the most common traits (Table 4.37 and 4.38). Two isolates (5%) were multiresistant, i.e. resistant to three or more antibiotics. Both had resistance to ampicillin and tetracycline in their phenotype.

Levels of resistance in *E. coli* from turkeys are low in an international perspective. The proportion of isolates susceptible to all antibiotics tested has increased since 2014 and been stable in the latest years (44% in 2014, 71% in 2016, 80% in 2018 and 80% in 2020). This change is driven by decreased occurrence of resistance to some substances, namely ampicillin, sulphonamides and tetracycline (Figure 4.15). The differences over time are statistically significant ($p<0.05$, X^2). The reason(s) for these changes is not known.

None of the isolates were resistant to cefotaxime or ceftazidime. Moreover, also when using selective culture, no ESC resistant *E. coli* was isolated from the 45 samples. For more details and comments on occurrence of resistance to ESC, see section Antibiotic resistance in animals, Notifiable disease.

Figure 4.15. Resistance (%) in *Escherichia coli* from turkeys 2013-2020. The number of isolates each year varies (n=44-85, 2020 n=44).

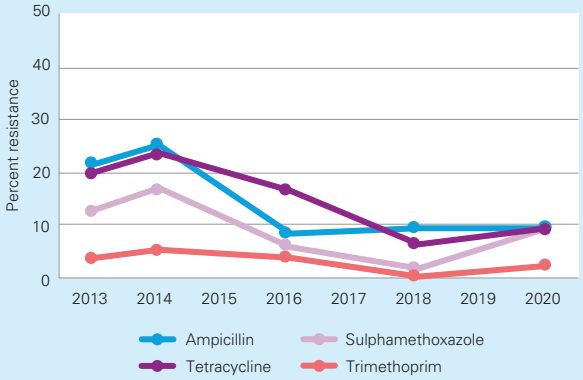


Table 4.37. Resistance (%) and multiresistance (%) in indicator *Escherichia coli* from broilers and turkeys, 2020. Most recent data on indicator *E. coli* from other sample categories are given for comparison.

Antibiotic	ECOFF (mg/L)	Resistance (%)									
		Broilers	Broiler meat	Cattle[b]	Laying hens	Pigs	Pig meat	Sheep	Turkeys	Dogs	Horses
		2020 n=172	2012 n=92	2015 n=101	2012 n=61	2019 n=174	2011 n=20	2006-09 n=115	2020 n=44	2012 n=74	2010-11 n=274
Ampicillin	>8	13	18	1	3	19	30	2	9	9	2
Azithromycin	>16	0	-	1	-	0	-	-	0	-	-
Cefotaxime	>0.25	0	0	0	2	0	0	0	0	1	0
Ceftazidime	>0.5	0	-	0	-	0	-	-	0	-	-
Chloramphenicol	>16	0	0	0	0	2	0	0	2	0	<1
Ciprofloxacin	>0.06	12	4	0	5	1	10	<1	5	3	<1
Colistin	>2	0	1	1	0	0	0	-	0	0	<1
Gentamicin	>2	<1	3	0	2	0	0	3	0	0	<1
Meropenem	>0.12	0	-	0	-	0	-	-	0	-	-
Nalidixic acid	>8	11	4	0	5	2	0	0	5	0	<1
Sulphamethoxazole	>64	15	16	2	8	18	10	7	9	4	15
Tetracycline	>8	7	14	1	13	13	0	<1	9	8	2
Tigecycline	>0.5	0	-	0	-	0	-	-	0	-	-
Trimethoprim	>2	9	7	0	5	15	10	2	2	1	16
Multiresistance[a]											
Susceptible to all above		72	66	96	80	71	70	89	80	84	83
Resistant to 1		15	18	2	7	6	10	8	14	8	2
Resistant to 2		3	7	2	7	12	5	3	2	7	12
Resistant to 3		6	3		7	6	15	<1	2		2
Resistant to >3		4	5			5			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 4.38. Distribution of MICs and resistance (%) in *Escherichia coli* from intestinal content from broilers (n=172) and turkeys (n=44), 2020.

Antibiotic	Source	Resistance %	Distribution (%) of MICs (mg/L)																
			≤0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	>1024
Ampicillin	Broilers	13							5.8	40.1	39.5	1.7				12.8				
	Turkeys	9							2.3	36.4	50.0	2.3	2.3			6.8				
Azithromycin	Broilers	0								2.3	44.8	51.7	1.2							
	Turkeys	0								11.4	47.7	40.9								
Cefotaxime	Broilers	0					100													
	Turkeys	0					100													
Ceftazidime	Broilers	0						100												
	Turkeys	0						100												
Chloramphenicol	Broilers	0										99.4	0.6							
	Turkeys	2										97.7				2.3				
Ciprofloxacin	Broilers	12	84.3	3.5		7.0	4.1	1.2												
	Turkeys	5	93.2	2.3		2.3	2.3													
Colistin	Broilers	0							99.4	0.6										
	Turkeys	0							100											
Gentamicin	Broilers	<1						88.4	9.3	1.7				0.6						
	Turkeys	0						90.9	9.1											
Meropenem	Broilers	0		100																
	Turkeys	0		100																
Nalidixic acid	Broilers	11									87.8	1.2	0.6	0.6	5.2	4.7				
	Turkeys	5									95.5				2.3		2.3			
Sulphamethoxazole	Broilers	15										54.1	30.2	0.6					1.2	14.0
	Turkeys	9										54.5	34.1	2.3					2.3	6.8
Tetracycline	Broilers	7								91.9	1.2			0.6	2.9	3.5				
	Turkeys	9								90.9				2.3	6.8					
Tigecycline	Broilers	0					99.4	0.6												
	Turkeys	0					100													
Trimethoprim	Broilers	9					44.8	41.3	4.1	0.6					9.3					
	Turkeys	2					65.9	20.5	11.4						2.3					
			≤0.016	**0.03**	**0.06**	**0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**256**	**512**	**1024**	**>1024**

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 2020) 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 2019 was used as a proxy for 2020 (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 2020, a total of 54.0 and 9.1 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. Penicillins (J01C and QJ01C) represent most of the amount in kg active substance of antibiotics for both humans and animals; 63 and 54%, 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 2020 are included.

Figure 5.1. Sales of beta-lactam antibiotics for human and veterinary medicine, kg active substance, 2020. Please note the difference in indexation of the x-axis between Figures 5.1 and 5.2.

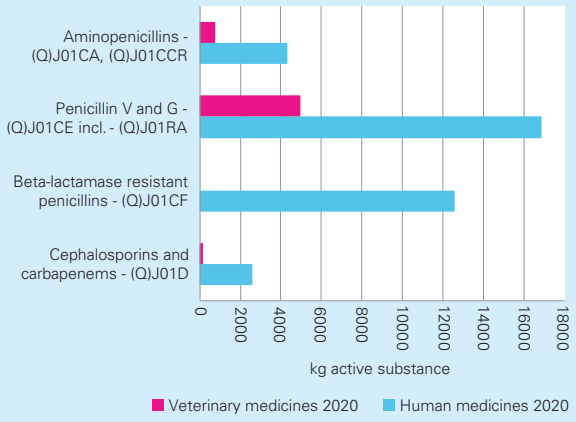
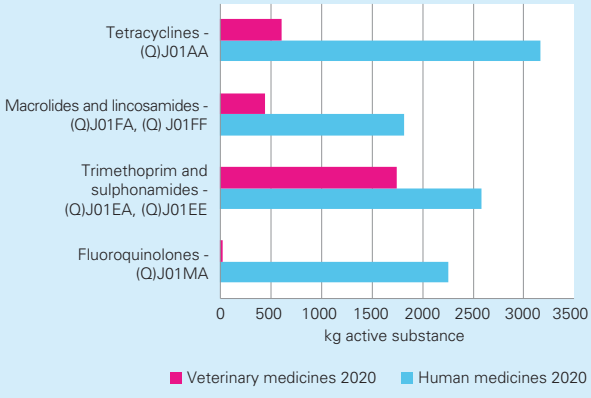


Figure 5.2. Sales of fluoroquinolones, macrolides, lincosamides, trimethoprim and sulphonamides and tetracyclines for human and veterinary medicine, kg active substance, 2020. Please note the difference in indexation of the x-axis between Figures 5.1 and 5.2.

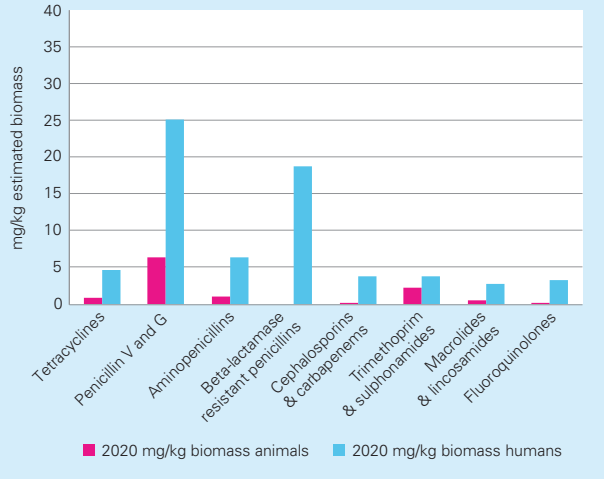


Comparison of sales expressed as mg per kg estimated biomass

In 2020, the sales were 79.8 and 11.9 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 103 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 2020.



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 rare in animals and on food in Sweden. Previously the occurrence in intestinal samples from broilers was high but it has decreased 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 is 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, is still commonly detected. In 2020, 10 of totally 27 cases of MRSA in horses were of this type. However, in 2019 a new *spa*-type, t1971, was notified (1 case) and in 2020 this *spa*-type dominated among reported isolates from horses with 14 of 27 cases. *Spa*-type t1971 is uncommon in humans in Sweden, in total three cases have been detected over the years.

MRSA CC398 acquired in Sweden is uncommon in humans. Among all MRSA cases with available typing results in 2020, there were 8 cases with isolates belonging to CC398, and the only *spa*-type found was t034. 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 2020, there were 5 reported cases with *spa*-types t373 (n=3), t3391 (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 from animals 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 needed 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 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 resistance 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.

For the majority of the domestically acquired infections in humans, the origin of the isolates is not known. 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 (20%) 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 43%, 24% and 1% respectively. From animals, 183 *C. jejuni* from broilers were tested. The resistance to fluoroquinolones was 21% and to tetracycline 5% no resistance to erythromycin was found.

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

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. 10.0 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)
Dog (UTI)	Urinary	2020	1 078	12.1	0.9[a]	0.6	2.2	0	0.2	7.0[b]
Cat (UTI)	Urinary	2020	470	15.3	0.6[a]	0.4	2.7	0	0	3.6[b]
Horse (e.g., endometritis)	Genital tract	2020	253	7.1	0.4[a]	0	5.2	0		14.6[b]
Dairy cow (mastitis)	Milk	2020	60	15.0	0[a]	0	1.7	0		5.0[b]
Calf (enteritis)	Faeces/Post-mortem	2019-20	37	43.2	0[a]	0	5.4	0		16.2[b]
Pig (enteritis)	Faeces/Post-mortem	2020	66	24.2	0[a]	0	3.0	0		27.3[b]
Pig (healthy)	Intestinal content	2019	174	19.0	0	0	0	0		14.9
Turkey (healthy)	Intestinal content	2020	44	9.1	0	0	0	0		2.3
Broiler (healthy)	Intestinal content	2020	172	12.8	0	0	0.6	0		9.3
Laying hens (e.g., salpingitis)	Post-mortem	2018	100	11.0	2.0[a]	0	1.0			3.0[b]
Humans (UTI)	Urinary	2020	199 172	29.2	10.7	3.9			1.2	19.9
Humans (bloodstream inf.)	Blood	2020	9 844		14.2	7.7	6.1	0		21.6[b]

[a]Enrofloxacin tested, BP >1mg/L; [b]Trimethoprim-sulphamethoxazole tested, BP >4 mg/L, NordicAST v. 10.0.

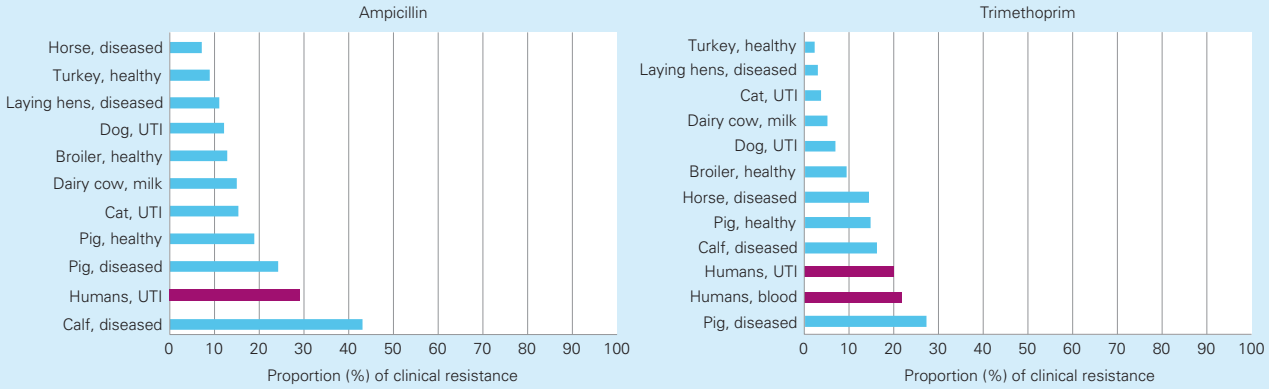
blood stream isolates from humans (Table 5.1). This agrees with a low use of these antibiotic classes in animals (see Sales of antibiotics for animals). However, although few isolates of *E. coli* from animals show clinical resistance to fluoroquinolones, reduced susceptibility (i.e. non wild-type) is common in some categories of diseased and healthy animals (See Antibiotic resistance in animals in this and previous reports). Possibly, the selection pressure from fluoroquinolone use 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. Proportion of resistance (%) to ampicillin and trimethoprim in *Escherichia coli* from humans and animals interpreted with clinical breakpoints. For details see Table 5.1.



Antibiotic resistance in *Campylobacter jejuni* from chicken meat and from Swedish patients

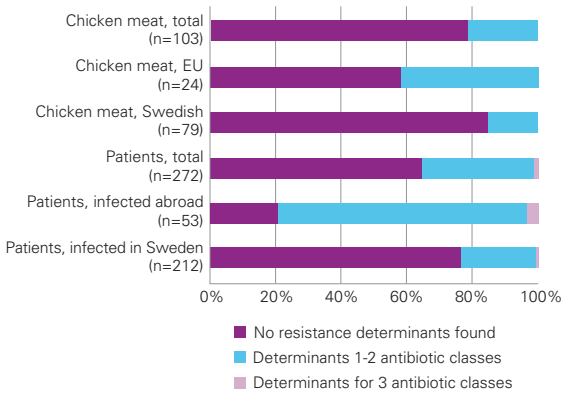
Introduction

Campylobacter is the major cause of bacterial gastroenteritis in Sweden and in the EU (EFSA & ECDC, 2021). Although *Campylobacter* infections are rarely treated with antibiotics, antibiotic treatment may be needed in severe cases, making antibiotic resistant *Campylobacter* a potential public health problem (Kaakoush et al., 2015). Macrolides are first-line antibiotics to treat severe *Campylobacter* infections, while fluoroquinolones, tetracyclines and aminoglycosides remain as alternative drugs (Kaakoush et al., 2015; ECDC, 2016; SRGA, 2019).

In 2016-2017, there was a large outbreak of campylobacteriosis in Sweden, linked to the consumption of domestic chicken meat (SVA, 2018). The importance of such meat as a source of *Campylobacter* infection has thereafter been investigated by the Swedish Food Agency and the Public Health Agency of Sweden (2018; 2019; 2020) in yearly comparative analyses between *Campylobacter* spp. isolates from chicken meat and Swedish patients.

The present study was performed using data from genome sequencing of *Campylobacter jejuni* isolates collected in 2018-2019. The aim was to investigate the occurrence of known genes and chromosomal mutations encoding antibiotic resistance in *C. jejuni* isolates from chicken meat obtained from the Swedish market and from human cases in Sweden, and to investigate the overlap between the resistance determinants identified in isolates from various categories of meat and patients.

Figure 1. The proportion of *Campylobacter jejuni* isolates from chicken meat at retail and from Swedish patients either fully lacking resistance determinants for quinolones, macrolides, tetracyclines and aminoglycosides (purple), or containing resistance determinants for 1-2 (blue) or 3 (light purple) of those antibiotic classes.



Method

Raw sequence reads of 79 *C. jejuni* isolates from Swedish chicken meat and 24 isolates from meat from other EU-countries, all sampled at retail, were included in the study. Sequence data from meat isolates were processed in the Swedish Food Agency's in-house bioinformatic pipeline (Östlund, 2019). Raw sequence reads of clinical isolates from the national surveillance program of *Campylobacter* were also included, of which 212 isolates were derived from domestically acquired infections, 53 were travel related and 7 lacked such information. Sequence data from human isolates were processed in the Public Health Agency's in-house bioinformatic pipeline Bacttyper (https://git.folkhalsomyndigheten.se). Antibiotic resistance genes and resistance-associated chromosomal mutations were identified in assembled contigs by applying AMRFinderPlus 3.10 and its associated database (NCBI; https://github.com/ncbi/amr). The study focuses on genes and mutations linked to resistance to clinically relevant antibiotic classes; quinolones, macrolides, tetracyclines and aminoglycosides.

Chi^2 tests were used in all comparisons to determine significant differences. A probability level of $p < 0.05$ was considered statistically significant.

Results and conclusions

In 85% of the *C. jejuni* isolates from Swedish chicken meat no genes or mutations encoding resistance to quinolones, macrolides, tetracyclines or aminoglycosides were identified, whereas 58% of the isolates from EU-produced meat lacked such resistance determinants (Figure 1). Among clinical isolates, 76% of the isolates from domestic cases and 21% of the isolates from cases infected abroad contained no such resistance determinants.

Three isolates from patients contained resistance determinants for three of the investigated antibiotic classes, whereas none of the meat isolates had such a multidrug resistance genotype (Figure 1). None of the isolates from either meat or patients harboured described genes or mutations encoding resistance to macrolides.

The same resistance genes or mutations for quinolones, tetracyclines and aminoglycosides were identified in isolates from both chicken meat and patients, except for the aminoglycoside gene *aadE*, which was found in two isolates from patients but not from meat (Table 1). The proportion of isolates containing the quinolone resistance mutation *gyrA*_T86I or the tetracycline resistance gene *tetO* was lowest for Swedish chicken meat and highest for patients infected abroad followed by meat imported from other EU countries (Table 1). In fact, the proportion of iso-

lates with these two respective resistance determinants was significantly higher for travel related cases compared to cases infected in Sweden as well as the three categories of chicken meat.

The most prevalent resistance determinant found among clinically relevant antibiotic classes was *gyrA*_T86I, where 17% of chicken meat and 33% of patients were positive. This was followed by *tetO* (chicken meat 10%, patients 19%) and the aminoglycoside resistance gene *aph(3')-IIIa* (chicken meat 4%, patients 1%) (Table 1). Overall, bla_{OXA} genes encoding resistance to beta-lactam antibiotics, which are not recommended for treatment, was the most common resistance trait (chicken meat 93%, patients 80%) (data not shown).

In conclusion, none of the isolates from either chicken meat or patients contained genes or mutations for resistance to macrolides. The determinants *gyrA*_T86I and *tetO*, encoding resistance to fluoroquinolones and tetracyclines respectively, were detected in isolates from all categories and were most frequently found in isolates from patients infected abroad.

The relatively high proportion of isolates lacking resistance determinants for the clinically relevant antibiotic classes investigated, which was noted for Swedish meat and domestic cases, could possibly reflect the generally lower usage of antibiotics in Sweden in relation to other countries, both in food-producing animals and in humans (EMA, 2020; ECDC, 2020).

Table 1. The proportion and number of *Campylobacter jejuni* isolates for various categories of chicken meat and patient groups containing resistance determinants for quinolones, tetracyclines or aminoglycosides. None of the isolates contained genes or mutations encoding resistance to macrolides.

Antibiotic class	Resistance determinant	Chicken meat, total (n=103) % (n)	Chicken meat, EU (n=24) % (n)	Chicken meat, Swedish (n=79) % (n)	Patients, total (n=272)[a] % (n)	Patients infected abroad (n=53) % (n)	Patients infected in Sweden (n=212) % (n)
Quinolone	*gyrA*_T86I	17 (18)	38 (9)	11 (9)	33 (91)	75 (40)	22 (47)
Tetracycline	*tetO*	10 (10)	25 (6)	5 (4)	19 (51)	51 (27)	10 (21)
Aminoglycoside	*aph(3')-IIIa*	4 (4)	13 (3)	1 (1)	1 (3)	4 (2)	<1 (1)
Aminoglycoside	*aadE*	0 (0)	0 (0)	0 (0)	1 (2)	2 (1)	<1 (1)

[a]including seven isolates from cases without travel information

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Background data, material, methods and references

Demographics and denominator data

Humans

Table 6.1. Inhabitants in Sweden, per region, per age group, 2020. 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	1 546	6 805	27 706	45 836	39 746	32 909	5 058	159 606
Dalarna	2 986	12 875	48 843	80 491	72 102	61 755	8 914	287 966
Gotland	516	2 294	9 528	16 205	15 864	13 454	1 825	59 686
Gävleborg	2 905	12 507	48 468	80 782	73 526	60 822	8 372	287 382
Halland	3 583	15 429	60 995	96 687	84 325	63 323	9 506	333 848
Jämtland	1 367	5 883	21 881	38 201	32 714	26 929	3 835	130 810
Jönköping	4 141	17 559	66 086	111 899	88 358	64 910	10 646	363 599
Kalmar	2 430	10 706	40 755	68 154	62 060	53 293	8 048	245 446
Kronoberg	2 328	9 676	36 297	63 022	47 441	36 608	6 097	201 469
Norrbotten	2 450	10 049	39 468	72 788	64 705	53 155	7 478	250 093
Skåne	15 889	66 679	244 261	449 382	331 957	234 819	34 840	1 377 827
Stockholm	28 474	118 239	424 513	843 910	582 570	333 546	45 829	2 377 081
Sörmland	3 217	14 390	54 136	84 978	73 789	58 870	8 160	297 540
Uppsala	4 324	18 452	66 887	133 734	89 020	62 681	8 615	383 713
Värmland	2 816	12 295	45 860	81 737	72 093	58 315	9 298	282 414
Västerbotten	2 952	12 194	45 233	89 574	64 151	50 355	7 277	271 736
Västernorrland	2 469	10 586	41 654	68 438	62 770	51 954	7 476	245 347
Västmanland	3 021	12 867	48 136	83 351	68 476	52 137	7 857	275 845
Västra Götaland	19 540	81 235	297 448	569 875	421 756	292 320	43 707	1 725 881
Örebro	3 344	14 142	53 297	95 557	73 591	56 900	7 974	304 805
Östergötland	5 085	21 473	80 560	150 546	112 331	83 056	12 444	465 495
Sweden	**115 383**	**486 335**	**1 802 012**	**3 325 147**	**2 533 345**	**1 802 111**	**263 256**	**10 327 589**

Table 6.2. Population in Sweden, per year, 2000-2020. 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

Table 6.3. Number of admissions and patient-days in somatic medical care in Sweden, 2016-2020. Data represent production by acute care hospitals in all regions except Dalarna for all years and Jämtland Härjedalen for 2020.

Year	Admissions	Patient-days
2016	1 360 540	6 140 745
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

Table 6.4. Number of admissions and patient-days in somatic medical care in the regions, 2020. Data represent production by acute care hospitals in all regions except Dalarna and Jämtland Härjedalen.

Region	Admissions	Patient-days
Blekinge	20 487	88 913
Gotland	9 697	38 290
Gävleborg	34 080	133 877
Halland	37 091	138 218
Jönköping	44 782	163 408
Kalmar	35 904	121 199
Kronoberg	22 072	93 604
Norrbotten	29 923	127 528
Skåne	163 442	704 339
Stockholm	294 912	1 240 819
Sörmland	33 776	152 001
Uppsala	45 811	234 213
Värmland	37 247	153 143
Västerbotten	42 120	188 861
Västernorrland	31 028	131 396
Västmanland	36 471	143 363
Västra Götaland	200 072	867 432
Örebro	38 949	163 274
Östergötland	59 566	221 222
Sweden	**1 217 430**	**5 105 100**

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 and numbers of holdings in Table 6.8 and 6.9.

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 on 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) 1980-2020. From the statistical database of the Board of Agriculture.

Animal Species	1980[a]	1985[a]	1990	1995	2000	2005	2010	2015	2018	2019	2020
Cattle											
Dairy cows	656	646	576	482	428	393	348	338	319	305	303
Beef cows	71	59	75	157	167	177	197	184	214	210	207
Other cattle >1 year	614	570	544	596	589	527	513	487	498	500	480
Calves <1 year	595	563	524	542	500	509	479	466	475	451	462
Total, cattle	1 935	1 837	1 718	1 777	1 684	1 605	1 537	1 475	1 507	1 466	1 453
Sheep											
Ewes and rams	161	173	162	195	198	222	273	289	296	280	263
Lambs	231	252	244	266	234	249	292	306	291	269	238
Total, sheep	392	425	406	462	432	471	565	595	587	549	501
Pigs											
Boars & sows	290	260	230	245	206	188	156	142	132	130	131
Fattening pigs >20 kg[a]	1 254	1 127	1 025	1 300	1 146	1 085	937	830	901	943	869
Piglets <20kg[b]	1 170	1 113	1 009	769	566	539	427	384	361	383	368
Total, pigs	2 714	2 500	2 264	2 313	1 918	1 811	1 520	1 356	1 393	1 456	1 368
Laying hens											
Hens	5 937	6 548	6 392	6 100	5 670	5 065	6 061	7 571	7 699	8 909	8 403
Chickens reared for laying	2 636	2 159	2 176	1 812	1 654	1 697	1 647	1 842	1 927	2 067	2 420
Total, hens	8 573	8 708	8 568	7 912	7 324	6 762	7 707	9 413	9 626	10 976	10 823
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, 1980-2020. From the statistical database of the Board of Agriculture.

Animal Species	1980	1985	1990	1995	2000	2005	2010	2015	2018	2019	2020
Cattle											
Cattle >1 year	574	584	523	502	490	433	425	406	410	418	420
Calves < 1 year	130	152	70	30	39	33	27	22	15	15	13
Total, cattle	704	736	593	532	529	466	453	428	426	433	434
Sheep	302	328	280	189	202	206	255	256	280	252	240
Pigs	4 153	4 283	3 653	3 743	3 251	3 160	2 936	2 560	2 646	2 573	2 623
Broilers	40 466[a]	36 410[a]	38 577[a]	61 313	68 617	73 458	78 507	95 974	100 535	106 121	110 335
Turkeys							495	475	526	508	521

[a]Data supplied by the National Food Administration.

Table 6.7. Quantity of livestock slaughtered (in 1000 tonnes) at slaughterhouses, 1990-2020. From the statistical database of the Board of Agriculture.

Animal Species	1990	1995	2000	2005	2010	2015	2018	2019	2020
Cattle									
Cattle >1 year	139.5	140.1	145.4	131.4	133.5	129.7	134.3	137.2	138.2
Calves < 1 year	6.8	3.2	4.4	4.5	4.3	3.5	2.5	2.4	2.2
Total, cattle	146.3	143.3	149.8	135.9	137.8	133.1	136.9	139.7	141.0
Sheep	5.0	3.5	3.9	4.1	5.0	4.2	5.6	5.1	4.9
Pigs	293.1	308.8	277.0	275.1	263.5	233.5	249.8	240.3	246.5
Broilers	44.0[a]	73.6[a]	89.9	96.2	112.0	137.7	149.3	159.2	166.8
Turkeys					3.2	3.8	4.4	4.6	4.7

[a]Data supplied by the National Food Administration.

Table 6.8. Average number of animals per holding 1995-2020. From the statistical database of the Board of Agriculture.

Animal Species	1995	2000	2005	2010	2015	2018	2019	2020
Cattle								
Dairy cows	27.2	33.7	46	61.9	81.5	91.8	93.9	98.3
Beef cows	9.2	12.0	13.8	16.2	17.7	20.6	20.5	20.6
Ewes and rams	19.5	24.8	29.2	31.7	31.8	32.4	33.1	33.2
Boars and sows	31	63	156	156	186	158	193	185
Fattening pigs	157	294	471	664	845	852	1 053	945
Laying hens	640	995	471	1 638	2 587	2 413	3 700	3 427

Table 6.9. Number of holdings with animals of different types, 1980-2020. From the statistical database of the Board of Agriculture.

Animal species	1980	1985	1990	1995	2000	2005	2010	2015	2018	2019	2020
Cattle											
Dairy cows	44 143	35 063	25 921	17 743	12 676	8 548	5 619	4 161	3 477	3 253	3 087
Beef cows	12 436	10 310	10 883	17 069	13 861	12 821	12 190	10 405	10 418	10 266	10 063
Calves <1 year	62 314	52 001	41 986	36 542	27 733	22 888	18 494	15 186	14 139	13 630	13 266
Total holdings with cattle	70 503	58 872	47 292	41 990	32 063	26 179	21 586	17 466	16 317	15 851	15 426
Sheep	10 238	10 595	9 749	10 037	8 089	7 653	8 657	9 110	9 120	8 463	7 956
Pigs	26 122	19 937	14 301	10 753	4 809	2 794	1 695	1 228	1 346	1 089	1 146
Laying hens	23 603	17 531	12 900	9 593	5 678	4 916	3 703	2 927	3 197	2 408	2 451

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. All 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 2020 version of the ATC/DDD index, available at https://www.whocc.no/atc_ddd_index/.

Antibiotic sales in humans

Swedish national statistics on drug utilisation

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.

Definitions of DDD 2020

Table 6.10. DDD for all antibiotic substances (J01) registered in Sweden in 2020.

	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	0.5
J01DC02 - cefuroxime - parenteral	3	J01MA14 - moxifloxacin	0.4
J01DC02 - cefuroxime - oral	0.5	J01XA01 - vancomycin	2
J01DC04 - cefaclor	1	J01XA02 - teicoplanin	0.4
J01DD01 - cefotaxime	4	J01XA04 - dalbavancin	1.5
J01DD02 - ceftazidime	4	J01XB01 - colistin - parenteral	9 MU
J01DD04 - ceftriaxon	2	J01XB01 - colistin - oral	3 MU
J01DD08 - cefixime	0.4	J01XB02 - polymyxin B	0.15
J01DD14 - ceftibuten	0.4	J01XC01 - fusidic acid	1.5
J01DD52 - ceftazidim and enzyme inhibitor	6	J01XD01 - metronidazole	1.5
J01DE01 - cefepime	4	J01XE01 - nitrofurantoin	0.2
J01DF01 - aztreonam - parenteral	4	J01XX01 - fosfomycin - parenteral	8
J01DF01 - aztreonam - inhalation	0.225	J01XX01 - fosfomycin - oral	3
J01DH02 - meropenem	3	J01XX04 - spectinomycin	3
J01DH03 - ertapenem	1	J01XX05 - methenamine - hippurate	2
J01DH51 - imipenem and enzyme inhibitor	2	J01XX05 - methenamine - mandelate	3
J01DH52 - meropenem and enzyme inhibitor	3	J01XX08 - linezolide	1.2
J01DH56 - imipenem and enzyme inhibitor	2	J01XX09 - daptomycin	0.28
J01DI01 - ceftobiprolmedocaril	1.5	J01XX11 - tedizolid	0.2
J01DI02 - ceftarolinfosamil	1.2		

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. The same applies for region Jämtland Härjedalen, for which data are excluded for 2020.

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, run 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.

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 kept 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 2020 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) 2016-2020 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. 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. 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.

Updates with new conversion factors for procaine benzylpenicillin

The protocol for the European surveillance of veterinary antimicrobial consumption has been updated with regard to conversion factors for certain benzylpenicillins (EMA, 2021). Benzylpenicillins, in particular procaine benzylpenicillin, constitute a large proportion of the total sales of antibiotics for animals in Sweden. Data for procaine benzylpenicillins from 1980 and onwards have therefore been recalculated with the new conversion factor (0.57 compared to previously 0.6).

Products sold with special licence

Antibiotic products sold with special licence (products prescribed and sold on exemption from general 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 broilers and turkeys as well as on samples of brolier meat.

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, 150 were selected in January-June and 150 in August-December. Each sample was from a unique flock but not always from a unique production site. Samples cultured were collected at seven abattoirs that in 2020 accounted for approximately 98% of the total volume of broilers slaughtered. The number of samples from each abattoir was roughly proportional to the annual slaughter volume of the abattoir.

Samples collected from turkey consists of caecal content of healthy turkeys sampled at slaughter. Each sample is from a unique flock but not always from a unique production site. Sampling was performed from January to December at two abattoirs that in 2020 accounted for approximately 90% of the total volume of turkeys slaughtered in Sweden.

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

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 the majority of isolates from notified incidents has been confirmed using molecular methods at SVA.

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.

VRE

Screening for VRE was performed on the same samples of intestinal content from caecas of healthy broilers as for ESBL (see above).

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

Campylobacter jejuni were isolated from caecal content from healthy broilers sampled at slaughter within the Swedish Campylobacter programme in which whole caeca are collected from each batch of broilers slaughtered. In 2020, one isolate from all 183 flocks positive for *C. jejuni* were selected for susceptibility testing. If *C. jejuni* was isolated more than once from the same flock, the isolate from the first sampling was chosen. The isolates were stored in -70°C until tested.

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.

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. are from the respiratory tract from calves.

In farmed fish, isolates of *Flavobacterium psychrophilum* and *Aeromonas salmonicida* 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 and the respiratory tract).

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

Indicator bacteria

The samples from intestinal content from healthy broilers and turkeys 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 broilers were cultured for indicator *E. coli* and these samples were evenly distributed over the year. From turkey, all collected samples 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 (previously Enterobaceriaceae) 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 (previously Enterobaceriaceae) 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. *Escherichia coli* like colonies on CC agar and CO agar were sub-cultured on MacConkeyagar, and if they were lactose positive, they were sub-cultured on horse-blood agar. Lactose positive isolates were species identified by MALDI-TOF MS and if positive for any Enterobacterales (previously Enterobaceriaceae) species the isolate would be further tested for ESBL production.

Clinical isolates from cats, dogs, and horses were submitted to the Dept. of Animal Health and Antimicrobial Strategies, SVA as bacterial strains. Isolates were species identified by MALDI-TOF MS.

MRSA and MRSP

Isolates were species identified by MALDI-TOF MS and tested for presence of *mecA* and *mecC* with PCR (see below). 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).

VRE

After the initial dilution in BPW (see screening for ESBL above), 100 µL was spread on Slanetz-Bartley agar with vancomycin (16 mg/L) and incubated for 48 hours at 37°C.

Two colonies, randomly chosen, were sub-cultured on horse-blood agar (5% v/v), (37°C, 24 h). Colonies with morphology consistent with enterococci, were identified to species level by MALDI-TOF MS. If available, one isolate of *E. faecium* and one isolate of *E. faecalis* were tested for antibiotic susceptibility.

Zoonotic pathogens

Salmonella

Salmonella was isolated and identified at the Dept. of Microbiology, SVA or at regional laboratories in accordance with standard procedures. All samples within official control programmes are cultured according to the procedures detailed by the MSRV (ISO 6579-1:2017). Confirmatory identification and serotyping were performed according to the procedures of White-Kauffmann-Le Minor. For certain isolates, the serovar was verified by whole genome sequencing.

Campylobacter

Campylobacter jejuni from broilers was isolated and identifed at the Dept. of Microbiology, SVA. Samples were cultured according to ISO 10272-1:2017 for detection of thermophilic *C. jejuni* by direct cultivation on mCCDA and incubation at 42°C for 48 h in a microaerophilic environment. Identification was based on colony morphology, microscopic appearance including motility. 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.

Indicator bacteria

Escherichia coli

After the initial dilution in BPW and incubation (see screening for ESBL above), 10 µL was spread on MacConkey agar and incubated overnight at 44°C.

Up to three lactose positive colonies with morphology typical for *E. coli* was sub-cultured on horse-blood agar (5% v/v), after which the isolate was tested for production of tryptophanase (indole). Only lactose and indole positive isolates with typical morphology were selected for susceptibility tests.

Susceptibility testing

Microdilution

At SVA, fast growing aerobic bacteria, *Campylobacter* and bacteria from fish are tested for antibiotic susceptibility with accredited methodology using dilution methods in cation adjusted Mueller-Hinton broth (CAMHB) (Difco). Tests are performed following the standards for microdilution of the Clinical and Laboratory Standards Institute (CLSI, 2018). The microdilution panels used are produced by Trek diagnostics LTD (Sensititre) and for *Brachyspira spp.*the panels are produced at Section of Substrate, SVA (VetMIC). Different panels are used depending on the bacterial species tested and the purpose of the investigation (monitoring or clinical diagnostics). Minimum inhibitory concentration (MIC) is recorded as the lowest concentration of an antibiotic that inhibits bacterial growth.

Some adaptations from the CLSI standard are employed. For *Pasteurella* spp. the tests are made by dilution in CAMHB supplemented with 5-10% horse serum followed by incubation in CO_2, 37°C for 16-18 hours. For testing of *A. pleuropneumoniae* dilution in HTM broth was used and with incubation in CO_2 at 37°C for 18-24 hours. *Streptococcus* spp. were tested using CAMHB supplemented with 5-10% horse serum followed by incubation at 35°C for 16-18 hours.

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

Susceptibility of *Brachyspira hyodysenteriae* and *B. pilosicoli*, was tested by a broth dilution method described by Karlsson et al. (2003), in tissue culture trays with 48 wells per plate. The wells were filled with 0.5 ml of a suspension of bacteria ($1x10^6$-$5x10^6$ CFU/ml) in brain heart infusion broth (BHI) with 10% foetal calf serum and incubated in an anaerobic atmosphere at 37°C for four days on a shaker.

Bacteria from fish are tested for antibiotic susceptibility by broth microdilution adapted for aquatic bacteria according to CLSI (2020b).

Phenotypic confirmatory tests for production of extended spectrum beta-lactamases (ESBLs) in Enterobacterales (previously Enterobaceriaceae) were performed with and without clavulanic acid in Sensititre EUVSEC2 microdilution panels and interpreted according to EUCAST.

Genotyping

Suspected isolates of MRSA and MRSP were confirmed by detection of the *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 (previously Enterobaceriaceae) 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 (previously Enterobaceriaceae), 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 (previously Enterobaceriaceae) 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. In addition, Dept. of Microbiology is accredited for isolation and identification of animal pathogens and of *Salmonella* according to the same standard.

For susceptibility tests of zoonotic, pathogenic and indicator bacteria, *Escherichia coli* ATCC 25922, *Enterococcus faecalis* ATCC 29212, *Staphylococcus aureus* CCUG 15915 (analogue to ATCC 29213), *Actinobacillus pleuropneumoniae* ATCC 27090, *Trueperella pyogenes* CCUG 13230, *Acinetobacter baumannii* 2012-70-100-69 - EURL 69 (used for control of higher concentrations of cephalosporins and carbapenems), *Aeromonas salmonicida* subsp. *salmonicida* CCUG 2116 (analogue to ATCC 14174) and *Campylobacter jejuni* CCUG 11284 (analogue to ATCC 33560) 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 6.11. Cut-off values (mg/L) for resistance. Values in red are current (March 21) EUCAST epidemiological cut-off values (ECOFFs), values in blue are CLSI ECVs, black underlined values deviate from ECOFFs and ECVs, and for values in black, ECOFFs or ECVs are not defined.

Antibiotic	*Actinobacillus pleuropneumonia*	*Aeromonas salmonicida*	*Brachyspira hyodysenteriae*	*Campylobacter jejuni*	*Campylobacter coli*	*Enterococcus faecium*	*Escherichia coli* (indicator)	*Escherichia coli* (pathogen)	*Flavobacterium psychrophilum*	*Klebsiella pneumoniae*	*Pasteurella multocida*	*Pseudomonas aeruginosa*	*Salmonella enterica*	*Staphylococcus pseudintermedius, S. felis, S. schleiferi*	*Staphylococcus aureus*	*Streptococcus zooepidemicus*
Ampicillin	>0.25					>4	>8	>8			>1		>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	>2
Chloramphenicol						>32	>16						>16		>16	
Ciprofloxacin				>0.5	>0.5	>8	>0.06						>0.06		>1	
Clindamycin														>0.5	>0.5[d]	>0.5
Colistin							>2	>2		>2		>4				
Daptomycin						>8										
Doxycycline			>0.5													
Enrofloxacin	>0.12						>0.12	>0.12		>0.12	>0.06[b]	>2		>0.5	>0.5	
Ertapenem							>0.03									
Erythromycin				>4	>8	>4								>0.5	>1	>0.5
Florfenicol	>0.5	>4							>2		>1					
Fusidic acid														>1	>0.5	
Gentamicin				>1	>1	>32	>2	>2		>2		>8	>1	>2	>2	
Imipenem							>0.5									
Linezolid						>4									>4	
Meropenem							>0.12	>0.12								
Nalidixic acid				>16	>16		>8						>4			
Narasin						>2										
Neomycin								>8		>8						
Nitrofurantoin								>64						>32 (UTI)	>32 (UTI)	
Oxacillin														>0.5		
Oxolinic acid		>0.12							>0.25							
Oxytetracycline	>1	>1														
Penicillin	>0.5										>0.5			[c]	[c]	>0.06
Streptomycin				>4	>4											
Sulphamethoxazole							>64						>256			
Teicoplanin						>2										
Temocillin							>16									
Tetracycline				>1	>2	>4	>8	>8	>0.12	>8	>2		>8	>1	>1	
Tiamulin			>0.25													
Tigecycline						>0.25	>0.5									
Trimethoprim							>2						>2		>2	
Trim & sulpha[a]	>1							>1		>0.5	>0.5			>0.5	>0.5	>0.5
Tylosin			>16													
Tylvalosin			>1													
Vancomycin						>4										
Valnemulin			>0.12													

[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 2000–2020

The number of isolates of different matrices reported in Svarm since 2000 is presented in the tables below.

Table 6.12. *Salmonella enterica*, number of isolates 2000-2020.

Source	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Warm-blooded animals	67	52	49	101	68	105	101	112	122	117	82	71	71	86	77	54	77	63	92	86	135
Cold-blooded animals										17											

Table 6.13. *Campylobacter* spp., number of isolates 2000-2020.

Source	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Cattle		67					68							109		23					
Pigs		98		105		100	46		97			83				108		171		171	
Broilers		50	100		100				38		100		100		102		170		170		183
Broiler meat														111							
Meat (different sources)		74																			
Water		19																			

Table 6.14. Indicator *Escherichia coli*, number of isolates 2000-2020.

Source	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Cattle	293						314			223				197		101		85			
Pigs	260	308		303		390			349			167				200		140		174	
Pig meat									19			20									
Broilers	274	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																			
Sheep									115												

Table 6.15. Indicator *Enterococcus faecalis* and *E. faecium*, number of isolates 2000-2020 *(E. faecalis/E. faecium)*.

Source	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Cattle	22/71						13/98			10/24				11/42							
Pigs	56/48	52/106		87/71		55/47			68/39			22/23									
Pig meat									17/3			29									
Broilers	24/151	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 6.16. Clinical isolates from farmed animals, number of isolates 2000-2020.

Animal species & bacterial species	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Cattle																					
Escherichia coli (enteric)			220		87	39	24			40	15	15	58	30	29	36	29	31	14	19	18
Escherichia coli (uterine)														60							
Escherichia coli (milk)				169										142	95	113	74	79	100	74	60
Klebsiella spp. (milk)				44			24							41	39	41	36	34	52	34	45
Pasteurella spp.	254			100				27	32	14	27	80	37	39	39	46	104	86	79	63	65
Staphylococcus aureus (milk)		100	100			96			87						74						
Streptococcus dysgalactiae (milk)			100																		
Streptococcus uberis (milk)			100																		
Fusobacterium necrophorum										41								24			
Pigs																					
Actinobacillus pleuropneumoniae	18							84	39	24	16	57	33	36	37	33	18	23	16	16	15
Brachyspira hyodysenteriae	50	75	109	100		31	26	23	15	24	9	7	7	8	7	7	11	15	5	7	12
Brachyspira pilosicoli				93		57	72	44	31	24	13	16	17	12	13	7	17	21	22	27	22
Escherichia coli (enteric)	399	82	340	340	386	325	298	93	83	102	94	91	74	142	118	84	67	222	52	75	66
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
Poultry (laying hens)																					
Escherichia coli (infection)								70											100		
Sheep																					
Staphylococcus aureus (udder)								25								30					
Fusobacterium necrophorum										24											
Mannheimia haemolytica and *Bibersteinia trehalosi*															44						
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				124
Flavobacterium psychrophilum								42	27	24	21	27	31	23	61	31	16	26	21	8	18

Table 6.17. Clinical isolates from companion animals and horses, number of isolates 2000-2020.

Animal species & bacterial species	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Horses																					
Actinobacillus spp.		40																			
Escherichia coli (genital)	323	103	166	188	188	161	124	273	174	210	236	174	196	140	229	188	324	240	309	244	253
Rhodococcus equi	73	20			187																
Streptococcus equi ssp. *zooepidemicus*	301	174	163	150	185	175	174	180	159	152	43	131	140	123	129	82	114	81	97	52	64
Staphylococcus aureus										308	131	135	145	139	132	116	75	127	118	104	131
Fusobacterium spp.																			40		
Dogs																					
Escherichia coli (urinary)	185	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
Pasteurella canis															207	194	253	152	232	157	248
Pasteurella multocida					231										29	46	23				
Pseudomonas aeruginosa				234						261	313	353	178	309	389	355	349	306	366	349	324
Staphylococcus pseudintermedius (skin)	145	156	133	102	159	126	89	220	258	381	444	388	229	566	513	393	376	417	515	507	567
Staphylococcus pseudintermedius (external ear)																		648	784	827	792
Staphylococcus pseudintermedius (wound)																		844	1 005	932	826
Staphylococcus schleiferi															297	201	163	175	240	233	236
Cats																					
Escherichia coli (urinary)			46	52	55	74	95	131	170	245	236	274	310	404	461	455	537	539	545	495	470
Betahemolytic streptococci												184									
Pasteurella dagmatis															20	22	19				
Pasteurella multocida															244	340	349	301	392	216	382
Staphylococcus felis															244	227	277	287	310	312	403

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SWEDRES | SVARM 2020

This annual report describes the monitoring of antibiotic resistance and antibiotic sales in human and veterinary medicine in Sweden in 2020.

The year 2020 was exceptional due to the COVID-19 pandemic. The impact of the pandemic 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 policy and recommendations. In relation to the COVID-19 pandemic, total sales for humans fell by approximately 17% during 2020.

While the sales of antibiotics indicate positive progress, the trends concerning antibiotic resistance are more concerning. Especially alarming is the number of cases of $ESBL_{CARBA}$ in humans. This increases the risk of introducing $ESBL_{CARBA}$ among vulnerable patients, which can have serious consequences. So far, $ESBL_{CARBA}$ has never been confirmed from Swedish animals.

For humans the COVID-19 pandemic had considerable impact on antibiotic resistance data as well. The number of reported cases of all mandatory resistance, except pneumococci with reduced susceptibility to penicillin, decreased. 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
- Reduced dispension of antibiotic prescriptions has not resulted in increased complications
- Primary Care Quality – Diagnosis-linked indicators for best practice in primary care
- Recently published, ongoing, and planned development of EUCAST criteria for antimicrobial susceptibility testing of organisms
- Antibiotic resistance in *Campylobacter jejuni* from chicken meat and from Swedish patients
- ESBL in broiler breeding animals 2010–2020
- Methicillin-resistant *Staphylococcus aureus* (MRSA) in horses
- Screening of healthy dogs for carriage of ESBL-producing Enterobacterales (previously Enterobacteriaceae) and methicillin-resistant coagulase-positive staphylococci
- SvarmPat – monitoring of resistance in pathogens from farm animals

The Public Health Agency of Sweden 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.