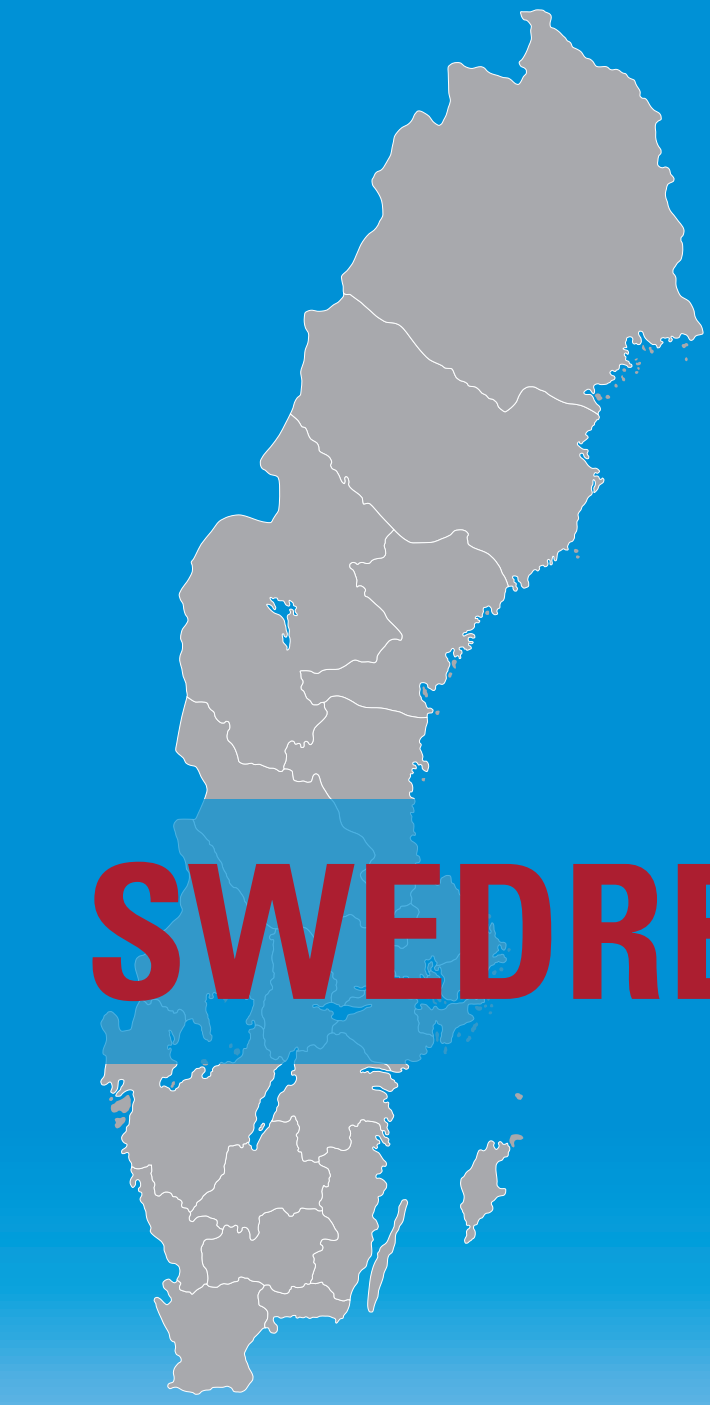

2018

SWEDRES | SVARM

Consumption of antibiotics and occurrence of antibiotic resistance in Sweden

Folkhälsomyndigheten
PUBLIC HEALTH AGENCY OF SWEDEN

SVA NATIONAL VETERINARY INSTITUTE

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

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Preface

This report from the monitoring of antibiotic resistance and antibiotic consumption in human and veterinary medicine, Swedres-Svarm, is an integrated report from the Public Health Agency of Sweden and the National Veterinary Institute with data from humans, animals, and food. This collaboration between the public health and veterinary sectors started in 2002.

The term global village was coined already during the 1960:s to describe the phenomenon of our world becoming more interconnected. Since then the term has been more popularised and is also sometimes used to describe our interdependence when it comes to antibiotic resistance: we are all in this together and geographic distance is no fail-proof protection. The best way to meet the challenge from widespread antibiotic resistance is through a one health approach. This means that we acknowledge the interconnection between people, animals, plants, and our shared environment and that we have a collaborative, multisectoral, and transdisciplinary approach to combat antibiotic resistance. This has also been the theme for the UN Interagency Coordination Group (IACG) on antibiotic resistance. The IACG's mandate is to provide practical guidance for approaches needed to ensure sustained effective global action to address antibiotic resistance. In doing so, IACG has put forward a set of recommendations to combat antibiotic resistance that was presented to the United Nations Secretary-General in a report published in April 2019.

The IACG was set up in response to the political declaration on antibiotic resistance made at the UN general assembly in 2016. The group is made up of representatives from the major UN and multi-sectoral agencies and a similar number of individual experts. It is co-chaired by the UN Deputy Secretary-General and WHO Director-General. The secretariat is hosted by WHO, with input from the Food and Agricultural Organisation of UN (FAO) and the World Organisation for Animal Health (OIE).

An integral part of any recommendations to combat antibiotic resistance and work towards a more prudent use of antibiotics is surveillance and monitoring systems. In this report we can show how the number of ESBL-forming *Escherichia coli* among poultry has been dropping substantially in Sweden. This is a consequence of our surveillance but would not have happened without close collaboration between authorities, farmers, trade organisations and individual companies. Collaboration is also something that Sweden emphasises in its response to IACG, if we want to push for a transformative change on how we combat antibiotic resistance we must engage with all stakeholders including across the agricultural sectors.

In the human sector, the national average for antibiotic prescription is now below 300 prescriptions per 1 000 inhabitants per year, which is a historically low level. This was accomplished through years of intensive work with antimicrobial stewardship lead by the regional and national Strama groups. Despite the comparatively good situation in Sweden regarding antibiotic resistance and antibiotic consumption, the preventive work needs to be continued and improved. Recent outbreaks of VRE in hospitals, and an increasing level of resistance to third generation cephalosporins in *E. coli* causing serious infections are two examples of development in this field that emphasise the need for further action.

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Thank you also to environmental departments in several municipalities for collecting samples of fresh meat from retail for ESBL-screening.

Content

Sammanfattning/Summary

Sammanfattning

När det gäller antibiotikaresistens hos bakterier från människor och djur har Sverige fortfarande en gynnsam situation vid en internationell jämförelse. Detta stöder att vi har effektiva strategier för att främja rationell användning av antibiotika och begränsa spridningen av antibiotikaresistens. Trots vårt jämförelsevis goda läge finns det problem med smittspridning och ökande antibiotikaresistens som motiverar fortsatta ansträngningar inom förebyggande arbete. Ett viktigt exempel är de återkommande utbrotten av vankomycinresistenta enterokocker på sjukhus. Detta beskrivs närmare i ett In Focus-avsnitt i denna Swedres-Svarm-rapport.

Antibiotikaanvändningen i Sverige har under de senaste årtiondena minskat inom både humanmedicin och veterinärmedicin. Dessutom har användningen av bredspektrumantibiotika minskat till fördel för antibiotika med smalare spektrum. Trots det har flera av de typer av resistens som övervakas ökat genom åren. Vissa undantag till dessa negativa trender finns dock.

Viktiga fynd 2018

- Två regioner nådde det nationella målet för antibiotikaförskrivning till människor på 250 recept per tusen invånare och år; Jämtland och Västerbotten. Detta långsiktiga mål är ett verktyg för att minska onödig antibiotikaanvändning.
- Det nationella genomsnittet för antibiotikaförskrivning till människor har nu nått under 300 recept per tusen invånare och år, vilket är en historiskt låg siffra.
- Ett stort och ett flertal mindre VRE-utbrott på sjukhus. VRE drabbar oftast känsliga patientgrupper där användningen av antibiotika är hög. Under året orsakade en utbrottsstam av VRE blodförgiftning hos fem patienter.
- Hög resistens mot ciprofloxacin hos Escherichia coli och Klebsiella pneumoniae, både från urin och blod från människor. Ciprofloxacin används vid behandling av febril urinvägsinfektion, det är viktigt att ta hänsyn till den höga resistensen vid empirisk behandling.
- Resistensen hos E. coli mot mecillinam och nitrofurantoin, förstahandsmedel vid okomplicerad urinvägsinfektion, är fortfarande låg, fyra respektive en procent.
- Höga nivåer av resistens hos Streptococcus agalactiae (GBS) mot erytromycin och klindamycin. Dessa antibiotika är alternativ till penicillin vid allergi. Barn kan drabbas av allvarliga infektioner i nyföddhetsperioden orsakade av S. agalactiae.
- Ökande antal fall av Enterobacteriaceae med $ESBL_{CARBA}$. De är extremt resistenta och det finns få behandlingsalternativ vid en eventuell infektion. Tidigt upptäckt och förhindrande av smittspridning inom humansjukvården är därför viktigt.
- Förbrukningen av antibiotika till djur är stabilt låg och domineras av penicillin med smalt spektrum.
- MRSA är ovanliga hos både lantbrukets djur och sällskapsdjur.
- Förekomsten av ESBL-bildande E. coli i tarm- och köttprov från slaktkyckling har minskat signifikant gentemot tidigare år.
- Bakterier som bildar $ESBL_{CARBA}$ har inte påvisats hos djur i Sverige.

Förbrukning av antibiotika

Antibiotikaförbrukning inom humanmedicin

Den totala antibiotikaförbrukningen i Sverige minskade med 4,4 procent mellan 2017 och 2018, till en nivå av 11,7 DDD per tusen invånare och dag. Detta mått omfattar antibiotika som sålts på recept till enskilda individer och antibiotika som ges till personer på olika vårdinrättningar såsom sjukhus, ungdomsmottagningar och särskilda boenden. För Region Dalarna ingår enbart den antibiotika som förskrivits på recept, eftersom regionen inte levererat statistik över försäljning till slutenvården under 2018. Sedan år 2000 har försäljningen av antibiotika i Sverige sjunkit med omkring 19 procent.

Öppenvård

Den minskade försäljningen av antibiotika på recept till patienter i öppenvården under 2018 omfattar de flesta antibiotikaklasser förutom betalaktamasstabila penicilliner (J01CF), trimetoprim med sulfonamid (J01EE) och nitrofurantoin (J01XE). Återkommande problem med tillgänglighet till antibiotika, dels till följd av restnotering av beredningar för oral suspension av amoxicillin med klavulansyra respektive cefadroxil, dels efter avregistreringen av ceftibuten under år 2017, kan bidra till den minskade försäljningen av kombinationer av penicilliner (J01CR) och cefalosporiner (J01DB-DE).

Antalet recept per tusen invånare i Sverige under 2018 var 296. Detta är en historiskt låg siffra, och den första gången sedan nationell övervakning av antibiotikaförrsäljningen startade som den nationella nivån varit under 300. För att nå det nationella målet på 250 recept per tusen invånare och år behövs dock ytterligare minskningar. Två regioner nådde målet under 2018.

Sjukhus och andra vårdformer

Under 2018 var försäljningen av antibiotika på rekvisition något lägre än under 2017, och det nationella medelvärdet är nu 1,52 DDD per tusen invånare och dag. Denna siffra omfattar försäljning av antibiotika som används till patienter på sjukhus samt sådan antibiotika som beställs till läkemedelsförråd på särskilda boenden och liknande inrättningar.

Data från akutsjukhus visar en något högre antibiotikaförsäljning 2018 jämfört med 2017, mätt som både DDD per hundra vårddagar och DDD per hundra vårdtillfällen. Betalaktamasstabila penicilliner (J01CF) fortsätter att vara den största anitbiotikaklassen mätt i antalet DDD. Det är stora skillnader mellan olika regioner, exempelvis vad gäller smalspektrumpenicilliner som utgör mellan omkring 6 och 18 procent av antibiotikaförsäljningen till akutsjukhusen mätt i DDD. Användningen av bredspektrumpreparat – cefalosporiner (J01DB-DE), karbapenemer (J01DH), fluorokinoloner (J01MA) och piperacillin med tazobactam (J01CR05) – visar stora regionala variationer i vilka preparat som används även om den sammanlagda nivån är lika.

Antibiotikaförbrukning inom veterinärmedicin

Den rapporterade försäljningen av antibiotika för djur uppgick 2018 till 10 042 kilogram varav 58 procent var penicillin med smalt spektrum. Motsvarande värden för 2009 var 15 368 kilogram och 50 procent.

Den totala försäljningen av antibiotika för djur har minskat med cirka två tredjedelar sedan 1986 då användningen av tillväxtbefrämjande antibiotika upphörde, korrigerat för att antalet av vissa djurarter har minskat 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 enskilda djur.

Jämförelse av försäljning inom human- och veterinärmedicin

Under 2018 såldes 59,5 respektive 10,0 ton antibiotika för allmänbehandling inom human- och veterinärmedicin. Mätt som milligram aktiv substans per skattad kilogram biomassa var förbrukningen 88,6 respektive 12,7 milligram per kilogram. Försäljning inom humanmedicin dominerade för alla inkluderade antibiotikaklasser utom för trimetoprim-sulfa.

Anmälningspliktig resistens

ESBL-producerande Enterobacteriaceae

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

Resultat 2018, Enterobacteriaceae med ESBL

- Antal rapporterade fall: 10 341 (föregående år 10 084), relativ förändring +2,5 procent.
- Antal fall med blodförgiftning: 703 (föregående år 594), relativ förändring +18 procent.
- Som tidigare år var Escherichia coli den vanligaste arten, 87 procent, följt av Klebsiella pneumoniae, 9 procent.

Resultat 2018, Enterobacteriaceae med $ESBL_{CARBA}$

- Antal rapporterade fall: 144 (föregående år 116), relativ förändring +24 procent.
- Antal fall med blodförgiftning: 7 (föregående år 2).
- Även bland Enterobacteriaceae med $ESBL_{CARBA}$ var E. coli den vanligaste arten, 60 procent, följt av K. pneumoniae, 33 procent.

Bakterier som bildar ESBL är inte anmälningspliktigt vid fynd hos djur. Sådana bakterier är, med undantag för slaktkycklingar, ovanliga hos djur i Sverige. Under 2018 undersöktes förekomsten av ESBL-bildande E. coli i tarm- och köttprov från slaktkyckling samt i tarmprov från kalkon och nötkreatur under ett år med selektiva metoder. Sådana bakterier hittades i 13 procent av tarmproven från slaktkyckling och i 12 procent av köttproven med svenskt ursprung. Detta innebär en signifikant minskad förekomst gentemot tidigare år. Bakterier som bildar $ESBL_{CARBA}$ har inte påvisats hos djur i Sverige.

Staphylococcus aureus resistenta mot methicillin (MRSA)

Samhällsförvärvad smitta är sedan länge den vanligaste typen hos människor, med mer än två tredjedelar av fallen. 2015 delades den upp i familje-/hushållssmitta och samhällsförvärvad smitta. Familje-/hushållssmitta utgjorde 39 procent av fallen under 2018.

Resultat 2018

- Antal rapporterade fall: 3 864 (föregående år 3 735), relativ förändring +3,5 procent.
- Antal fall med blodförgiftning: 64 (föregående år 55), relativ förändring +16 procent.
- Ett trettiotal mindre smittspridningar inom vård och omsorg rapporterades.

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. MRSA med *mecC* påvisades, inom ramen för ett forskningsprojekt, hos igelkott. Hos hundar och katter dominerar samma typer av MRSA som hos människor, vilket tyder på att människor är smittkällan. Hos hästar är lantbruksdjurstypen MRSA CC398 vanligast.

MRSP

Under 2018 var antalet anmälde fall av meticillinresistenta Staphylococcus pseudintermedius (MRSP) hos djur på samma nivå som de senaste åren. Totalt anmäldes 57 fall av MRSP (56 från hund och 1 från katt) till Jordbruksverket. De första åren efter att MRSP hade hittats hos djur i Sverige var i princip alla fall av en viss sekvenstyp (ST71). Numera förekommer dock ett flertal olika sekvenstyper och ST71 förekommer i princip inte alls.

MRSP är inte anmälningspliktig vid förekomst hos människa.

Streptococcus pneumoniae med nedsatt känslighet för penicillin (PNSP)

Resultat 2018

- Antal rapporterade fall: 91 (föregående år 61), relativ förändring +50 procent.
- Antal fall med blodförgiftning: 3 (föregående år 5).
- Ett utbrott på förskolor rapporterades från Örebro, det omfattade 18 fall.

Enterococcus faecium och faecalis resistenta mot vankomycin (VRE)

Resultat 2018

- Totalt rapporterades 444 fall: (föregående år 244), relativ förändring +82 procent.
- Antal rapporterade fall av E. faecium med vankomycinresistens: 438 (föregående år 236), relativ förändring +54 procent.
- Antal rapporterade fall (av E. faecalis): 6 (föregående år 8).
- Antal fall av VRE med blodförgiftning 9 (föregående år 2).
- Nitton sjukhusrelaterade utbrott rapporterades under året. Ett större (261 fall), tre mindre med 5-15 fall vardera, övriga var små spridningar med 2-4 fall vardera.

Resistens hos zoonotiska smittämnen

Salmonella är ovanligt hos djur i Sverige och isolerade stammar är oftast känsliga för antibiotika. Överförbar resistens mot tredje generationens cefalosporiner har aldrig påvisats hos isolat från djur i Sverige, och resistens mot antibiotikagruppen fluorokinoloner är mycket ovanlig. För Salmonellaarter var resistensen bland isolat från människor högst mot kinoloner, 22%. Ingen resistens mot meropenem rapporterades. Salmonella från svenska djur är en osannolik källa till invasiva infektioner hos människor. För det första rör det sig vanligen om olika typer av stammar, och för det andra är kinolonresistens vanlig hos isolat från människor till skillnad från isolat från djur.

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 50 procent och mot tetracyklin 31 procent 2018. En procent var resistenta mot erythromycin.

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

Resistens hos kliniska isolat från människor

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

- E. coli: Resistens hos blodisolat mot cefotaxim och ceftazidim var 7-8 procent, att jämföra med antalet anmälningar av E. coli ESBL från blod 2018: 470. Resistens mot ciprofloxacin är nu 18 respektive 12 procent hos isolat från blod respektive urin, ett observandum vid val av empirisk behandling av febril urinvägsinfektion.
- K. pneumoniae: Resistens hos blodisolat mot ccefotaxim och ceftazidim var 5 procent, att jämföra med antalet anmälningar av K. pneumoniae ESBL från blod 2018: 66. Liksom för E. coli är resistens mot ciprofloxacin nu relativt hög, 10-11 procent hos isolat från blod och urin.
- Resistensen hos E. coli mot mecillinam och nitrofurantoin, försthandsmedel vid okomplicerad urinvägsinfektion, är fortfarande låg, fyra respektive en procent.
- Staphylococcus aureus: Resistens mot cefoxitin (som indikerar MRSA) hos isolat från blod och prover från hud- och mjukdelar var 1,9 procent, att jämföra med antalet anmälningar av MRSA från blod 2018: 64.
- S. agalactiae (GBS): Resistens mot erytromycin och klindamycin har gradvis ökat och är nu cirka 20 procent för vart och ett av dessa antibiotika hos isolat från blod.
- Clostridioides difficile: Incidensen har minskat med 25 procent från 2009 till 2016 och därefter varit oförändrad. I likhet med tidigare år var alla undersökta isolat känsliga för metronidazol och vankomycin.

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. 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

The situation in Sweden regarding antibiotic resistance in bacteria in humans and animals is still favourable from an international perspective. This confirms that our strategies to promote the rational use of antibiotics and to limit the spread of antibiotic resistance are effective. Despite our comparatively good situation, there are problems with cross infection and increasing antibiotic resistance, which motivates continued efforts in preventive work. An important example is the recurrent outbreaks of vancomycin-resistant enterococci (VRE) in hospitals. This is described in more detail in an In Focus section of this Swedres-Swarm report.

Over the last decades the consumption of antibiotics in Sweden has decreased in both humans and in animals. In addition, the sales of broad-spectrum antibiotics have decreased while the use of narrow-spectrum antibiotics has increased. Despite this, many of the monitored types of antibiotic resistance have continued to increase over the years, even if exceptions to these negative trends occur.

Key findings 2018

- Two regions, Jämtland and Västerbotten, reached the national target for antibiotic prescriptions to humans of 250 prescriptions per 1 000 inhabitants per year. This long-term goal is intended to reduce unnecessary antibiotic use.
- The national average for antibiotic prescription to humans is now below 300 prescriptions per 1 000 inhabitants per years, which is a historically low level.
- One large and several small VRE outbreaks occurred in hospitals. VRE usually affects sensitive patient groups where the use of antibiotics is high. During the year, an outbreak strain of VRE caused septicaemia in five patients.
- High resistance to ciprofloxacin was seen in *Escherichia coli* and *Klebsiella pneumoniae*, both from urine and blood from humans. Ciprofloxacin is used in the treatment of febrile urinary tract infection, and when used for empirical treatment it is important to consider this high level of resistance.
- Resistance in *E. coli* to mecillinam and nitrofurantoin, used for first-line treatment of uncomplicated urinary tract infection, is still low, four and one percent respectively.
- High levels of resistance to erythromycin and clindamycin were observed in *Streptococcus agalactiae* (GBS). These antibiotics are alternatives to penicillin in cases of allergy. *S. agalactiae* can cause severe infections in children in the neonatal period.
- Increasing numbers of Enterobacteriaceae with $ESBL_{CARBA}$ were observed. These are extremely resistant, and there are few treatment options in case of infection. Early detection and prevention of spread within human health care is therefore important.
- Consumption of antibiotics for animals is stable at a low level and is dominated by narrow-spectrum penicillin.
- MRSA is unusual among both farm and companion animals.
- The occurrence of ESBL-producing *E. coli* in caecal and meat samples from broilers has decreased significantly compared to previous years.
- $ESBL_{CARBA}$-producing bacteria have not been detected in animals in Sweden.

Consumption of antibiotics

Antibiotic consumption in humans

The total sales of antibiotics to humans in Sweden was 4.4% lower in 2018 than in 2017 and the national average is now 11.7 DDD per 1 000 inhabitants per day. This figure encompasses all antibiotics sold on prescription to individuals, as well as antibiotics sold to hospitals and other health care facilities for dispensing to patients and clients. For the Region Dalarna, only prescription data are included because the region failed to supply data on hospital sales during 2018. The sales of antibiotics have decreased by approximately 19% since the year 2000.

Outpatient care

The decrease in sales in outpatient care during 2018 encompasses the majority of all antibiotic groups, except beta-lactamase resistant penicillins (J01CF), trimethoprim with sulphonamides (J01EE), and nitrofurantoin (J01XE). Persistent availability problems affecting oral suspensions of amoxicillin with clavulanic acid and cefadroxil, as well as the withdrawal of ceftibuten in 2017, might partly explain the lower sales of combinations of penicillins (J01CR) and cephalosporins (J01DB-DE).

Hospitals and other health and social care facilities

In 2018, sales were slightly lower than in 2017 and the overall figure is now 1.52 DDD per 1 000 inhabitants per day. This reflects all antibiotics sold for dispensing in hospitals, nursing homes and other healthcare facilities.

Data from acute care hospitals show that the consumption of antibiotics was slightly higher in 2018 compared with 2017, both when measured as DDD per 100 patient-days and as DDD per 100 admissions. Beta-lactamase-resistant penicillins (J01CF) still represent the greatest number of DDDs. There are large differences in consumption of antibiotics between Swedish acute care hospitals, for example, in the relative use of narrow-spectrum penicillins, which make up between 6.1% and 18.6% of the total acute care hospital consumption measured in DDDs. The use of broad-spectrum antibiotics – cephalosporins, carbapenems, fluoroquinolones, and piperacillin with tazobactam – also shows regional variation in terms of which substances are used, although the overall level is similar within the country.

Sales of antibiotics for animals

In 2018, reported sales of antibiotics for animals were 10 042 kg, of which 58% were narrow-spectrum penicillins. The corresponding figures for 2009 were 15 368 kg and 50%, respectively.

Since the withdrawal of growth-promoting antibiotics from the market in 1986, the total sales of antibiotics have decreased by around 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 consumption of antibiotics in human and veterinary medicine

In 2018, a total of 59.5 tonnes of antibiotics were sold for human use and 10.0 tonnes were sold for animal use. Measured as milligrams of active substance per kilogram biomass, the consumption was 88.6 and 12.7 milligrams per kilogram, respectively. Consumption by humans still dominates for all included classes of antibiotics except for trimethoprim-sulphonamides.

Notifiable resistance

ESBL-producing Enterobacteriaceae

ESBL-producing Enterobacteriaceae in humans have been subject to mandatory notification since 2007. This is the most common of the antibiotic resistance types where notification is required.

Results 2018, Enterobacteriaceae with ESBL

- The number of reported cases: 10 341 (previous year 10 084), relative change +2.5%.
- The number of cases of septicaemia: 703 (previous year 594), relative change +18%.
- As in previous years, *E. coli* was the most common species, 87%, followed by *K. pneumoniae*, 9%.

Results 2018, Enterobacteriaceae with $ESBL_{CARBA}$

- The number of reported cases: 144 (previous year 116), relative change +24%.
- The number of cases with septicaemia: 7 (previous year 2).
- Among Enterobacteriaceae with $ESBL_{CARBA}$, *E. coli* was the most common species, 60%, followed by *K. pneumoniae*, 33%.

ESBL-producing Enterobacteriaceae are, with the exception of broilers, rare among animals in Sweden. In 2018, the occurrence of ESBL-producing *E. coli* in caecal and meat samples from broilers, caecal samples from turkeys, and intestinal samples from cattle under one year of age were investigated with screening methods. Such bacteria were isolated from 13% of the intestinal samples and 12% of the meat samples from broilers of Swedish origin. This is a significant decrease from previous years and is most likely explained by decreased occurrence of ESBL-producing *E. coli* in the breeding pyramid. Bacteria that form $ESBL_{CARBA}$ have not been detected in animals in Sweden.

MRSA

Community-acquired infection has long been the most common type in humans, with more than two-thirds of the cases. In 2015, it was divided into family-/household-related infection and community-acquired infection. Family/household-related infections accounted for 39% of the cases in 2018.

Results 2018

- The number of reported human cases: 3 864 (previous year 3 735), relative change + 3.5%.
- The number of cases with septicaemia: 64 (previous year 55), relative change + 16%.
- About 30 smaller outbreaks in health- and elderly care were reported.

The occurrence of MRSA in animals in Sweden is still low, which limits the spread from animals to humans. MRSA was found sporadically in cats, dogs and horses in 2018, and MRSA with *mecC* was detected in samples from hedgehogs in a research project. 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 is the most common.

MRSP

In 2018, there were 57 cases of methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) notified to the Swedish Board of Agriculture. All cases except one were related to dogs. This number is about the same level as in recent years. The epidemiology of MRSP is becoming more diverse compared to earlier years with several sequence types occurring.

MRSP in humans is not notifiable.

PNSP

Results 2018

- The number of reported cases: 91 (previous year 61), relative change + 50%.
- The number of cases with septicaemia: 3 (previous year 5).
- An outbreak in preschools in Örebro county that included 18 cases.

VRE

Results 2018

- The number of reported cases: 444 (previous year 244), relative change + 82%.
- The number of reported cases of *E. faecium* with vancomycin resistance: 438 (previous year 236), relative change +54%.
- The number of reported cases: of *E. faecalis* with vancomycin resistance: 6 (previous year 8).
- The number of cases with septicaemia: 9 (previous year 2).
- Nineteen hospital-related outbreaks were reported during the year, including one larger (261 cases), three smaller with 5-15 cases each, and the rest with only 2-4 cases each.

Zoonotic pathogens

Salmonella is rare in animals in Sweden, and few incidents involve antibiotic-resistant strains. Strains with ESBL resistance have never been found in isolates from animals in Sweden, and resistance to fluoroquinolones is rare. Isolates from human invasive infections are markedly more resistant, which makes animals in Sweden an unlikely source for these infections.

Campylobacter from animals in Sweden are generally susceptible to relevant antibiotics, and resistance to erythromycin, for example, is most uncommon.

Infections, either in humans or in animals, caused by *Salmonella* and *Campylobacter* are usually not treated with antibiotics. In humans, only a small proportion are tested for susceptibility, and most of these isolates 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 laboratories and the Public Health Agency.

- *E. coli*: Resistance in blood isolates to cefotaxime and ceftazidime was 7-8%, to compare with the 470 reported cases of *E. coli* ESBL from blood in 2018. Resistance to ciprofloxacin is now 18 and 12%, in isolates from blood and urine, respectively and this needs to be noted when choosing empirical treatment for febrile urinary tract infection. Resistance in *E. coli* to mecillinam and nitrofurantoin, used for first-line treatment of uncomplicated urinary tract infection, is still low, four and one percent respectively.
- *K. pneumoniae*: Resistance of blood isolates to cefotaxime and ceftazidime was 5%, to compare with the 66 reported cases of *K. pneumoniae* ESBL from blood 2018: 66. As for *E. coli*, resistance to ciprofloxacin is now relatively high, 10-11% in isolates from blood and urine.
- *S. aureus*: Resistance to cefoxitin (which is indicative of MRSA) in isolates from blood and samples from skin and soft tissue was 1.9%, to compare with the 64 of reported cases of MRSA from blood 2018.
- *S. agalactiae* (GBS): Resistance to erythromycin and clindamycin has gradually increased and is now about 20% for both of these antibiotics in blood isolates.
- *Clostridioides difficile*: The incidence has decreased by 25% from 2009 to 2016 and subsequently remained unchanged. Like previous years, all isolates tested were susceptible to metronidazole and vancomycin.

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. 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 generally low, and the situation is favourable in an international perspective.

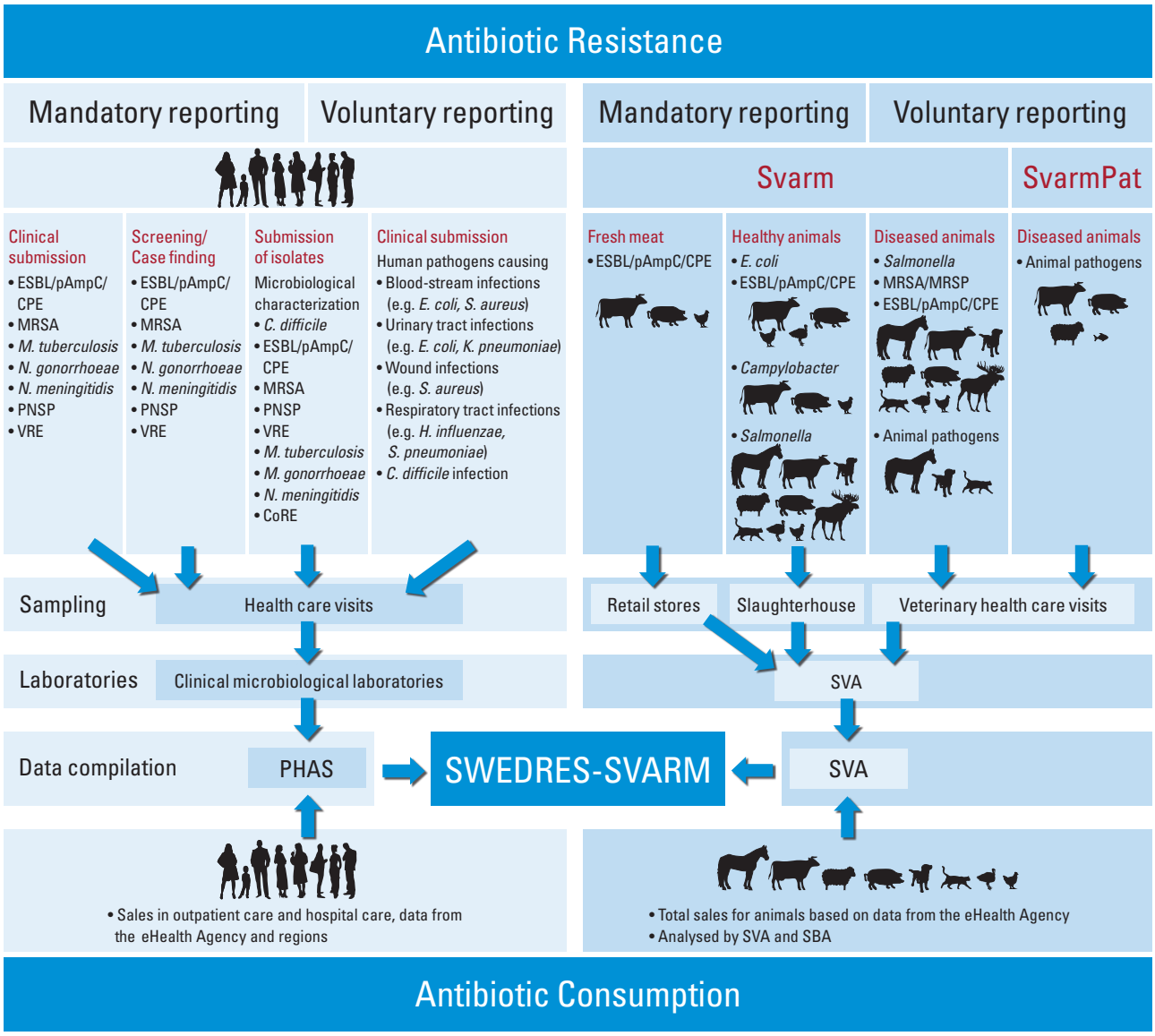
Guidance for readers

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 use of antibiotics and on antibiotic resistance in a joint report.

Data on occurrence of notifiable diseases caused by resistant 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 obtained from several sources and national programs and 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.

FIGURE 1.1. Schematic view of antimicrobial consumption and resistance monitored in Sweden 2018. Resistance in bacteria from humans and consumption for humans to the left and resistance in bacteria from animals and food and consumption 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 consumption

Antibacterials for systemic use in human are indexed as J01 in the Anatomical Therapeutic Chemical classification system. Unfortunately, the J01 group also includes the antiseptic substance methenamine. This is not an antibiotic and has no influence on antibiotic resistance. Throughout this report, methenamine is consequently excluded whenever antibiotics are referred to or presented as a group.

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

Wherever sales of antibiotics to a certain group of people is displayed (children 0-6 years, women 18-79 years, inhabitants in a region), the denominator is the number of individuals in the same group.

In this report the term 'outpatient care' includes all antibiotic sales on prescriptions to individuals. 'Hospital care' includes sales of antibiotics to hospitals, nursing homes and other health and social care facilities). Since national data on antibiotic consumption in hospitals in Sweden is thus combined with sales to some nursing homes and other facilities, the figure is 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.

National treatment recommendations may be adapted with local variations by the regional drug and therapeutics committees, 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 resistance in tables or graphs. The methods used for antibiotic susceptibility testing, whether MIC determination or disk diffusion inhibition zones, 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

The vast majority of 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, 2018a). 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	Pen	Penicillin G
Azt	Azithromycin	Flf	Florfenicol	Ptz	Piperacillin-Tazobactam
Bac	Bacitracin	Fox	Cefoxitin	Rif	Rifampicin
Caz	Ceftazidime	Fus	Fusidic acid	Str	Streptomycin
Cdr	Cefadroxil	Gen	Gentamicin	Sul	Sulphonamide
Cer	Ceftiofur	Imp	Imipenem	Tet	Tetracycline
Cet	Cephalothin	Kan	Kanamycin	Tgc	Tigecycline
Chl	Chloramphenicol	Lin	Linezolid	Tmp	Trimethoprim
Cip	Ciprofloxacin	Mec	Mecillinam	Tsu	Trimethoprim-sulfonamide
Cli	Clindamycin	Mer	Meropenem	Tob	Tobramycin
Col	Colistin	Nal	Nalidixic acid	Van	Vancomycin
Ctx	Cefotaxime	Nar	Narasin		
Enr	Enrofloxacin	Oxa	Oxacillin		

Abbreviations

AST	Antimicrobial Susceptibility Testing
ATC	Anatomical therapeutic chemical classification system
CDI	*Clostridioides difficile* infection
CMO	County medical officer
DDD	Defined daily dose
ECDC	European Centre for Disease Prevention and Control
ECOFF	Epidemiological cut-off value for non-susceptibility
EARSS/EARS-Net	European antimicrobial resistance surveillance system/network
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	Group A streptococci or *Streptococcus pyogenes*
GBS	Group B streptococci or *Streptococcus agalactiae*
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
PNSP	Penicillin non-susceptible pneumococci
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
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*)

Consumption of antibiotics in humans

Total consumption of antibiotics in humans

In 2018, the total sales of antibiotics (J01 excl. methenamine) in Sweden (outpatient care and hospital care) was 4.4% lower than in 2017 (12.3 and 11.7 DDD per 1 000 inhabitants per day, respectively). This adds to an overall downward trend, with approximately 19% less sales compared to the year 2000. A comparison with EU/EEA countries (European Centre for Disease Prevention and Control, 2018), where figures range from 34.1 to 11.0 DDD per 1 000 inhabitants per day with a population-weighted mean of 23.4, gives an indication of Sweden's restrictive position regarding antibiotic prescribing. However, there are considerable differences within Sweden with total sales ranging from 13.6 DDD per 1 000 inhabitants per day in Region Gotland to 9.7 in Region Jämtland, Figure 1.1. Region Dalarna is not included in the statistics showing total sales, due to failure to report data for sales of antibiotics to hospitals and other care facilities.

FIGURE 1.1. Sales of antibiotics (J01 excl. methenamine) to humans, all genders, per region, 2003-2018 in three-year intervals, DDD/1 000 inhabitants per day. Data includes prescriptions to individuals as well as antibiotics dispensed in hospitals, nursing homes etc.

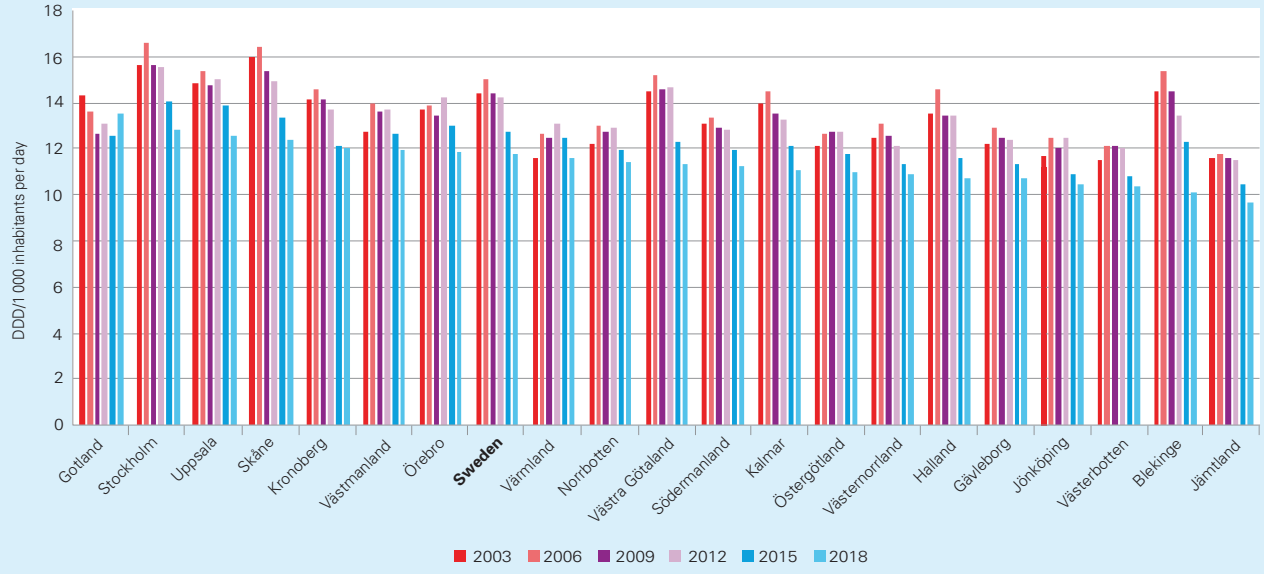
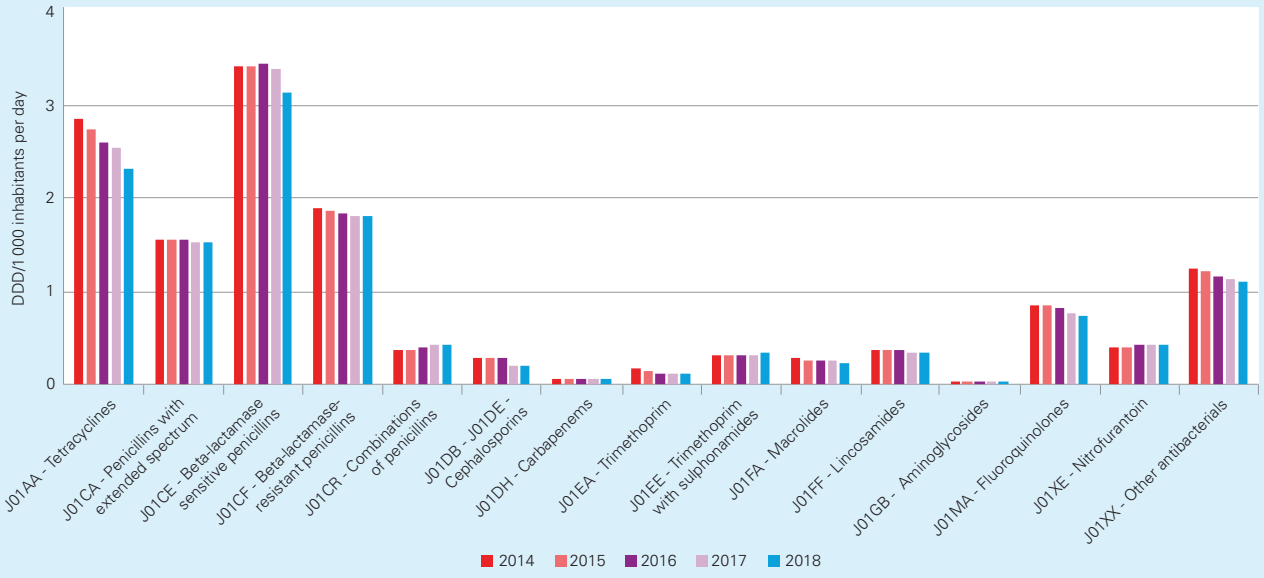


FIGURE 1.2. Sales of antibiotics to humans, all genders, ATC-5, 2014-2018, DDD/1 000 inhabitants per day. Data includes prescriptions to individuals as well as antibiotics dispensed in hospitals, nursing homes etc.



Approximately 85% (measured as DDD) of antibiotics in Sweden 2018 were sold on prescriptions in outpatient care. Beta-lactamase sensitive penicillins and tetracyclines were the two most sold antibiotic groups in Sweden during 2018, despite decreased sales. Overall, the sales of tetracyclines and fluoroquinolones continues the decrease seen in recent years. Nitrofurantoin, a recommended first-line treatment for urinary tract infections, continues to increase, Figure 1.2.

Antibiotics in outpatient care

The statistics for outpatient care reported in Swedres-Svarm includes all sales of antibiotics on prescriptions issued to individuals; from healthcare centres in the community and from hospitals. Since 1992, the total sales of antibiotics on prescriptions has decreased by 47.2%, Figure 1.3. The greatest change during these years is seen among young children (the age group 0-4 years), where sales decreased by 75.9%, from 1 328 prescriptions per 1 000 inhabitants per year in 1992 to 320 in 2018. A multitude of structural factors may have contributed to this marked change, for example altered supply chains for medicines, extension of the vaccination programme for children, organizational changes in the health care system, or demographic changes. Long-term strategic work targeting the quality of prescribing are described by Mölstad and colleagues in *Lessons learnt during 20 years of the Swedish strategic programme against antibiotic resistance* (Mölstad S, Löfmark S, et al. 2017).

The sales of antibiotics in outpatient care was 4.2% lower in 2018 than in 2017; 309 versus 296 prescriptions per 1 000 inhabitants per year, respectively. A statistically significant decrease is seen across all age groups (data not shown), and the rate of change appears higher over time. Less seasonal variation in sales of antibiotics is seen over the years (data available at https://www.folkhalsomyndigheten.se/folkhalsorapportering-statistik/statistikdatabaser-och-visualisering/antibiotikastatistik/sverige/), which could indicate increased adherence to prescribing guidelines (Coenen S, Ferech M, et al. 2007).

The decrease in sales in outpatient care during 2018 encompasses a majority of all antibiotic groups, except beta-lactamase resistant penicillins (J01CF), trimethoprim with sulphonamides (J01EE), and nitrofurantoin (J01XE), Figure 1.4. Persistent availability problems affecting oral suspensions of amoxicillin with clavulanic acid and cefadroxil, as well as the withdrawal of ceftibuten in 2017, may partly explain the lower sales of combinations of penicillins (J01CR) and cephalosporins (J01DB-DE).

Beta-lactamase sensitive penicillins (J01CE) and tetracyclines (J01AA) were the most commonly sold antibiotics in 2018, measured as DDD per 1 000 inhabitants per day.

FIGURE 1.3. Sales of antibiotics (J01 excl. methenamine) in outpatient care, to humans, all genders, per age, 1987-2018, prescriptions/1 000 inhabitants per year.

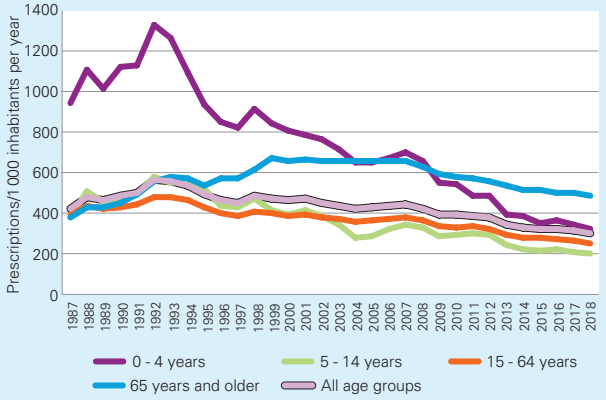
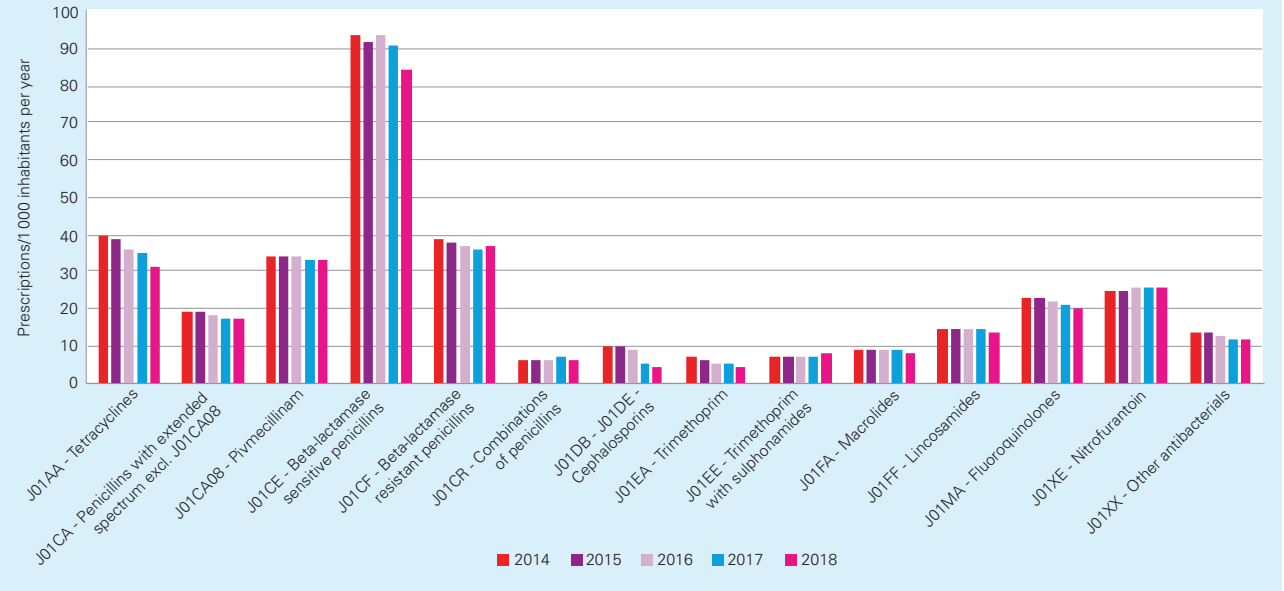


FIGURE 1.4. Sales of antibiotics in outpatient care, to humans, all genders, ATC-5, 2014-2018, prescriptions/1 000 inhabitants per year.



Doxycycline (J01AA02) represents the major part of the tetracycline DDDs. If measured prescriptions, beta-lactamase sensitive penicillins (J01CE) and beta-lactamase resistant penicillins (J01CF) were the most commonly sold antibiotics, Figure 1.4 and Table 1.1.

Antibiotics commonly used to treat respiratory tract infections, urinary tract infections, and skin and soft tissue infections

National treatment and prescribing recommendations for infectious diseases, including documentation of the assessment of supporting evidence, are published by the Medical Products Agency. A short, accessible version for use in daily practice is made widely available for clinicians through a collaboration with Strama and the Public Health Agency of Sweden (The Public Health Agency of Sweden, 2019).

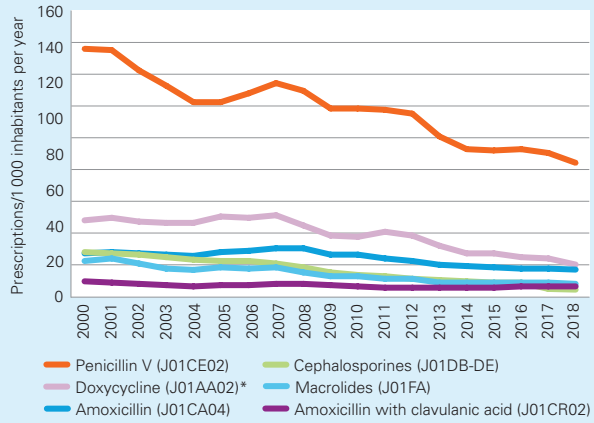
Antibiotics commonly used to treat respiratory tract infections (RTI) are overall the most frequently prescribed antibiotics in Sweden. The antibiotics included in this measure are doxycycline (J01AA02; excluding packages larger than 50 tablets), narrow spectrum penicillin (J01CE02), amoxicillin (J01CA04), amoxicillin with enzyme inhibitor (J01CR02), cephalosporins (J01DB-DE), and macrolides (J01FA), Figure 1.5. Here we also find the greatest decrease over time in terms of number of prescriptions per 1 000 inhabitants per year, from 294 in 2000 to 142 in 2018. Between 2017 and 2018 the combined sales of RTI antibiotics decreased by 8.2%.

Narrow spectrum penicillin, (J01CE), is the recommended first line antibiotic for treatment of community acquired RTI in Sweden (the 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 1.5 and Table 1.1. The sales of tetracyclines commonly used to treat respiratory tract infections (packages containing less than 50 tablets) has decreased over the last decades, possibly reflecting increasing adherence to the recommendation that acute bronchitis shall not be treated with antibiotics.

Beta-lactamase resistant penicillins (J01CF) were the second most frequently prescribed antibiotic in outpatient care measured in prescriptions per 1 000 inhabitants. The sales of this group increased by 1.6% in 2018 compared with 2017 and represent 12.4% of the total sales of antibiotics in outpatient care in 2018, Table 1.1.

National treatment recommendations for urinary tract infections (UTIs) (the Swedish Medical Products Agency, 2017), recommends pivmecillinam (J01CA08) and nitrofurantoin (J01XE01) over trimethoprim (J01EE01) against uncomplicated UTIs in women aged 15 years or older. Prescribers are also encouraged to minimise the use of fluoroquinolones (J01MA) due to increasing resistance among gram negative pathogens. The trend towards increased use of first-line antibiotics continues, showing that sustainable change in prescribing is possible, Figure 1.6. The overall sales of antibiotics commonly prescribed against UTI in women has decreased slowly over the years; by 8.5% since 2000 measured in prescriptions per 1 000 women aged 18-79 years. However, if measured as DDD per 1 000 women per day, sales have decreased by 18.9% in the same period. This suggests a move towards shorter treatment durations for this condition, which is also according to recommendations.

FIGURE 1.5. Sales of antibiotics commonly used to treat respiratory tract infections, outpatient care, humans, all genders, 2000-2018, per year, prescriptions/1 000 inhabitants.



* Excludes packages larger than 50 tablets

Figure 1.6. Sales of antibiotics commonly used to treat urinary tract infections in women, outpatient care, humans, 2000-2018, per year, prescriptions/1 000 women per year.

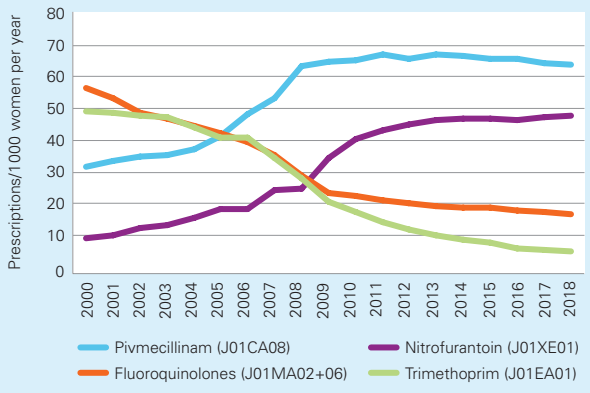
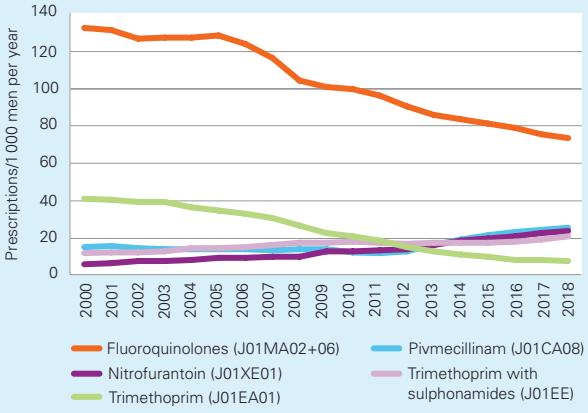


Figure 1.7. Sales of antibiotics commonly used to treat urinary tract infections in men, outpatient care, humans, 2000-2018, per year, prescriptions/1 000 men per year.



The total sales of antibiotics commonly used to treat UTI in men aged 65 years and older has decreased by 26.8% since 2000, Figure 1.7. However, data for 2018 indicates a slight increase from the previous year, from 149 to 151 prescriptions per 1 000 men per year. Due to increasing resistance in gram-negative bacteria, the use of fluoroquinolones has been questioned and nitrofurantoin and pivmecillinam are now recommended as first line antibiotics for treatment of symptomatic UTI without fever in men (the Swedish Medical Products Agency, 2017). Sales of these two antibiotics, measured as prescriptions per 1 000 men per year, have increased by 4.7 and 4.6%, respectively between 2017 and 2018. The changes are significant ($p<0.001$) and the rate gets higher over time. Meanwhile, sales of fluoroquinolones to men aged 65 years and older has decreased significantly $p<0.001$ since 2000. The sales decreased further in 2018; by 2.4% compared with 2017.

Age and gender differences

Antibiotics that are commonly prescribed against RTI are the most frequently sold to the age group 0-4 years, among both girls and boys, and represent 84% of the total antibiotic sales in this age group. Overall, RTI antibiotics are prescribed more to women than to men, apart from those aged 80 years or older, Figure 1.8.

In the older age groups (from 70-79 years for women and 80 years and older for men) antibiotics commonly used to treat UTIs are the most frequently prescribed antibiotics. These antibiotics are also prescribed to a larger extent to women of all ages, probably due to the higher prevalence of lower UTI among women, Figure 1.9. This measure includes pivmecillinam (J01CA08), trimethoprim (J01EA01), ciprofloxacin (J01MA02) and nitrofurantoin (J01XE01).

Figure 1.8. Sales of antibiotics that are commonly prescribed against respiratory tract infections to humans in 2018, outpatient care, prescriptions/1 000 inhabitants in 2018 per year. This measure includes doxycycline(J01AA02; excluding packages larger than 50 tablets), narrow spectrum penicillin (J01CE02), amoxicillin (J01CA04), amoxicillin with enzyme inhibitor (J01CR02), cephalosporins (J01DB-DE), and macrolides (J01FA).

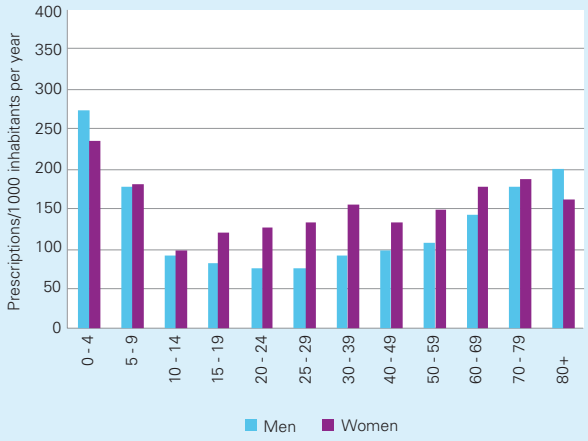


Figure 1.9. Sales of antibiotics that are commonly prescribed against urinary tract infections to humans in 2018, outpatient care, prescriptions/1 000 inhabitants in 2018 per year. This measure includes pivmecillinam (J01CA08), trimethoprim (J01EA01), ciprofloxacin (J01MA02) and nitrofurantoin (J01XE01).

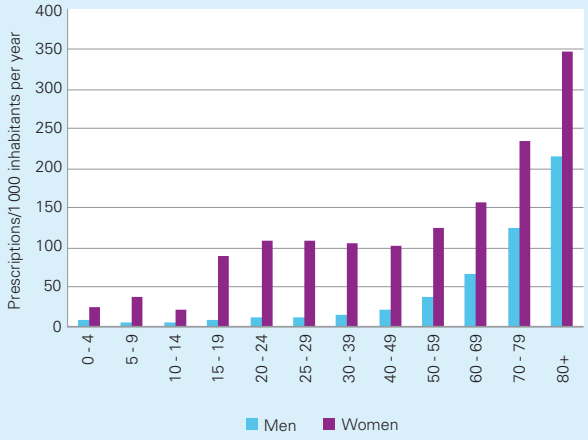


Figure 1.10. Sales of antibiotics that are commonly prescribed against skin and soft tissue infections to humans in 2018, outpatient care, prescriptions/1 000 inhabitants in 2018 per year. This measure includes clindamycin (J01FF01) and flucloxacillin (J01CF05).

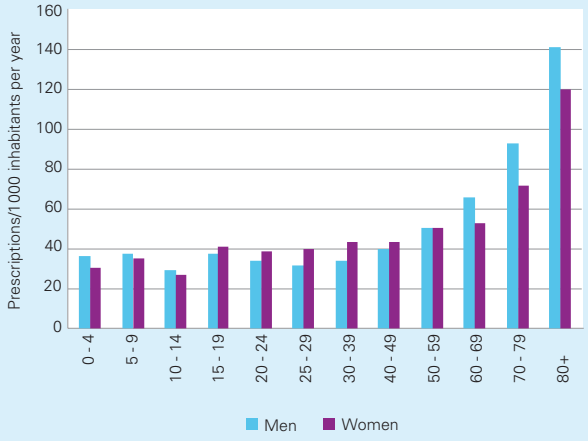
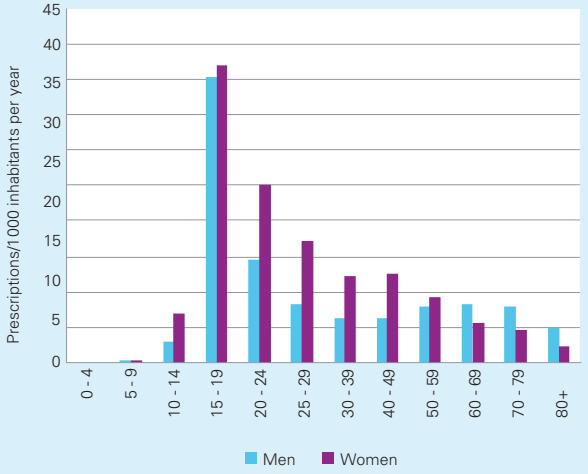


Figure 1.11. Sales of antibiotics that are commonly prescribed against skin and soft tissue infections (acne) to humans in 2018, outpatient care, prescriptions/1 000 inhabitants in 2018 per year. This measure includes doxycycline (J01AA02; packages over 50 tablets), lymecycline (J01AA04), oxytetracycline (J01AA06) and tetracycline (J01AA07).



The prescribing of antibiotics that are commonly used against skin and soft tissue infections (SSTI) is similar to men and women and between age groups, with a slight increase towards the elderly, Figure 1.10. Included in this measure are clindamycin (J01FF01) and flucloxacillin (J01CF05). Antibiotics commonly used to treat acne are mainly used by teenagers of both genders (15-19 years), Figure 1.11. This measure includes doxycycline (J01AA02; packages over 50 tablets), lymecycline (J01AA04), oxytetracycline (J01AA06) and tetracycline (J01AA07).

Overall, 60% of all antibiotic prescriptions in Sweden during 2018 were issued to women. This proportion has been stable over time. During 2018, women were prescribed 354 antibiotic prescriptions per 1 000 inhabitants per year while men were prescribed 233. The greatest differences in prescriptions between men and women are seen in the age groups 20-39 years (20-29 and 30-39), where 68-70% of the total antibiotic sales were to women, Figure 1.12.

Comparison across age groups shows that the use of antibiotics is greatest among people that are 80 years and older; 627 prescriptions per 1 000 inhabitants per year. As mentioned in the chapter "Guidance for readers", parts of the antibiotic use among the elderly are not included in the statistics for outpatient care and therefore a possible underestimation in the age group 80+ cannot be ruled out.

Antibiotic consumption among children

Sales of antibiotics to children aged 0-6 years was 4.6% lower in 2018 than in the previous year; 311 prescriptions per 1 000 children compared to 326. Different kinds of penicillins are the most commonly prescribed antibiotics in this age group; penicillin V (J01CE02), amoxicillin (J01CA04) and flucloxacillin (J01CF05) represent 59.5%, 12.5% and 9.1% respectively of the total sales to this age group in 2018, Table 1.1.

The decrease encompasses 17 out of 21 regions. There are still large variations within Sweden regarding antibiotic sales to children between 0 and 6 years; from 351 prescriptions per 1 000 children per year in Region Stockholm to 161 in Region Jämtland, Figure 1.13. The last few years have also seen substantial changes in some regions, notably Stockholm, Skåne and Uppsala.

Figure 1.12. Sales of antibiotics (J01 excl. methenamine) to humans, 2018, per age and gender, prescriptions/1 000 inhabitants per year.

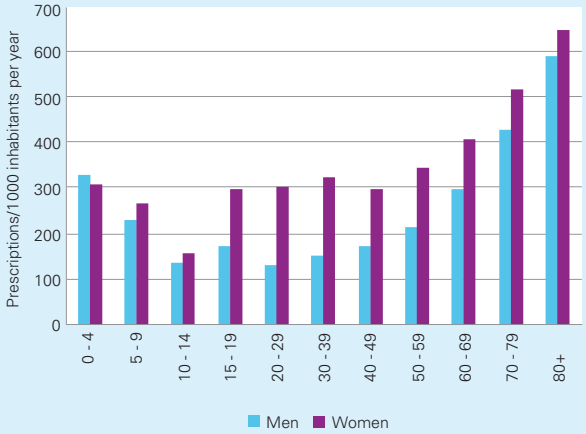


Figure 1.13. Sales of antibiotics (J01 excl. methenamine) in outpatient care, to humans, all genders, children 0-6 years, per region, 2014-2018, prescriptions/1 000 children per year.

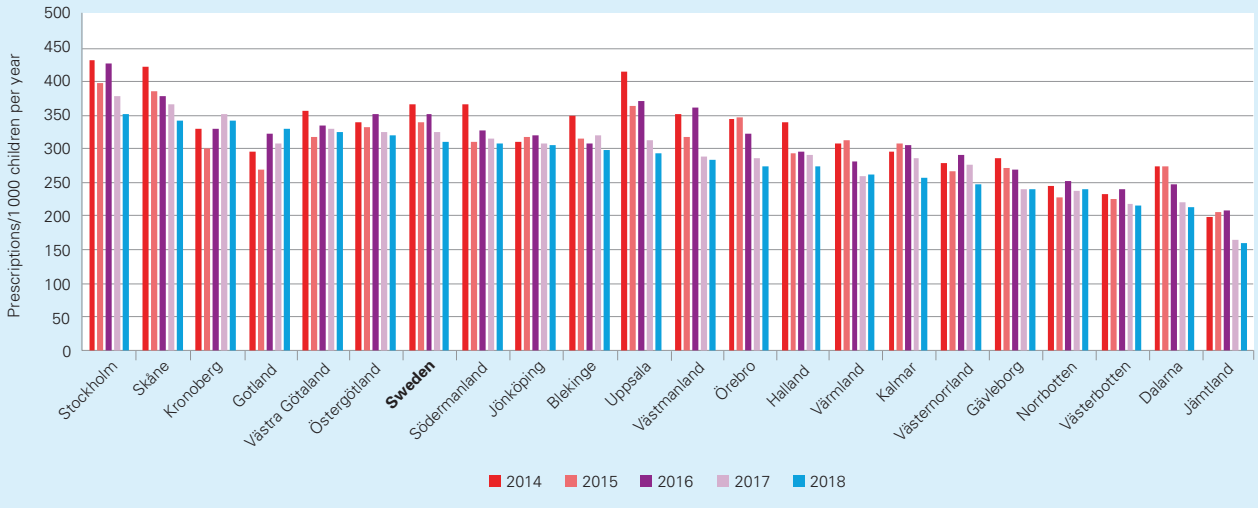


Table 1.1. Sales and consumption of antibiotics in outpatient care, humans, all genders, by antibiotic class or substance, age groups, per year, 2014-2018. DDD/1 000 inhabitants per day, prescriptions/1 000 inhabitants per year, users/1 000 inhabitants per year.

Age groups (years)	DDD/1 000 per day					Prescriptions/1 000 per year					User/1 000 per year				
	2014	2015	2016	2017	2018	2014	2015	2016	2017	2018	2014	2015	2016	2017	2018
Tetracyclines (J01AA)															
0-6	0.00	0.00	0.00	0.01	0.01	0.05	0.05	0.07	0.28	0.30	0.0	0.0	0.1	0.2	0.2
7-19	2.82	1.99	2.09	2.65	2.59	25.1	17.4	17.6	22.8	21.2	15.5	14.6	14.8	15.0	14.1
20-64	2.92	2.78	2.55	2.47	2.26	43.1	41.4	37.5	35.8	32.0	32.9	31.6	29.1	27.8	25.1
65-79	3.06	3.02	2.78	2.82	2.54	60.4	59.9	54.3	54.9	49.1	46.2	44.9	41.6	42.3	38.1
80+	1.97	2.06	1.90	2.05	1.90	45.7	48.0	43.8	46.9	42.5	36.3	38.4	35.2	37.4	34.2
All age groups	2.66	2.55	2.40	2.35	2.16	39.8	38.7	35.6	34.6	31.1	29.8	28.8	26.8	26.3	23.8
Penicillins with extended spectrum (J01CA) excl. pivmecillinam (J01CA08)															
0-6	1.08	1.04	1.06	0.95	0.97	43.7	42.3	42.6	37.6	38.7	33.5	30.3	30.2	28.3	29.1
7-19	0.31	0.32	0.32	0.31	0.31	8.2	8.5	8.4	7.8	7.9	6.7	6.4	6.4	6.1	6.1
20-64	0.56	0.55	0.53	0.51	0.51	13.2	13.1	12.2	11.8	11.4	10.5	10.2	9.6	9.3	8.9
65-79	1.44	1.45	1.42	1.44	1.42	32.4	32.6	31.1	31.0	30.0	25.2	24.6	23.9	24.1	23.1
80+	1.71	1.81	1.75	1.86	1.85	36.8	38.1	36.2	37.7	37.0	29.4	30.1	28.7	30.0	29.5
All age groups	0.76	0.76	0.74	0.73	0.73	19.3	19.0	18.2	17.7	17.3	15.0	14.5	13.9	13.6	13.3
Pivmecillinam (J01CA08)															
0-6	0.01	0.01	0.01	0.02	0.02	1.0	0.8	1.0	1.4	1.7	1.0	1.0	1.1	1.3	1.6
7-19	0.20	0.13	0.14	0.19	0.19	13.4	9.2	9.4	12.9	12.7	11.7	10.9	11.1	11.2	11.1
20-64	0.48	0.47	0.47	0.47	0.46	29.8	29.4	29.5	29.1	28.8	24.6	24.1	24.3	24.0	23.8
65-79	1.00	1.01	1.02	1.00	1.00	59.5	59.4	59.1	58.3	58.3	44.2	43.1	43.7	43.3	43.4
80+	1.92	1.91	1.94	1.92	1.92	114.7	114.1	114.2	113.0	112.7	82.1	81.4	81.6	81.0	80.8
All age groups	0.55	0.55	0.56	0.55	0.54	34.0	33.7	33.8	33.3	33.1	26.5	26.0	26.2	26.0	25.9
Beta-lactamase sensitive penicillins (J01CE)															
0-6	2.82	2.54	2.86	2.68	2.53	211.5	196.1	211.8	196.1	185.0	159.2	146.4	155.7	147.1	140.0
7-19	2.66	2.48	2.59	2.63	2.43	94.0	94.7	98.7	92.5	86.0	75.7	73.3	77.0	73.4	68.7
20-64	3.24	3.22	3.19	3.17	2.93	77.6	77.2	76.5	75.8	70.3	66.2	65.3	65.2	64.7	59.9
65-79	3.58	3.62	3.51	3.61	3.36	83.4	84.4	81.4	84.0	77.9	70.4	69.5	68.1	70.5	65.6
80+	3.07	3.17	3.05	3.10	3.05	73.9	76.7	73.4	74.3	72.7	63.3	65.1	62.3	63.5	62.1
All age groups	3.21	3.19	3.20	3.15	2.93	93.1	92.1	93.2	90.8	84.4	75.8	73.9	74.8	73.7	68.8
Beta-lactamase resistant penicillins (J01CF)															
0-6	0.26	0.23	0.23	0.27	0.28	26.2	24.4	23.6	27.3	28.3	20.6	19.5	19.0	21.6	22.3
7-19	0.77	0.68	0.67	0.72	0.73	27.4	25.6	24.7	25.2	26.2	22.2	20.9	20.4	20.0	20.9
20-64	1.30	1.26	1.25	1.21	1.22	32.1	30.8	30.3	29.6	30.0	25.5	24.3	24.1	23.4	23.9
65-79	2.74	2.69	2.64	2.54	2.60	56.2	54.9	53.4	51.9	53.2	37.3	35.4	35.4	34.4	35.7
80+	5.18	5.22	5.26	5.23	5.21	102.6	101.6	100.4	99.1	98.8	62.8	61.2	61.2	59.9	60.9
All age groups	1.56	1.54	1.53	1.48	1.49	38.5	37.4	36.7	36.0	36.6	28.2	26.9	26.7	26.2	26.9
Combinations of penicillins (J01CR)															
0-6	0.21	0.18	0.18	0.20	0.15	13.5	12.0	12.0	12.8	9.3	8.3	7.2	6.9	7.7	5.7
7-19	0.14	0.14	0.15	0.17	0.16	4.0	4.2	4.3	4.8	4.1	2.7	2.7	2.7	2.8	2.6
20-64	0.24	0.25	0.25	0.27	0.29	5.0	5.1	5.3	5.6	5.7	4.0	4.1	4.3	4.4	4.5
65-79	0.37	0.40	0.44	0.50	0.52	7.5	8.2	8.8	9.9	10.0	5.6	6.0	6.4	7.1	7.2
80+	0.35	0.39	0.44	0.52	0.58	6.7	7.6	8.8	10.1	11.0	5.0	5.8	6.5	7.5	8.0
All age groups	0.25	0.26	0.27	0.30	0.31	6.1	6.2	6.5	7.0	6.7	4.5	4.5	4.7	5.0	4.9
Cephalosporins (J01DB-DE)															
0-6	0.27	0.24	0.24	0.03	0.01	26.9	25.1	24.7	2.9	1.0	22.2	20.7	20.0	2.6	0.8
7-19	0.13	0.13	0.13	0.05	0.04	9.3	9.5	9.5	3.7	2.6	7.6	7.2	7.1	3.1	2.2
20-64	0.11	0.11	0.11	0.08	0.07	6.7	6.6	6.4	5.1	4.6	5.5	5.3	5.1	4.1	3.7
65-79	0.17	0.18	0.17	0.12	0.10	9.4	9.7	9.4	7.5	6.7	7.0	6.9	6.9	5.6	4.9
80+	0.29	0.29	0.30	0.21	0.19	17.0	17.4	17.6	13.6	12.5	13.1	13.2	13.2	10.4	9.6
All age groups	0.14	0.14	0.14	0.08	0.07	9.8	9.6	9.4	5.5	4.8	7.8	7.5	7.3	4.4	3.7

Age groups (years)	DDD/1 000 per day					Prescriptions/1 000 per year					User/1 000 per year				
	2014	2015	2016	2017	2018	2014	2015	2016	2017	2018	2014	2015	2016	2017	2018
Trimethoprim (J01EA)															
0-6	0.07	0.06	0.06	0.06	0.06	9.2	8.1	7.6	7.8	8.2	6.9	6.1	5.6	5.8	6.2
7-19	0.04	0.04	0.03	0.03	0.03	2.8	2.4	2.0	1.9	1.7	2.2	1.8	1.6	1.4	1.3
20-64	0.10	0.09	0.07	0.06	0.06	3.9	3.3	2.6	2.2	2.0	3.0	2.5	1.9	1.6	1.5
65-79	0.34	0.31	0.25	0.24	0.23	13.5	11.8	9.5	9.0	8.3	9.2	8.1	6.5	5.9	5.6
80+	0.71	0.69	0.62	0.58	0.54	35.5	32.7	30.3	28.4	26.4	18.8	17.1	14.2	12.9	12.4
All age groups	0.15	0.14	0.12	0.11	0.10	7.2	6.4	5.4	5.0	4.7	4.9	4.3	3.5	3.2	3.0
Trimethoprim with sulphonamides (J01EE)															
0-6	0.09	0.08	0.07	0.09	0.09	9.6	8.6	7.8	10.3	11.0	5.7	4.8	4.6	6.6	7.0
7-19	0.10	0.10	0.10	0.11	0.11	3.8	4.1	4.1	4.6	4.8	2.0	1.9	1.8	2.3	2.3
20-64	0.20	0.21	0.20	0.20	0.21	4.8	4.8	4.9	5.1	5.3	2.7	2.6	2.7	2.8	2.9
65-79	0.57	0.60	0.62	0.62	0.67	13.0	13.2	13.7	14.5	15.6	8.6	8.4	8.9	9.2	9.8
80+	0.51	0.53	0.55	0.54	0.62	13.2	13.1	14.0	14.9	16.7	9.9	9.7	10.3	10.7	11.5
All age groups	0.25	0.26	0.26	0.26	0.28	6.8	6.8	6.9	7.4	7.9	4.0	3.9	4.0	4.4	4.6
Macrolides (J01FA)															
0-6	0.26	0.23	0.25	0.26	0.24	12.4	11.2	12.0	12.4	11.5	9.7	8.5	9.0	9.5	8.6
7-19	0.22	0.19	0.21	0.22	0.19	8.6	7.8	8.2	9.4	7.8	6.1	5.7	6.1	6.5	5.1
20-64	0.24	0.23	0.23	0.21	0.19	9.1	8.9	8.4	8.2	7.5	6.8	6.5	6.3	6.3	5.7
65-79	0.30	0.30	0.29	0.32	0.28	9.0	9.0	8.3	9.0	8.3	5.9	5.7	5.4	5.7	5.0
80+	0.19	0.21	0.22	0.22	0.21	5.8	6.5	6.3	6.6	6.4	4.0	4.2	4.0	4.4	3.9
All age groups	0.25	0.24	0.24	0.24	0.22	9.2	9.0	8.9	9.2	8.2	6.7	6.3	6.2	6.4	5.6
Lincosamides (J01FF)															
0-6	0.02	0.02	0.02	0.04	0.03	5.1	4.5	4.8	7.7	7.1	3.6	3.3	3.7	5.7	5.4
7-19	0.11	0.09	0.09	0.12	0.11	7.3	6.3	6.3	7.7	7.4	5.7	5.4	5.7	6.0	5.8
20-64	0.31	0.30	0.30	0.29	0.28	14.7	14.5	14.3	13.6	13.1	11.5	11.3	11.4	10.8	10.3
65-79	0.56	0.57	0.56	0.56	0.53	22.9	23.0	22.5	21.9	21.4	15.7	15.3	15.6	15.1	14.6
80+	0.73	0.72	0.72	0.75	0.72	29.9	30.2	30.0	30.0	29.4	18.9	18.6	18.8	18.5	18.2
All age groups	0.32	0.32	0.32	0.31	0.30	14.9	14.8	14.8	14.5	13.9	11.0	10.8	10.9	10.7	10.2
Fluoroquinolones (J01MA)															
0-6	0.02	0.01	0.02	0.02	0.02	0.8	0.7	0.8	1.0	1.1	0.4	0.5	0.5	0.6	0.6
7-19	0.10	0.08	0.07	0.10	0.09	3.4	2.8	2.3	3.5	3.3	2.7	3.0	2.5	2.7	2.6
20-64	0.59	0.57	0.55	0.52	0.49	18.9	18.4	17.6	16.8	16.1	13.8	13.3	12.8	12.2	11.7
65-79	1.61	1.58	1.53	1.47	1.41	54.8	53.6	51.7	50.0	48.2	37.6	35.6	35.2	34.0	32.6
80+	1.95	1.91	1.90	1.83	1.83	72.5	71.0	70.1	67.3	67.5	51.4	49.8	49.1	47.2	46.7
All age groups	0.69	0.68	0.66	0.63	0.60	23.3	22.9	22.1	21.2	20.5	16.4	15.9	15.5	14.8	14.3
Nitrofurantoin (J01XE)															
0-6	0.06	0.05	0.05	0.06	0.07	7.2	6.8	7.1	8.0	7.5	5.2	5.2	5.5	6.1	6.1
7-19	0.13	0.09	0.09	0.12	0.11	9.8	7.1	7.1	9.2	8.7	8.3	7.8	7.7	7.8	7.4
20-64	0.31	0.31	0.31	0.32	0.33	21.1	20.9	20.9	21.5	21.9	17.0	16.7	16.8	17.2	17.5
65-79	0.74	0.76	0.76	0.78	0.80	44.9	45.2	45.2	45.7	46.2	32.5	31.7	32.2	32.4	32.5
80+	1.30	1.35	1.38	1.44	1.46	84.0	87.0	87.7	90.4	91.6	53.8	53.8	53.1	53.7	53.6
All age groups	0.38	0.38	0.39	0.40	0.40	25.1	25.2	25.3	25.9	26.0	18.9	18.6	18.7	19.0	19.1
All agents (J01 excl. methenamine)															
0-6	5.15	4.70	5.06	4.69	4.50	367.2	340.9	356.1	325.9	310.9	222.7	206.4	213.2	200.2	193.3
7-19	7.75	6.48	6.71	7.45	7.13	217.8	200.0	203.1	206.5	195.0	141.8	136.1	138.9	133.6	127.8
20-64	10.62	10.38	10.04	9.80	9.30	280.8	275.2	267.2	260.9	249.2	175.8	171.3	168.4	164.8	158.1
65-79	16.55	16.54	16.06	16.09	15.53	468.7	466.3	450.0	449.1	434.5	246.5	238.9	235.4	236.2	228.1
80+	19.95	20.34	20.10	20.30	20.13	640.3	645.9	634.7	634.1	626.9	307.8	306.7	301.2	301.5	298.1
All age groups	11.20	11.04	10.86	10.62	10.15	328.0	322.8	317.7	308.9	295.9	191.7	186.0	184.5	180.7	174.0

In Sweden, the proportion of children (0-6 years) treated with at least one course of antibiotics in 2018 was 19.3%, which is less than in 2017, Figure 1.14. The proportion decreased in 17 out of 21 regions during 2018 and it ranges from 351 users per 1 000 children in Region Stockholm to 161 users per 1 000 children in Region Jämtland.

Regional comparisons

In 2018, 17.4% of the Swedish population filled at least one prescription for antibiotics, compared to 2017 when the corresponding figure was 18.1%, Table 1.1. However, the proportion of people using antibiotics varies between the regions, from 19.5% in Region Gotland to 13.9% in Region Västerbotten. The proportion decreased in all 21 regions from 2017 to 2018, Figure 1.15. On a national level, the proportion of people treated with antibiotics during the last five years has decreased by 1.7 percentage points since 2014. The corresponding number for children is 2.9.

In 2018, the average sales of antibiotics in outpatient care measured in prescriptions per 1 000 inhabitants in Sweden was 296. This is a historically low figure, and the first time since national monitoring started that the annual average has been below 300 prescriptions per 1 000 inhabitants per year. However, to reach the Swedish long-term target of 250 prescriptions per 1 000 inhabitants per year, further reduction (by 15.5%) is needed, Figure 1.16. Two regions, Jämtland and Västerbotten, now reach the target.

In 2018, the number of prescriptions per 1 000 inhabitants was reduced in all 21 regions, Figure 1.16. A contributing factor to the lower sales throughout most regions in the last few years might be the patient safety initiative that started in 2011 and continued until the end of 2014. This performance-based initiative was launched by the Swedish government and the Association for Local Authorities and Regions, and one of its objectives was to optimise prescribing of antibiotics in accordance with guidelines using financial incentives. The initiative is described in Swedres-Svarm

Figure 1.14. Proportion (%) of children aged 0-6 years that have filled at least one prescription for antibiotics (J01 excl. methenamine), outpatient care, humans, all genders, per region, 2014-2018.

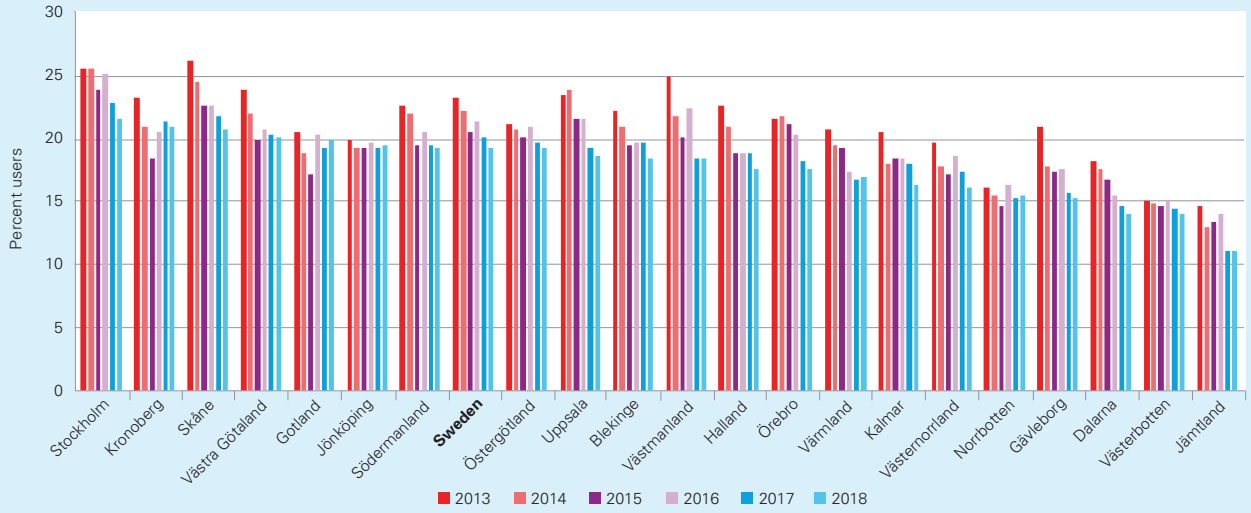
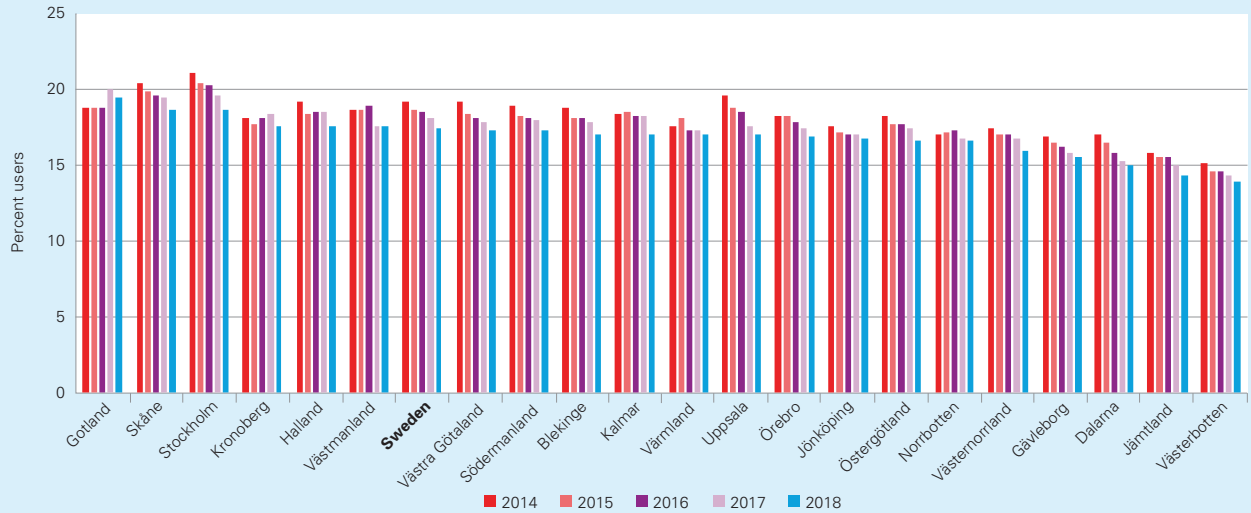


Figure 1.15. Proportion (%) of the population that have filled at least one prescription for antibiotics (J01 excl. methenamine), outpatient care, humans, all genders, per region, 2014-2018.



2014; chapter "National campaign for improved patient safety" (Swedres-Svarm 2014, 2015). In addition to this particular effort, regional and national stakeholders continue their long-term strategic work for good quality in antibiotic prescribing. However, regional variation remain in Sweden and the number of prescriptions per 1 000 inhabitants range from 340 in Region Gotland to 240 in Region Västerbotten.

As mentioned in earlier editions of Swedres-Svarm, Strama has proposed two quality targets for antibiotic prescribing in outpatient care; one focusing on the use of narrow-spectrum penicillins in children and the other on fluoroquinolones in the treatment of UTI in women.

The target for narrow-spectrum penicillins in children between 0 and 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 2018 the proportion of penicillin V was 75% on a national level, compared with 74% in 2017. Region Värmland had the largest proportion, 84%, and Region Stockholm the smallest, 71%, Figure 1.17.

The target for fluoroquinolone prescribing to women between 18 and 79 years of age is 10% or less of prescriptions. Here, the numerator is ciprofloxacin (J01MA02) and norfloxacin (J01MA06) and the denominator is pivmecillinam (J01CA08), trimethoprim (J01EA01), ciprofloxacin (J01MA02), norfloxacin (J01MA06) and nitrofurantoin (J01XE01). The national average proportion of fluoroquinolones in Sweden in 2018 was 13%. Region Västerbotten had the highest proportion (15%) and Region Stockholm the lowest proportion (11%), Figure 1.18.

Figure 1.16. Sales of antibiotics (J01 excl. methenamine) in outpatient care, to humans, all genders, per region, per year, 2003-2018 (three year intervals), prescriptions/1 000 inhabitants per year.

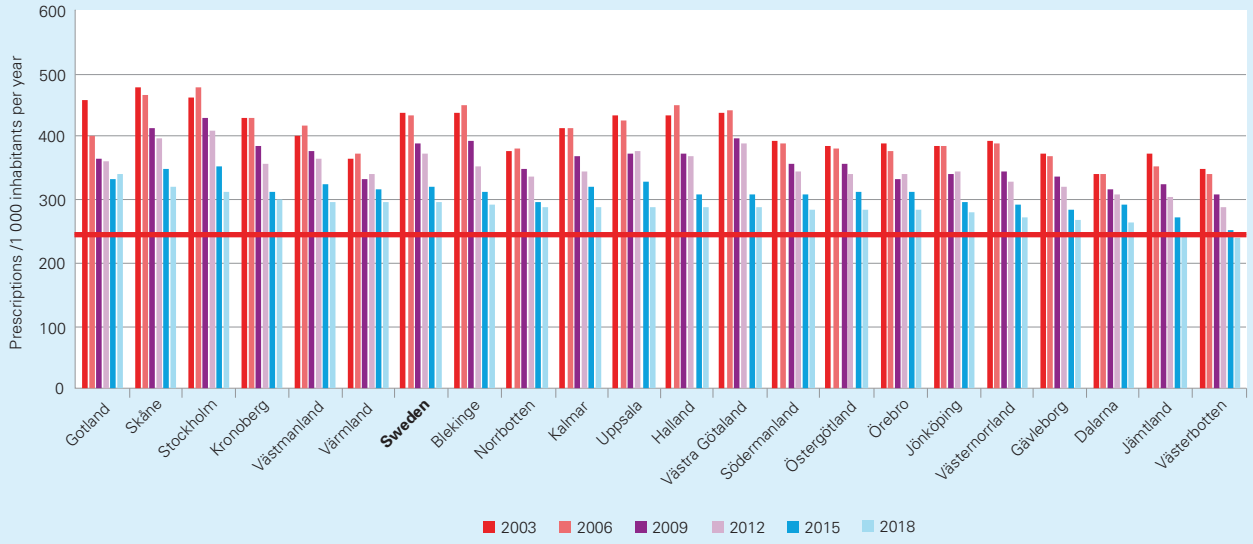


Figure 1.17. Proportion penicillin V of antibiotics that are commonly prescribed to treat respiratory tract infections in children 0-6 years, outpatient care, humans, all genders, per region 2017 and 2018. The red line indicates Strama's target at a minimum of 80%.

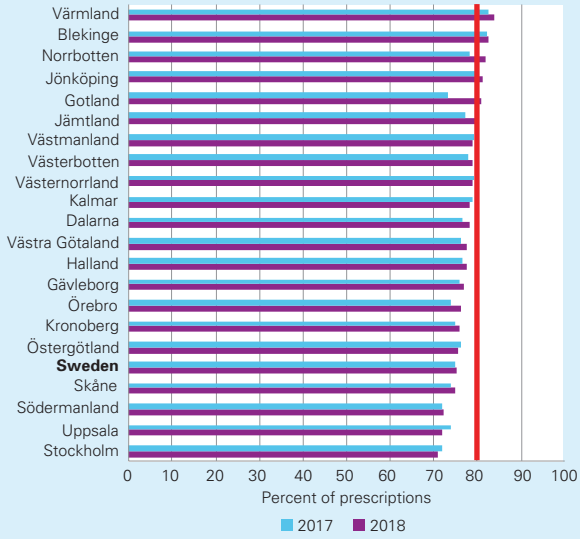
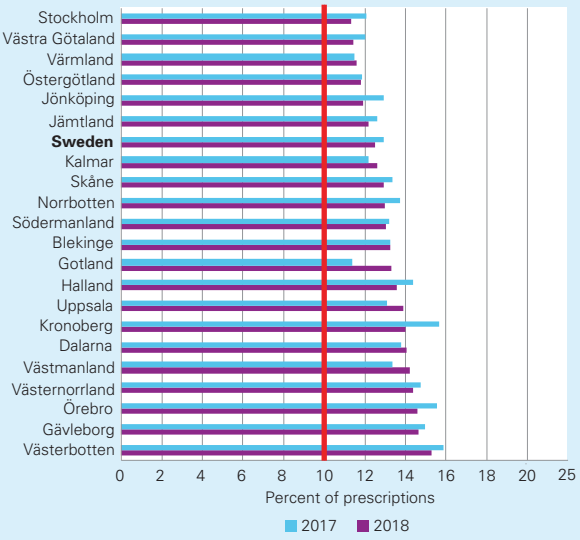


Figure 1.18. Proportion fluoroquinolones of antibiotics commonly prescribed to treat urinary tract infections in women 18-79 years, outpatient care, humans, per region, 2017 and 2018. The red line indicates Strama's target of maximum 10% fluoroquinolones.



Antibiotics in dentistry

In 2018 the sales of J01 and metronidazole (P01AB01) prescribed by dentists decreased by 7.4% compared with 2017. The sales decreased from 21 to 20 prescriptions per 1 000 inhabitants per year, Figure 1.19. Penicillin V (J01CE02) is the most commonly prescribed antibiotic followed by amoxicillin (J01CA04) and clindamycin (J01FFA01). These antibiotic substances represent 74.3%, 9.6%, and 8.2% respectively of all antibiotics prescribed by dentists.

The greatest decrease in sales in 2018 was seen for erythromycin (12.2%) and clindamycin (9.7%), measured in prescriptions per 1 000 inhabitants per year. Amoxicillin has decreased by 25% between 2013 and 2018. The explanation for this might be the new stricter treatment recommendations for the use of antibiotic prophylaxis implemented in 2012 (Läkemedelsverket, 2012). A big increase was seen for clindamycin between 2001 and 2011. However, since 2012, the trend has reversed and the sales of clindamycin have decreased each year. The age group 65-79 years is the group with the highest consumption of antibiotics prescribed by dentists, followed by the age groups 80 years and older and 20-64 years. Between 2000 and 2007, an increase was seen in the consumption in all age groups (data not shown), but since 2007 there has been an overall decrease, Figure 1.20. A possible explanation for the relatively high level of prescribing to older people could be an earlier dental care policy that made complicated prosthetic treatment available at a lower cost to people over 65. In such treatments, the use of antibiotics as prophylaxis was common. The reform ended in 2008.

Dentists account for around 6% of all antibiotics prescribed in outpatient care in Sweden. The proportion varies between 4.2% and 7.1% between the regions. The total sales of antibiotics (J01 and metronidazole), measured as prescriptions per 1 000 inhabitants per year, was lower in 20 of 21 regions in 2018 compared with 2017. There are large regional differences; more pronounced here than when all outpatient care is combined. Dentists in Region Skåne prescribed the most (25 prescriptions per 1 000 inhabitants) and more than twice as much as dentists in Region Västerbotten

Figure 1.19. Sales of antibiotics prescribed by dentists in outpatient care, humans, all genders, 2014-2018, prescriptions/1 000 inhabitants per year.

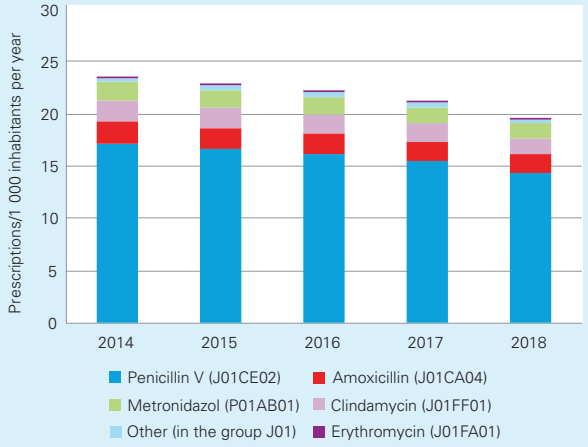


Figure 1.20. Sales of antibiotics (J01 excl. methenamine; metronidazole P01AB01) prescribed by dentists in outpatient care, humans, all genders, 2008, 2013 and 2018, by age group, prescriptions/1 000 inhabitants per year.

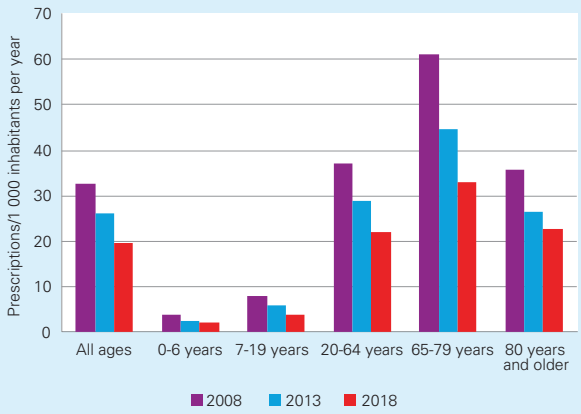
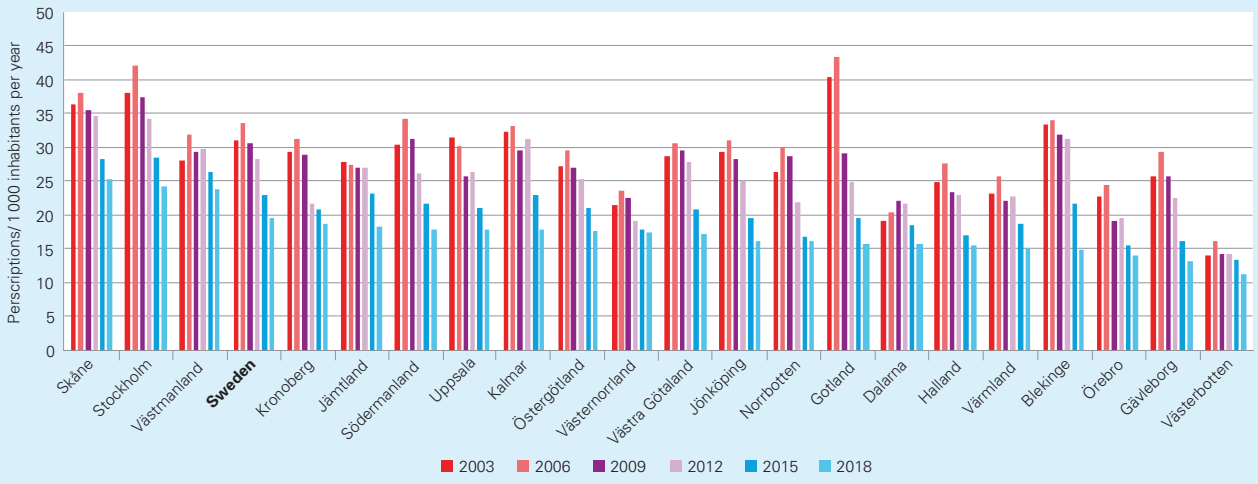


Figure 1.21. Antibiotics (J01 excl. methenamine; metronidazole P01AB01) prescribed by dentists in outpatient care, humans, all genders, 2003-2018 (every third year), presciptions/1 000 inhabitants per year.



who prescribed the least (11 prescriptions per 1 000 inhabitants) in 2018. Sales of antibiotics have decreased in all regions since the early 2000's, after a peak in consumption some ten years ago, Figure 1.21.

Antibiotics in hospital care

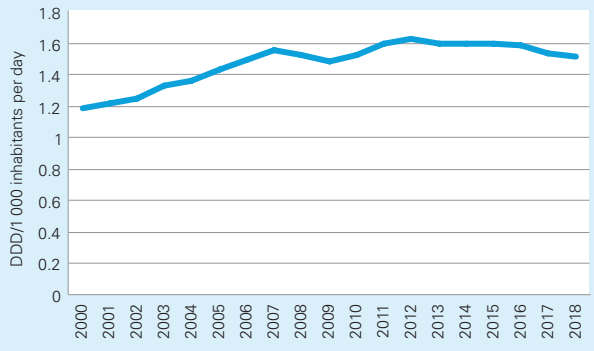
Data shown in this section includes sales from all Swedish hospitals and some other facilities, covering acute care hospitals as well as nursing homes and other institutions within health and social care that order antibiotics for dispensing to patients or clients. To provide a more detailed picture of antibiotic use in secondary care, there are also displays of sales to acute care hospitals only, related to the 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 the national level, the proportion of antibiotics in hospital care sold to acute care hospitals is about 70%. In some regions, almost all antibiotics in hospital care are sold to acute care hospitals and in other regions the proportion is as low as 50%.

Antibiotic consumption in hospitals and other health and social care facilities

The total sales of antibiotics to hospital care in Sweden was increasing between 2000 and 2012; J01 excluding methenamine shows a near-30% change from 1.18 to 1.63 DDD per 1 000 inhabitants per day. Since then, the level has been relatively stable. In 2018, sales were slightly lower than in 2017 and the overall figure is now 1.52 DDD per 1 000 inhabitants per day.

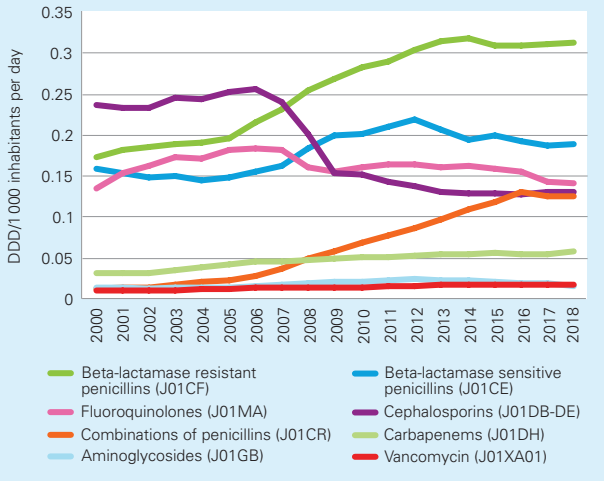
Figure 1.22. Sales of antibiotics (J01 excl. methenamine) in hospital care, to humans, all genders, 2000-2018, DDD/1 000 inhabitants per day.



A closer look at the antibiotics sold for dispensing in hospitals and other care facilities shows increasing figures for antibiotics with narrower spectrums, e.g. beta-lactamase resistant penicillins (J01CF), of which flucloxacillin represents the biggest part. The marked change in the sales of cephalosporins around 2006-2009 is explained in part by a shift from one substance to another (cefuroxime to cefotaxime) meaning that the number of DDDs appear lower. However, some of the decrease in cephalosporins was due to altered prescribing; since then more narrow-spectrum penicillins (J01CE) and penicillins with enzyme inhibitor (J01CR), mainly piperacillin/tazobactam, have gradually replaced the cephalosporins. There were no major changes during 2018 compared with 2017 in any of the antibiotic groups, Figure 1.23.

The Strama network, together with local drug and therapeutic committees, continues to promote appropriate prescribing of antibiotics in hospitals, focusing on the following areas: 1) Moderately severe (CRB-65 0-1) community acquired pneumonia should be treated with narrow spectrum penicillins; 2) Surgical prophylaxis should normally be given as one dose. In high risk situations, treatment can be given during 24 h maximum with few exceptions; 3) Uncomplicated lower urinary tract infections in women should be treated with pivmecillinam or nitrofurantoin, including hospital inpatients, whereas the use of fluoroquinolones should be restricted; 4) Extended spectrum cephalosporins and fluoroquinolones should not be used in situations where treatment with a narrow spectrum penicillin is an alternative. (Hanberger H et al., 2014). Some of these efforts are reflected in the statistics and seen in figure 1.23.

Figure 1.23. Sales of antibiotics in hospital care, to humans, all genders, ATC-5 and ATC-7, 2000 to 2018 DDD/1000 inhabitants per day.



Antibiotic consumption in Swedish acute care hospitals

Data from acute care hospitals shows that the consumption of antibiotics was slightly higher in 2018 compared with 2017, measured both as DDD per 100 patient-days and as DDD per 100 admissions, Table 1.2. The overall figures are 301.4 DDD per 100 admissions and 69.1 DDD per 100 patient-days.

Beta-lactamase resistant penicillins (J01CF) are the most common antibiotics, making up around 21% of both DDD/100 admissions and DDD/100 patient-days. They are used in surgical prophylaxis, and the recommended strategy is a single pre-operative dose. The national average in 2018 was 14.9 DDD per 100 patient-days. Other major classes are the beta-lactamase sensitive penicillins (J01CE), cephalosporins (J01DB-DE), penicillins with extended spectrum (J01CA) and combinations of penicillins (J01CR), which mainly consists of piperacillin with tazobactam (J01CR05), and fluoroquinolones (J01MA). They all represent around 10% each of sales to acute care hospitals.

The largest changes in sales between 2017 and 2018 are seen in antibiotics that make up a small part of the total sales to acute care hospitals, e.g. moxifloxacin (J01MA14), vancomycin (A07AA09) and imidazole derivatives (J01XD). Cefalosporins (J01DB-DE) and carbapenems (J01DH) have shown increasing sales over the last few years and continue to do so in 2018. They now represent 11% and 5%, respectively.

According to available data, there are large differences in consumption of antibiotics between Swedish acute care hospitals. One example is the use of narrow spectrum penicillins (J01CE), which ranges from 6.1% to 18.6% of the total acute care hospital consumption measured in DDDs, Figure 1.24. The use of narrow spectrum antibiotics increased in 14 of 20 regions in 2018 compared with 2017 (Region Dalarna is excluded from the analysis in 2018 due to failure to report data). Notable here is that there are great differences with regards to the dosage of penicillin G between the regions. The DDD for penicillin G is 3.6 g, but within Sweden the prescribed dose varies from 1 g three times a day to 3 g three times a day. The type of hospital, case mix and patient demographics may also influence the statistics and should be taken into account when comparing these data. For example, the regions Uppsala, Stockholm, Västerbotten, Västra Götaland, Skåne, Östergötland and Örebro all have tertiary referral hospitals.

In acute care hospitals the use of cephalosporins varied between 3.3% and 14.4% during 2018, and the corresponding numbers for fluoroquinolones was 6.7% to 14.8%. Piperacillin-tazobactam varied between 4.9% and 12.4% and carbapenems between 1.7% and 6.7%, Figure 1.25.

Table 1.2. Sales of antibiotics to acute care hospitals, humans, all genders, ATC-5 and ATC-7, 2014 to 2018. DDD/100 admissions and DDD/100 patient-days.

	DDD/100 admissions					DDD/100 patient-days				
	2014	2015	2016	2017	2018*	2014	2015	2016	2017	2018*
Tetracyclines (J01AA)	23.0	23.1	22.2	20.9	20.0	5.2	5.2	4.9	4.8	4.6
Penicillins with extended spectrum (J01CA)	32.0	32.7	33.4	32.9	32.7	7.2	7.4	7.4	7.5	7.5
Beta-lactamase sensitive penicillins (J01CE)	31.5	33.3	33.8	34.6	36.3	7.1	7.5	7.5	7.9	8.3
Beta-lactamase resistent penicillins (J01CF)	56.6	56.8	61.0	60.9	64.8	12.7	12.9	13.5	14.0	14.9
Combinations of penicillins (J01CR)	25.0	27.7	32.9	31.0	32.1	5.6	6.3	7.3	7.1	7.4
Cephalosporins (J01DB-DE)	28.5	29.2	31.1	29.9	33.0	6.4	6.6	6.9	6.9	7.6
Carbapenems (J01DH)	12.7	13.3	13.9	13.4	14.9	2.8	3.0	3.1	3.1	3.4
Trimethoprim (J01EA)	1.7	1.7	1.1	0.7	0.7	0.4	0.4	0.2	0.2	0.2
Trimethoprim with sulphonamides (J01EE)	10.5	10.5	11.7	11.1	11.7	2.3	2.4	2.6	2.5	2.7
Macrolides (J01FA)	4.2	4.7	5.4	5.5	5.3	0.9	1.1	1.2	1.3	1.2
Lincosamides (J01FF)	8.5	8.3	8.7	8.4	8.5	1.9	1.9	1.9	1.9	1.9
Aminoglycosides (J01GB)	5.4	5.3	5.2	4.6	4.1	1.2	1.2	1.2	1.1	0.9
Fluoroquinolones (J01MA)	28.6	28.6	29.3	27.1	27.1	6.4	6.5	6.5	6.2	6.2
Glycopeptides (J01XA)	4.3	4.6	4.8	4.7	4.9	1.0	1.0	1.1	1.1	1.1
Imidazole derivates (J01XD)	4.4	4.2	4.1	4.3	4.8	1.0	1.0	0.9	1.0	1.1
Nitrofurantoin (J01XE)	2.3	2.2	2.3	2.3	2.2	0.5	0.5	0.5	0.5	0.5
Vancomycin (A07AA09)	0.3	0.3	0.3	0.3	0.4	0.1	0.1	0.1	0.1	0.1
Pivmecillinam (J01CA08)	9.2	9.1	8.8	8.2	8.4	2.1	2.1	2.0	1.9	1.9
Piperacillin and tazobactam (J01CR05)	20.2	22.0	26.0	23.2	23.6	4.5	5.0	5.7	5.3	5.4
Moxifloxacin (J01MA14)	1.7	1.6	1.9	2.0	2.6	0.4	0.4	0.4	0.5	0.6
Methenamine (J01XX05)	2.3	2.3	2.0	1.9	1.7	0.5	0.5	0.4	0.4	0.4
Linezolid (J01XX08)	0.6	0.6	0.9	0.8	0.8	0.1	0.1	0.2	0.2	0.2
All agents (J01)	283.4	290.4	305.3	296.3	301.4	63.5	65.8	67.5	67.9	69.1

*Denominator data from 2017

The proportion of all broad spectrum antibiotics (fluoroquinolones, cephalosporins, piperacillin with tazobactam and carbapenems) in Swedish acute care hospitals varied from 27.4% in Region Jämtland, to 37.0% in Region Uppsala. In general, there are major differences in the distribution regarding which group of broad spectrum antibiotics that is used, but the overall consumption of broad spectrum antibiotics is quite similar between the regions.

Figure 1.24. Proportion (%) of narrow spectrum penicillins (penicillin V and G, J01CE) of all antibiotics in Swedish acute care hospitals per region, 2017 and 2018.

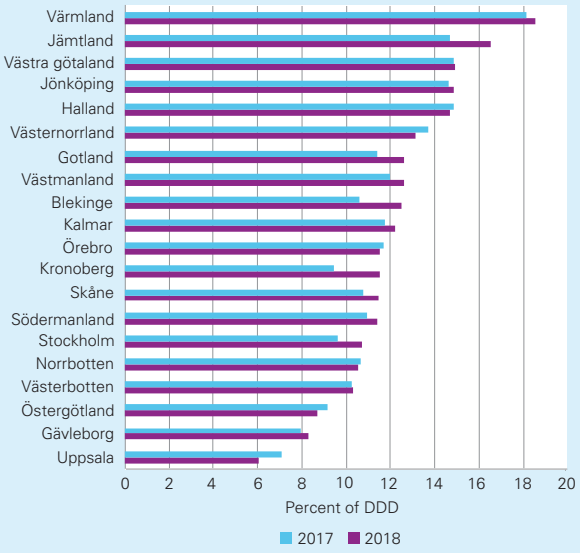
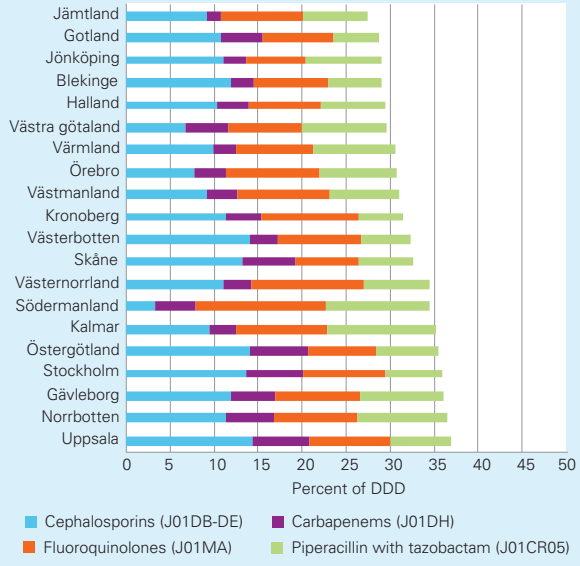


Figure 1.25. Proportion (%) of broad spectrum antibiotics (cephalosporins, carbapenems, fluoroquinolones and piperacillin with tazobactam) of all antibiotics in Swedish acute care hospitals 2018, per region, 2018.



Adverse reactions related to antibiotic use

Spontaneously reported drug-related adverse reactions are continuously entered into BiSi, a national database administered by the Swedish Medical Products Agency. The reports originate from health care professionals as well as patients. The antibiotic-related adverse reactions reported from health care professionals and patients between 2014 and 2018 were analysed for various groups of agents. There were 2 924 reports of side effects caused by the use of antibiotics during this period. The following organ system groups received most reports related to the use of systemic antibiotic drugs (J01): skin- and subcutaneous tissue disorders (n=1 415), gastrointestinal disorders (n=621), general disorders (n= 344), neurological reactions (n=360), respiratory disorders (n=231), immune system disorders (n=186), musculoskeletal disorders (n=171), investigations (n=126), hepato-biliary disorders (n=143), psychiatric disorders (n=100), renal and urinary disorders (n=111) and blood and lymphatic system disorders (n=73). The majority of the reports (63%) concern female patients, which corresponds to the gender difference seen in antibiotic use. The ten antibiotic substances most commonly associated with adverse reactions in the last five years, unadjusted for consumption and regardless of the cause of the report, are presented in Table 1.6.

Table 1.6. The most frequently reported adverse drug reactions related to antibiotics, reported to the Swedish Medical Products Agency 2014-2018.

Antibiotic	Total number of adverse drug reaction reports 2014 to 2018	Number of 'serious' reports	Number of fatal cases
Phenoxymethyl-penicillin	389	120	0
Flucloxacillin	312	150	9
Ciprofloxacin	266	165	4
Clindamycin	234	103	2
Nitrofurantoin	231	95	3
Sulfamethoxazole and trimethoprim	169	112	3
Amoxicillin	155	60	0
Doxycycline	142	40	0
Piperacillin and beta-lactamase inhibitor	126	80	3
Cefotaxime	95	50	2

New DDDs for antibiotics

Since January 2019, several antibiotic substances have been assigned new DDDs (defined daily doses). This will have consequences for the longitudinal monitoring of antibiotic consumption.

What is a DDD?

A DDD (defined daily dose) is a technical unit for measuring the use of medicines. It is defined as "the assumed average maintenance dose per day for a drug used for its main indication in adults". Hence, a DDD does not necessarily reflect a recommended or clinically relevant dose of a medicine. The therapeutic dose, i.e. what is actually prescribed, will take into account characteristics of the patient (for example age, body weight, and renal function) and the type and severity of the condition.

A DDD often reflects a compromise between the doses used in different countries. Although DDD comparisons do not show how many people are using a medicine or how many times it has been prescribed, they provide an overall measurement of the use of a substance in a geographical area or over time. One DDD is assigned per ATC code and route of administration (e.g. oral, parenteral). Many antibiotics were assigned their DDD in the 1970's, when the ATC/DDD system was developed by the WHO Collaborating Centre for Drug Statistics Methodology in Oslo.

How has the change come about?

The WHO and ECDC arranged a joint expert meeting in 2017, with the purpose of suggesting new DDD for antibiotics that are widely used from an international perspective. After discussions it was decided to assign new values for nine substances, see Table 1. All DDDs are higher than the previous values, reflecting the use of higher doses today than when they were originally decided. One reason for higher therapeutic doses is the development of antibiotic resistance.

Table 1. New and old (2018 and 2019) DDD values of the recently updated antibiotics.

ATC	Formulation	DDD 2018	DDD 2019
J01CA01 ampicillin	P	2 g	6 g
J01CA04 amoxicillin	O	1 g	1.5 g
J01DE01 cefepime	P	2 g	4 g
J01DH02 meropenem	P	2 g	3 g
J01MA02 ciprofloxacin	P	0.5 g	0.8 g
J01XB01 colistin	P	3 MU	9 MU
J01CR02 amoxicillin and beta-lactamase inhibitor	O	1 g	1.5 g
Not registered in Sweden			
J01CA04 amoxicillin	P	1 g	3 g
J01CA17 temocillin	P	2 g	4 g

Effects for monitoring of antibiotic consumption

An increased DDD value for a medicinal substance means a lower numerator when the amount of antibiotics used is displayed in relation to population (DDD/1 000 inhabitants), hospital admissions, (DDD/100 admissions), etc. Thus, if antibiotic use is compared over time, it will appear as if less antibiotics are used after the alteration. Trends over longer periods of time will remain, but the values for each time point will be lower. Comparisons of for example the number of prescriptions per 1 000 inhabitants per year will not be affected. Figure 1 shows the effect of the DDD change on the total sales of antibiotics in Sweden from year 2000. With the updated DDDs, the values are on average 3.5 percent lower. Notable for stakeholders that monitor the sales and use of antibiotics over time is that when older datasets are updated with current figures, the number of DDDs for the affected substances need to be re-calculated.

Depending on the ratio of the use of antibiotics with adjusted DDDs to those with unchanged DDDs, the benchmarking of for example regions or countries could be affected. Figure 2. Since all the antibiotics with new, higher DDDs are broad-spectrum substances, countries or regions that use narrow-spectrum antibiotics will appear to have a smaller reduction.

Figure 1. Sales of antibiotics to humans, all genders, DDD/1 000 inhabitants per day, 2000-2018, DDD 2018 and DDD 2019.

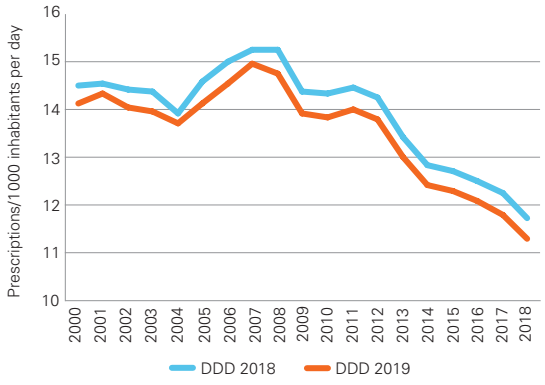
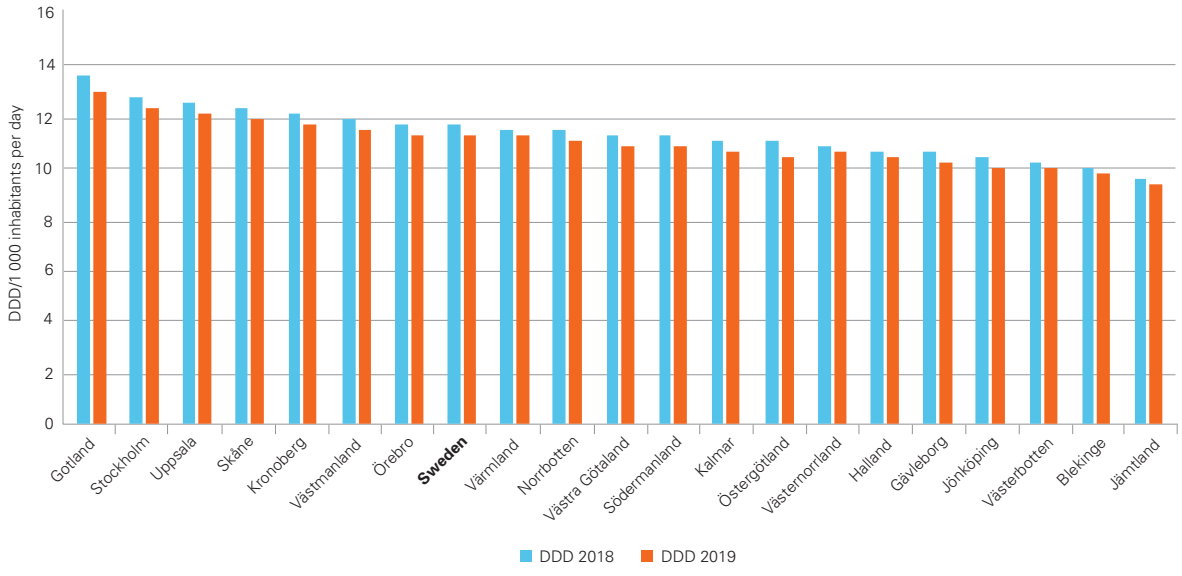


Figure 2. Sales of antibiotics to humans, all genders, DDD/1 000 inhabitants per day, 2018, per region, DDD 2018 and DDD 2019.



IMPACT – a One Health collaboration on antibiotic resistance for sustainable change

The One Health approach is an imperative way forward to contain antibiotic resistance, on the global, EU and national levels alike (WHO 2015, European Commission 2017, Regeringskansliet 2016). Cooperation between sectors, countries, and research disciplines helps us understand the problems more fully, and also to inform action for sustainable change.

Swedish-Chinese collaboration regarding antibiotics

China and Sweden have collaborated on issues related to antibiotic resistance since 2010, framed by Memorandums of Understanding between the two countries' governments. Starting in 2014 leading Chinese and Swedish researchers in human health, animal health and environmental sciences have been collaborating in a One Health project called the Sino-Swedish integrated multisectoral partnership for antibiotic resistance containment; IMPACT. The project was funded for five years by the Swedish Research Council (VR) and the National Natural Science Foundation of China (NSFC).

IMPACT is a mixed methods project, employing a combination of epidemiological, health systems and laboratory investigations. For the purpose of informing national and international policies, IMPACT has further investigated interventions that could lead to sustainable behavioural change. The interventions included efforts to prevent infections, improve antibiotic use in humans and animals, and limit the spread of resistant bacteria.

In total 10 organisations (Table 1) have worked together around three main areas:

- knowledge, attitudes and practice concerning human and animal antibiotic use
- distribution of resistant bacteria and genetic elements within the human, animal, environmental and health care sectors
- design, implementation and evaluation of strategies to promote rational use of antibiotics and to limit the spread of antibiotic resistance in all sectors

Examples of One Health studies within IMPACT

Knowledge, attitudes and practices were addressed in a questionnaire study conducted among residents in 12 villages in the province of Shandong, where around one third of the households kept pigs in their backyards (Dyar O J, Yin J 2018). The researchers also observed medicines for people and animals stored in the households to see whether antibiotics were kept at hand. People that kept pigs in their backyards seemed to have better knowledge about which medicines classify as antibiotics and what antibiotics should be used for (e.g. pneumonia, urinary tract infections). However, the pig farmers were also more likely to believe that antibiotics were needed to prevent a cold from developing into a more severe disease in a person. Around one fourth of participants stated that bacteria can become resistant to antibiotics, and a similar proportion said that people or animals can become

Table 1. Partnering organisations in IMPACT.

China	Sweden
Zhejiang University (PI)	Public Health Agency of Sweden (PI)
China Agricultural University (co-PI)	Karolinska Institutet (co-PI)
Shandong University (co-PI)	Linköping University (co-PI)
Shandong Academy of Agricultural Sciences	Swedish National Food Agency
Shandong Center for Disease Control and Prevention	Swedish National Veterinary Institute

resistant. Less than one fifth of all respondents thought that their own behaviour could contribute to controlling antibiotic resistance, although this proportion was higher among those that had more formal knowledge about antibiotics.

The same villages in rural parts of the Shandong province were used in another study, which investigated the possible relatedness between MRSA isolates from humans and pigs (Bi Z, Sun C 2018). Isolates from humans isolates of MRSA were identified from 13 (1.7%) households (from seven different villages); isolates from pigs of MRSA were identified from seven (2.8%) households (from five different villages). In three households, both human and pig isolates of MRSA were identified. Community-associated MRSA and livestock-associated MRSA, belonging to ST59 and ST9, respectively, were identified in both humans and pigs. The genotypic and phenotypic comparison of isolates indicated bidirectional transmission of MRSA between humans and pigs in the villages.

The prevalence of resistant bacteria in well water, used for drinking and irrigation, was also investigated in Shandong, in areas that had either extensive pig breeding or vegetable cultivation which was fertilised by chicken manure (Sun P, Bi Z 2017). Ten ESBL-producing *E. coli* isolates were detected in a total of 71 sampled wells. The *mcr-1* gene (coding for colistin resistance) was identified in two isolates from two different samples that also carried genes for CTX-M (which codes for ESBL). No carbapenemase genes were detected.

Lessons learned

There are few examples of research that truly applies a One Health approach and therefore IMPACT also contributes valuable insights from organising and delivering research across disciplines, institutions and geographical regions (Cars O, Xiao Y 2016). Key aspects of working in a complex project, representing challenges as well as potential success factors, include finding effective ways to communicate, the sharing of conceptual frameworks, conflicts and issues of leadership and power, and the need for enough time to establish a collaborative structure across several disciplines and sectors.

More information about IMPACT, including a full list of publications, is available at https://www.folkhalsomyndigheten.se/impact.

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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 and methodology

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. Data presented here include sales of veterinary medicinal products with antibiotics indicated for terrestrial animals (topical products excluded). Thus, sales for use in aquaculture are not included.

As the result of a new interpretation of existing legislation on confidentiality, it has not been possible for SVA to obtain raw data per product for calculation to kg active substance and subsequent analyses. Therefore, the Board of Agriculture of Sweden has performed the calculations and aggregated the data for this report. The data source is the same as before, i.e. information in the database of the eHealth Agency on sales from pharmacies to animal owners (prescriptions dispensed) or to veterinarians (requisition).

Because of this altered process, we can only present information on aggregated overall sales this year. Further details on data source and inclusion criteria are given in Materials and methods, sales of antibiotics.

Completeness of data

In 2011, it was noted that the information on sales of products with special license was 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 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.

Trends in animal populations

Changes in the numbers of animals may affect trends in statistics on consumption of antibiotics. Compared to 2009, the number of pigs slaughtered in 2018 has decreased by 10%, while the number of broilers has increased by 34%. The number of dairy cows decreased by 10% 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 729 000 in 2006. Further details on animal numbers and data sources are found in Demographics and denominator data in this report.

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

ATCvet code	Antimicrobial class	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
QJ01AA, QG01A	Tetracyclines	1 174	1 115	1 073	881	935	787	685	515	521	515
QJ01CE, -R, QJ51	Benzylpenicillin[b]	7 721	7 546	6 696	6 362	5 954	5 509	5 861	5 997	5 940	5 848
QJ01CA, QJ01CR	Aminopenicillins	1 068	907	723	649	645	635	642	677	640	678
QJ01D	Cephalosporins	738	575	498	410	330	299	267	242	210	187
QA07AA, QJ01G, -R, QJ51R	Aminoglycosides and polymyxins	609	557	503	483	341	378	414	385	357	351
QA07AB, QJ01E	Sulphonamides	2 128	1 998	1 867	1 813	1707	1 699	1 634	1 643	1 678	1 448
QJ01E	Trimethoprim & derivatives	379	357	338	329	320	314	313	318	326	279
QJ01F	Macrolides & lincosamides	988	739	648	632	564	484	485	472	514	578
QJ01MA	Fluoroquinolones	164	148	120	106	52	45	34	30	26	29
QJ01BA, QJ01XX92, - 94	Amphenicols and pleuromutilins	398	174	140	100	129	121	133	264	99	129
	Total sales	**15 368**	**14 117**	**12 606**	**11 763**	**10 975**	**10 270**	**10 468**	**10 543**	**10 310**	**10 042**

[a]Data from 2010-2015 are uncertain because of a lack of completeness mainly affecting injectable products. [b]Also includes small amounts of phenoxymethylpenicillin and penicillinase stable penicillins.

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.

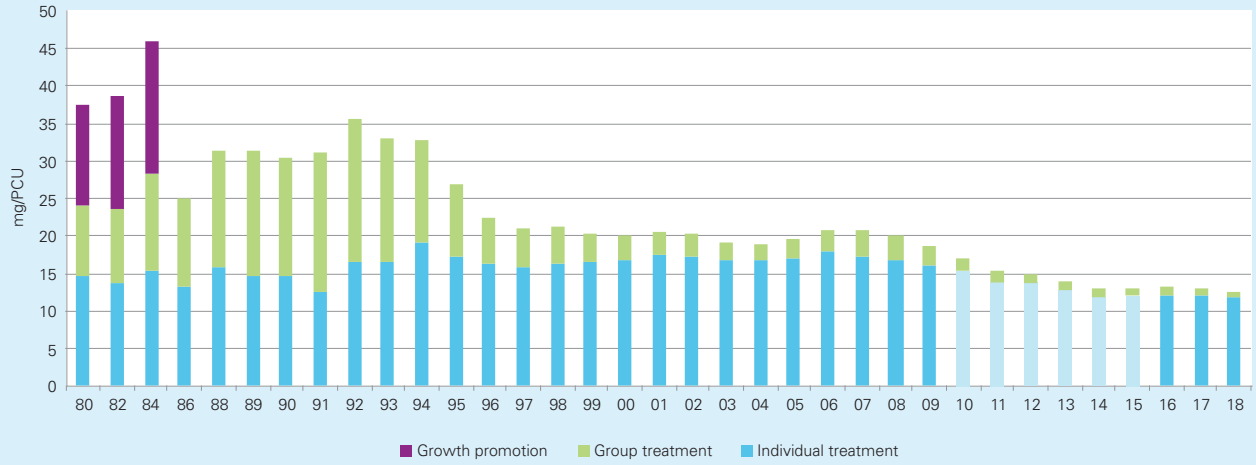
Of the overall sales expressed as kg active substance, more than 90% are products formulated for treatment of individual animals (injectables, tablets, intramammaries) and less than 10% for treatment of groups or flocks (premixes, oral powders, solutions for in water medication). In 2018, the total reported sales from Swedish pharmacies of antibiotics for animals were 10 042 kg, of which 58% was benzylpenicillin. The corresponding figures for 2009 were 15 368 kg and 50%.

Since 2009, sales of all classes of antimicrobials have decreased notably. In the past five years (since 2014), sales of narrow spectrum penicillins (mainly benzylpenicillin), aminopenicillins, aminoglycosides and polymyxins, macrolides and lincosmides and amphenicols and pleuromutilins have been relatively unchanged. Sales of other classes have decreased by more than 10%.

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 2016 as a proxy for PCU in 2017 and 2018. As sales for use in aquaculture are not included, the biomass of fish was not included in the PCU. The overall sales have decreased by around 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.

The WHO classifies 3rd generation cephalosporins, fluoroquinolones and polymyxins as "highly prioritised critically important antimicrobials". In 2018, the sales of these three classes of antibiotics were 0.002, 0.037 and 0.044 mg/PCU, respectively. This represent decreases since 2009 by 92%, 82% and 66%, respectively. For the 3rd generation cephalosporins and fluoroquinolones, the decrease is partly explained by a regulation limiting veterinarians' rights to prescribe these types of antimicrobials (SJVFS 2013:42). As to polymyxins, the recent findings of transferable resistance to colistin were communicated to stakeholders during 2016. 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.

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.

Antibiotic resistance in humans

Overview of surveillance systems

All surveillance of antibiotic resistance in Sweden rely on results from the clinical microbiological laboratories. The laboratories uses the methods and breakpoints recommended by NordicAST for susceptibility testing. This Nordic organization support the implementation of EUCAST recommendations in the Nordic countries.

Notifiable diseases

For humans four bacterial types of antibiotic resistance 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 (*vanA* or *vanB*, VRE), and Enterobacteriaceae with ESBL or $ESBL_{CARBA}$. As in previous years, the reports of ESBLs have outnumbered the other three types manifold.

Voluntary surveillance based on clinical samples

From 2015 and onwards, all voluntary 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 19 laboratories deliver data to Svebar. It is not possible to deduplicate Svebar data since patient identification is not permitted in the system. Consequently, duplicate findings from blood and other samples will be reported. For unusual resistance types, this can result in differences in proportion of resistance compared to previous years so all resistance trends should be interpreted with caution. Data analysed for volontary surveillance are collected from ten, eleven, and nine laboratories respectively for the years 2015-2016, 2017, and 2018.

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

Microbiological characterisation program

The Public Health Agency of Sweden offers laboratories to participate in microbiological characterisation programs by sending isolates for verification and characterisation. Regarding antibiotic resistance there are currently programs for, *Clostridioides difficile*, Enterobacteriaceae with ESBL or $ESBL_{CARBA}$, MRSA, PNSP, and VRE. During late 2017, two additional programs have been added, cephalosporin resistance in *H. influenzae* and colistin resistance in Enterobacteriaceae. For *C. difficile* all isolates from two weeks during the spring and during the fall are ribotyped and tested for antibiotic susceptibility to indicatior antibiotics. For Enterobacteriaceae with ESBL all cefadroxil resistant *E. coli* and *K. pneumoniae* isolates from urine are collected during one month every other year, the isolates are characterised genotypically and phenotypically. All isolates carrying $ESBL_{CARBA}$ are collected and characterised by whole genome sequencing. For MRSA *spa*-type and PVL-status is determined. All PNSP isolates are characterised with serotyping. Isolates from all VRE cases are characterised by whole genome sequencing, MLST and resistance genes.

TABLE 3.1. Summary of species and types of resistance included in national sureveillance of antibiotic resistance in Sweden.

Species, group or type	Sampling
Mandatory reporting (SmiNet)	
Enterobacteriaceae with ESBL	Samples of all types for clinical, screening or case finding purposes.
Enterobacteriaceae with $ESBL_{CARBA}$	
Staphylococcus aureus resistant to methicillin	
Streptococcus pneumoniae non-susceptible to penicillin	
Enterococcus faecium or *faecalis* resistant to vancomycin	
Mycobacterium tuberculosis *	
Neisseria gonorrhoeae *	
Neisseria meningitidis *	Invasive disease (blood, CSF, or other normally sterile sample).
Voluntary surveillance (Svebar)	
Escherichia coli *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	Clinical sampling from faeces.
Salmonella spp**	Clinical sampling from faeces and urine.
Campylobacter spp**	Clinical sampling from faeces.
Microbiological characterisation programme	
Colistin resistance in Enterobacteriaceae	All isolates from clinical, screening or case finding samples.
Enterobacteriaceae with $ESBL_{CARBA}$	All isolates from clinical, screening or case finding samples.
Staphylococcus aureus resistant to methicillin	All isolates from clinical samples.
Streptococcus pneumoniae non-susceptible to penicillin	All isolates from clinical, screening or case finding samples.
Enterococcus faecium or *faecalis* resistant to vancomycin	All isolates from clinical, screening or case finding samples.
Clostridioides difficile	All isolates from clinical samples during weeks 11-12 and 39-40.
Haemophilus influenzae, cephalosporin resistance	All isolates from clinical, screening or case finding samples.
Escherichia coli and *Klebsiella pnemoniae*, cefadroxil resistant	Consecutive samples from urine during one month every three years, 600-800 isolates

*All infections with these bacteria are mandatory to report. Antibiotic resistance data are acquired from these surveillance programs.

**All infections with these bacteria are mandatory to report. However, the antibiotic resistance data are acquired through the voluntary reporting in Svebar.

National reference laboratories for antibiotic resistance in humans in Sweden

The WHO Global Antimicrobial Resistance Surveillance System (GLASS) promotes the establishment of well-functioning AMR systems in all Member States. A key component is the set-up of at least one national reference laboratory (NRL) dealing with different aspects of antimicrobial resistance. The organization of such functions will vary between countries, but should promote and facilitate good laboratory practice and harmonization of methodology and standards used nationally. An important role of the NRL is to provide overall laboratory expertise and guidance as well as facilitate collaboration with local surveillance sites and laboratories. Here we describe how reference functions of importance for surveillance of antibiotic resistance are organised in Sweden.

Swedish Network of Microbiology Laboratories (SLIM)

SLIM is a collaborative network of human, clinical microbiological laboratories. It was initiated in 2017, and is owned, and governed by the regions in Sweden, and the Public Health Agency of Sweden. The regions are responsible for health care in Sweden and the Public Health Agency has a coordinating responsibility for communicable disease control. By developing this network, they share the responsibility to provide rarely used diagnostic tests within microbiology, and to provide expertise on methods necessary for communicable disease control. The functions requested from a reference laboratory are divided into five areas, namely providing reference diagnostics, providing reference material, providing support by experts, engage in development and collaboration, monitoring new developments and preparedness.

National reference laboratories (NRL) for 36 microbiological areas were considered necessary to provide at a national level and was included in this agreement. There are currently 27 clinical microbiological laboratories in Sweden, and all laboratories can apply for one or more of these NRLs. Laboratories can collaborate in taking responsibility for a NRL.

The governing body of SLIM decides which laboratory/laboratories to choose as NRL for each area, and the laboratories are reimbursed by the regions for the functions they provide.

National reference laboratory for antibiotic resistance

Three laboratories collaborate to provide the required services. The main NRL is the Department of Clinical Microbiology, Central hospital, Växjö. In addition there are two auxiliary NRLs for antibiotic resistance: Department of Clinical Microbiology, Karolinska University Hospital, and the Public Health Agency of Sweden.

Reference diagnostics

Department of Clinical Microbiology, Central hospital, Växjö

The laboratory offers MIC determination with broth microdilution technique (accredited reference methodology) as well as susceptibility testing with disc diffusion technique (accredited reference methodology) of clinically relevant bacteria against clinically relevant antibiotics.

Department of Clinical Microbiology, Karolinska University Hospital

MIC determination with agar dilution technique (international reference methodology) of clinically relevant bacteria against clinically relevant antibiotics. In particular, this methodology is used for anaerobic bacteria.

Public Health Agency of Sweden

The agency provides whole genome sequencing and analysis of genomic data for genotypic resistance characterization.

Unusual resistance phenotypes are characterised if considered needed based on assessment of the potential clinical consequences. This is done free of charge within the framework of the national microbial surveillance.

The agency is accredited for resistance detection for *Enterococcus faecium* and *faecalis* and will in the near future apply for accreditation for more analyses. Sequence data from other laboratories can also be sent to the agency for analysis. The proprietary software not only identifies the gene that in itself gives rise to resistance but also mutations in genes such as structural genes (eg proton pumps) that have an effect on bacterial resistance. For other bacteria the laboratory perform species identification, analysis of clonal relatedness with SNPs, and matching to the databases ResFinder and Plasmidfinder.

Reference material

In general, the NRL recommends that the users should order reference strains of accredited collections (ATCC, NTCC, CCUG, etc.) directly from the curator for each collection.

Department of Clinical Microbiology, Central hospital, Växjö
Characterized clinical isolates with specific resistance mechanisms and / or established MIC values may, under special circumstances (the stability of the resistance, ownership, etc.), be provided for a fee.

Department of Clinical Microbiology, Karolinska University Hospital
A reference collection of bacteria with known resistance mechanisms and / or established MIC values by agar dilution is under construction and can, under special circumstances (stability, ownership, etc.), be provided for a fee.

Public Health Agency of Sweden
Bacteria with known resistance mechanisms and/or established MIC values may, under special circumstances (stability, ownership, etc.) be provided for a fee. New variants of resistance genes will be made available through public databases.

Expert support

Department of Clinical Microbiology, Central hospital, Växjö
The laboratory provides problem solving for laboratories in the field of resistance determination with phenotypic methods.

It advises both clinical colleagues and laboratory staff in the field of antibiotics and susceptibility testing. The laboratory offers help with methodological troubleshooting and testing of material (media, antibiotics, etc.) where quality defects in manufacturing, storage, etc. are suspected.

The laboratory organizes reocurring courses in phenotypic susceptibility testing for laboratory staff. The courses are arranged as not-for-profit. Information about these courses and application forms can be found at http://www.nordicast.org/workshops (Theoretical and practical training in the EUCAST disc diffusion method). The laboratory also arranges training for medical staff free of charge. This ranges from 1 to 14 days of training in susceptibility testing techniques.

Department of Clinical Microbiology, Karolinska University Hospital
The laboratory provides problem inventory in the field of phenotypic susceptibility testing (problem solving for laboratories with problems in the field of susceptibility testing with phenotypic methods).

The laboratory advises both clinical colleagues and laboratory staff in the field of antibiotics and susceptibility testing. Assistance can be given in verifying unusual resistance. Methods for detection of important resistance mechanisms can be provided. A senior consultant in bacteriology is always available during the laboratory's opening hours and expert competence on antibiotic resistance (not limited to anaerobes) is generally available, even when requested urgently. The laboratory is also open on weekends and always has a medical doctor on call.

Public Health Agency of Sweden
The agency can assist the country's health and medical services with expert support with analyses of sequence data for genotypic resistance characterization, independent of sequencing platform. This includes detection of resistance genes, determination of resistance mutations, investigation of resistance mechanisms, and management and updating of databases. The agency also handles identification and characterization of newly discovered resistance genes, mechanisms and mutations.

Development and collaboration

Department of Clinical Microbiology, Central hospital, Växjö
The laboratory is responsible for a global network of laboratories with specialist knowledge in resistance testing. The nodes in this network are often specialised in one area (agar dilution method, *Listeria monocytogenes*, anaerobic bacteria, *Neisseria gonorrhoeae* etc). The laboratory collaborates with several organizations in the world, such as Clinical and Laboratory Standards Institute, CLSI (USA), to prepare and maintain reference intervals for type strains with and without defined resistance mechanisms (http://www.eucast.org/ast_of_bacteria/qc_tables/). A good example is the development of a specific reference strain for the quality assurance of resistance testing to colistin.This was done in collaboration with The Public Health Laboratory (Colindale), London. The laboratory monitors methodological problems, and publishes warnings on EUCAST's NordicASTs websites and other information about tests or materials that should not be used for various reasons. On behalf of other laboratories in Sweden, the reference laboratory communicate with suppliers about substandard products. It works together with both other reference laboratories and laboratories in clinical microbiology in various projects. The reference laboratory annually updates Nordic laboratories at NordicAST's workshop.

Department of Clinical Microbiology, Karolinska University Hospital
Through participation in various national and international networks the laboratory monitors international developments and initiates discussions on diagnostic needs. An employee of the laboratory has a coordinating role of President of EUCAST. The laboratory cooperate with the Department of Clinical Microbiology in Odense, on developing susceptibility testing methodology for anaerobic bacteria. The laboratory will work with EUCAST to develop disk diffusion methodology for both anaerobic and Neisseria spp.

Public Health Agency of Sweden
The agency develops and validates of new analyzes based on national needs. The knowledge base for analysis and interpretation of sequencing results is continuously developed through our national surveillance programs, national studies, and participation in national and international networks. The agency has an important role in national collaboration on genotypic resistance characterization with whole genome sequencing. It also participates in a large number of international collaboration groups.

Monitoring new developments and preparedness.

Department of Clinical Microbiology, Central hospital, Växjö
The laboratory is internationally engaged in development and validation of phenotypic susceptibility testing international, which assures up-to-date expertize in the field. The laboratory always has one representative in the EUCAST Steering Committee, two persons are affiliated to NordicAST (the Nordic method group in the field of susceptibility testing) and one person is a member of CLSI's working group in quality control within susceptibility testing.

Department of Clinical Microbiology, Karolinska University Hospital
The laboratory has through Christian Giske's and Carl-Erik Nord's central positions within European microbiology in Europe an obvious monitoring of developments in the area. The laboratory currently has a representative in EUCAST Steering Committee, two persons in the NordicAST committee, and one person who advises CLSI, including the Working Group for Anaerobes.

Public Health Agency of Sweden
Databases of genetic resistance markers and software used to analyze sequence data is continuously updated through structured external monitoring. The microbial surveillance programs are an important platform for detecting national dissemination of resistant bacteria. The agency continuously monitors international publications and media for new discoveries of resistance mechanisms. These are included in the analyzes provided at the agency.

National reference laboratory for epidemiological typing of bacteria

This function is provided by the Public Health Agency of Sweden. Epidemiological typing is needed in the management of outbreaks, and to investigate more insidious spread of resistance. Currently most typing of bacteria at the agency concerns different resistant isolates. The laboratory at the Public Health Agency of Sweden offers a wide range of epidemiological typing, both more traditional methods, e.g. serotyping, and typing based on whole genome sequencing.

Conclusion

The SLIM organization has so far been proven a success in providing reference microbiology, and expert advice within human, clinical microbiology in Sweden.

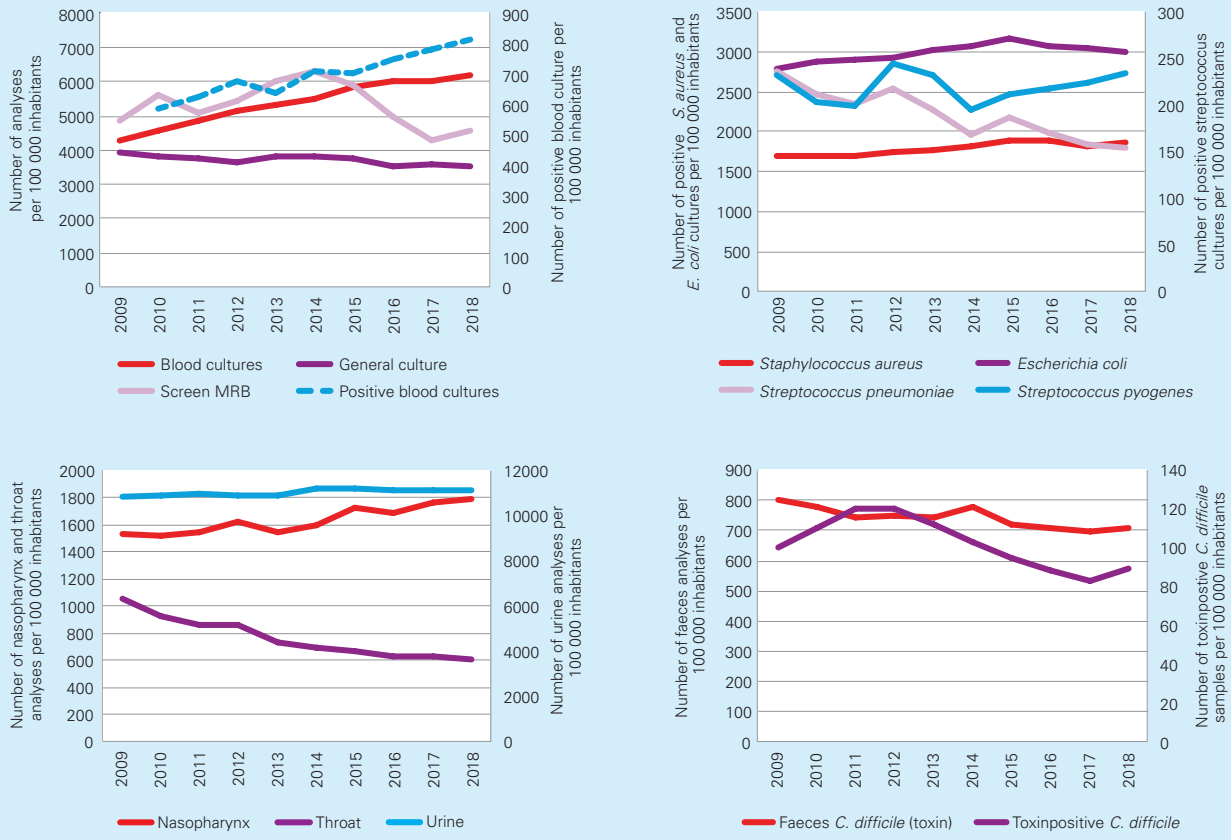
Reference functions and collaboration within the profession are essential for the continuous national work with antibiotic resistance and susceptibility testing. In addition to the described NRLs there are several other collaborations or organizations with important functions for work against antibiotic resistance. One example is the national Strama-group, working with antimicrobial stewardship and issuing treatment guidelines for common infections. Another example is the Reference group for antibiotics – and expert group, which collaborates with EUCAST and EMA concerning break points for susceptibility testing. They also give advice on dosage of antibiotics and which antibiotics to select for susceptibility testing for different specimen types and different bacteria.

In general, there has been a long term tradition of collaboration within the profession in Sweden, and this is now even further strengthened with the building up of the national network for microbiological laboratories.

Overview of sampling and culture results

Denominator data have been collected since 2001 on a voluntary basis directly from the microbiology laboratories in Sweden and reported each year in Swedres-Svarm. This year some of the data is derived from Svebar. The reporting laboratories, this year 25 out of 26, cover more than 95 percent of the population. Complete data for 2018 are given in the section Demographics and denominator data. In the following Figure 3.1 the annual numbers of requested analyses per 100 000 inhabitants are presented for: blood culture, MRB screening culture, general culture, throat culture, nasopharynx culture, urine culture, and *C. difficile*. The number of positive blood cultures per 100 000 inhabitants and the number of isolated *S. aureus*, *E. coli*, *S. pneumoniae*, *and S. pyogenes* in all specimen types per 100 000 inhabitants are also given. The trend for blood cultures requested annually have increased continuously. After some years of decreasing numbers a slight increase in MRB screening cultures is seen. The trends for number of positive blood cultures, and isolated *E. coli* and *S. aureus*, regardless of specimen type, were also increasing although numbers of *E. coli* and *S. aureus* seem to level off. Throat cultures have decreased the past years, likely due to an increased use of near patient testing for streptococcal tonsillitis and the publication of national guidelines for the management of pharyngitis. Though for *S. pyogenes* there is an increased number of isolates the last years.

Figure 3.1. Denominator data for humans. Number of requested analyses, and number of positive analyses or isolates. All per 100 000 inhabitants.



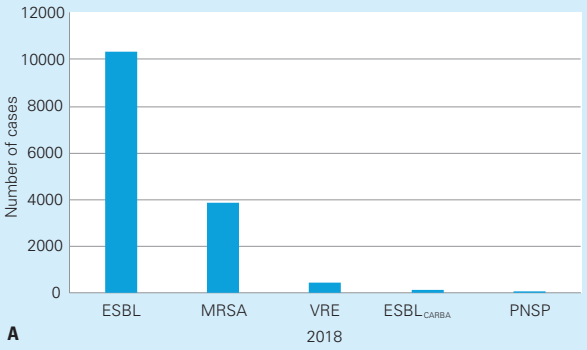
Source: The Public Health Agency of Sweden

Overview of mandatory reported antibiotic resistance

Table 3.2. Summary of results for mandatory reported antibiotic resistance 2018

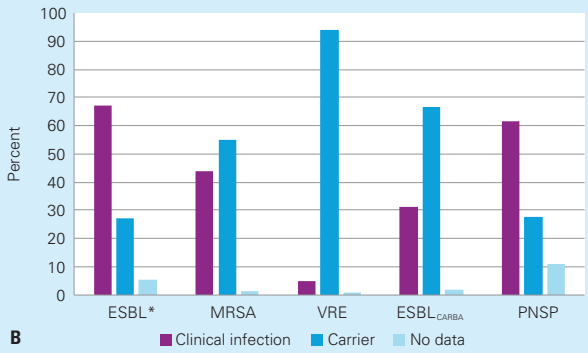
	ESBL	$ESBL_{CARBA}$	MRSA	PNSP	VRE
No of cases (incidence)	10 341 (101)	144 (1.4)	3 684 (38)	91 (0.9)	444 (4.3)
Proportion clinical infection	67%	31%	44%	62%	5%
Gender	66% women	59% men	52% women	52% men	62 % men
Median-age (range)	55 year (0-100+)	62 year (0-90)	29 year (0-97)	26 year (0-86)	71 year (0-98)
Proportion of domestic cases	no information	19%	49% (5% no data)	69% (24% no data)	81%
Short epidemiological information	Community and health-care	Hospital abroad	Community	Community	Hospital, domestic spread
Blood stream infections	703 (550 new cases 2018, 153 cases known from previous years)	7 (6 new cases 2018, one case known from previous years)	64 (52 new cases 2018, 12 cases known from previous years)	6	9

Figure 3.2 A, B. Number of mandatory reported cases during 2018 (A) and the proportion of clinical infection versus carriers (B).



A

Source: The Public Health Agency of Sweden



B

*ESBL data, based on sample types, clinical infection (blood, liquor, urine), carrier (feces, rectum, perineal), No data (other sample materials or not specified).
Source: The Public Health Agency of Sweden

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

Mandatory reporting of ESBL-producing Enterobacteriaceae

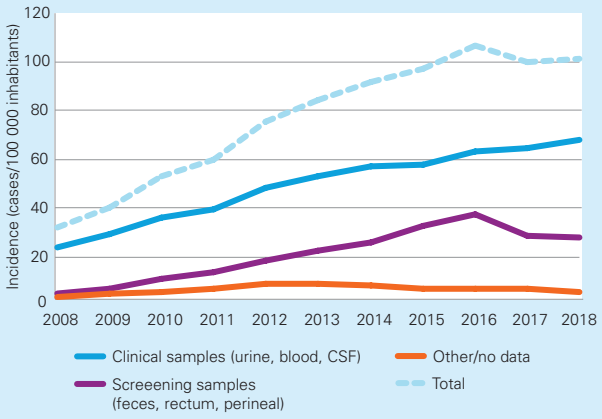
Results from 2018

- Number of reported cases 10 341 (previous year 10 084), relative change +2.5%
- Number of bloodstream infections 703 (previous year 594), relative change +18%

Trends

The incidence of ESBL has increased steadily under many years but has remained stable since 2016 and in 2018 the incidence was 101 new cases per 100 000 inhabitants, see Figure 3.3. During the same period there was a drop in cases with samples taken for screening purposes (feces, rectum and perineal) while cases with mostly clinical samples (urine, blood and CSF) increased slowly. All 21 counties in Sweden reported ESBL-cases and a 2.5 fold difference in incidence was noted, from 69 to 172 cases per 100 000 inhabitants. The large variation could partly be explained by different local practices in sampling.

Figure 3.3. The incidence (cases/100 000 inhabitants) of cases with ESBL-producing Enterobacteriaceae in relation to type of infection, year 2009–2018.

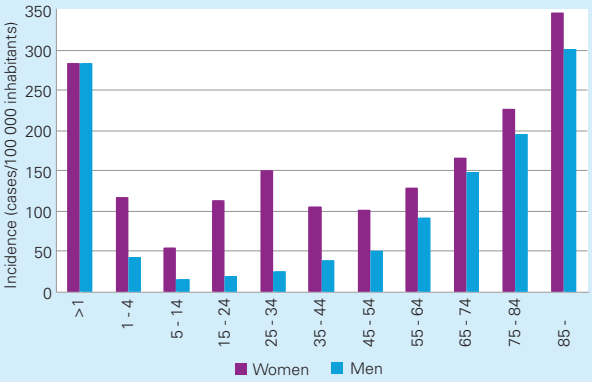


Source: The Public Health Agency of Sweden

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 (Figure 3.4). 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 several other species of Enterobacteriaceae (for detailed information see attached file Figure 3.3).

Figure 3.4. Incidence (cases/100 000 inhabitants) per age group of notified cases of ESBL-producing Enterobacteriaceae 2018.



Source: The Public Health Agency of Sweden

Outbreaks

Small clusters with both ESBL-producing *K. pneumoniae* and *E. coli* have been noted at both neonatal units and other units in different parts of Sweden during 2018, but outbreaks with ESBL-producing Enterobacteriaceae are not consistently reported.

Comments

Since 2016 the total incidence of ESBL-producing Enterobacteriaceae has remained stable, but the incidence for cases discovered in clinical samples has increased constantly during the years. Differences in sampling, screening and contact tracing practices in the regions highly influences these results.

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

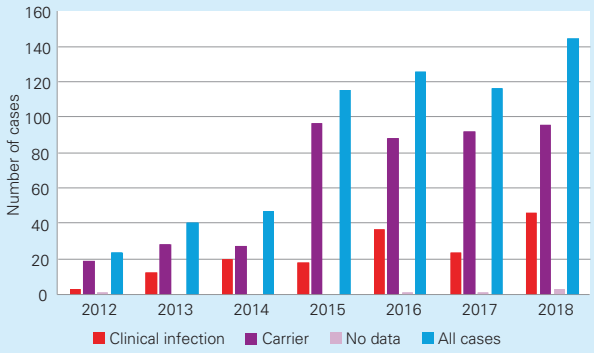
Results from 2018

- Number of reported cases: 144 (previous year 116), relative change +24%
- Number of bloodstream infections: 7 (previous year 2)

Trends

In 2018, the incidence for ESBL$_{CARBA}$ producing Enterobacteriaceae was 1.4 cases per 100 000 inhabitants, an increase with 23% (28 cases) compared with 2017. Nearly two thirds of the cases were carriers (Figure 3.5). Cases were reported from 18 of 21 counties in Sweden. The majority of cases were reported as acquired abroad (78%, n=112) and identified in targeted screening after hospitalization abroad. Of the 27 domestic cases, 24 were identified by investigation of clinical infection. The number of domestic cases with hospital acquired ESBL$_{CARBA}$ remained at the same level as previous years (2016 and 2017). For 15 domestic cases information on acquisition was missing. The cases were unequally distributed between women and men (41% women, 59% men) with median ages of 56 years for women and 65 years for men.

Figure 3.5. Number of notified cases with ESBL$_{CARBA}$ producing Enterobacteriacae, 2012-2018.

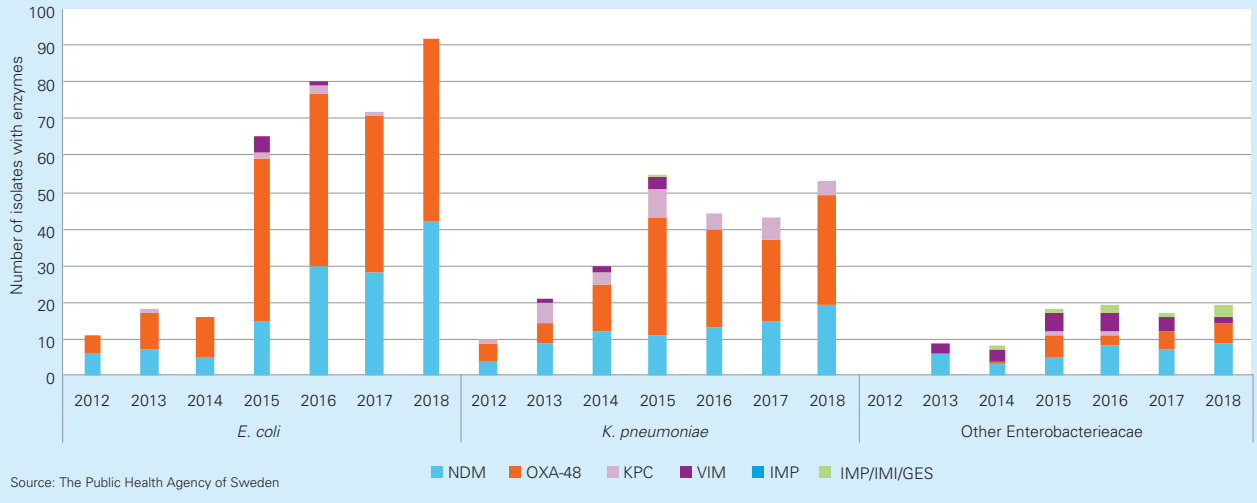


Soure: The Public Health Agency of Sweden

Epidemiological typing of ESBL$_{CARBA}$

All ESBL$_{CARBA}$ isolates from notified cases in 2018 have been characterised using whole genome sequencing (WGS). The most common carbapenemase-producing Enterobacteriaceae was *E. coli* accounting for 60% of all cases, followed by *K. pneumoniae* with 33%. Genes coding for carbapenem resistance have also been detected in several other species of Enterobacteriaceae. The most prevalent enzyme type in 2018 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 3.6). Apart from the genotypic analysis, phenotypic susceptibility testing was performed on all ESBL$_{CARBA}$ isolates. Table 3.3 shows antibiotic resistance of ESBL$_{CARBA}$ cases, no major changes in resistance have occurred between 2017 and 2018.

Figure 3.6. Number of isolates and types of ESBL$_{CARBA}$ in Enterobacteriaceae in Sweden 2012-2018.



Source: The Public Health Agency of Sweden

Table 3.3. Antibiotic resistence in isolates from human cases with $ESBL_{CARBA}$ divided by species.

	KPC-MBL positive isolates[3]		OXA-48-like positive isolates[4]	
Antibiotic	*E. coli* % R **(n=39)**	*K. pneumoniae* % R **(n=22)**	*E. coli* % R **(n=49)**	*K. pneumoniae* % R **(n=23)**
Amikacin	36	65	2	8
Cefotaxim	100	100	82	96
Ceftazidim	100	100	65	96
Ciprofloxacin	92	96	37	88
Gentamicin	46	70	20	79
Imipenem[1]	46	70	0	13
Mecillinam	38	52	12	29
Meropenem	62	74	2	42
Nitrofurantoin[2]	8	-	4	-
Piperacillin/ Tazobactam	100	100	100	100
Tobramycin	62	91	12	92
Trimethoprim	90	78	63	92

[1]Gradient test, [2]Clinical breake-points are valid only for E. coli, [3]Other CPE n=12, [4]Other CPE n=3

Outbreaks

In 2018, two observed clusters of $ESBL_{CARBA}$ occurred in Sweden, which affected 2 patients each. During the spring a cluster of OXA-48-producing *K. pneumoniae* ST392 was detected by WGS. Six patients were affected. After additional epidemiological information from the county medical officers it was shown that all cases had been hospitalized in Gran Canaria. Epidemiological information shared with ECDC revealed additional cases in Norway with the same ST-type and SNP analysis showed a thight genetic relationship between the bacterial isolates from the cases. (ECDC 2018).

Comments

The number of $ESBL_{CARBA}$ cases is low in Sweden and the majority of cases are identified in screening programs after hospitalization abroad. The lack of information on the acquisition route for a rather large number of domestic cases is worrisome. National surveillance is important for at an early stage try to limit a national spread but also to follow the development of $ESBL_{CARBA}$ in the coming years.

Escherichia coli, from blood and urine cultures

Results from 2018

- Number of reported cases with $ESBL_{CARBA}$-producing *E. coli*: 87
- Number of reported cases with bloodstream infections caused by $ESBL_{CARBA}$-producing *E. coli*: 1
- Number of reported cases with ESBL-producing *E. coli*: 9 205
- Number of reported cases with bloodstream infections caused by ESBL-producing *E. coli*: 470

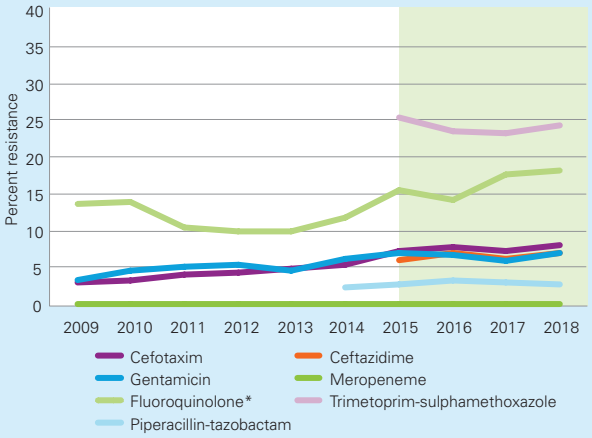
Table 3.4. Proportion (%) of antibiotic resistant *E. coli* from blood and urine 2018.

Antibiotic	Blood isolates % R **(n=5 383)**	Urine isolates % R **(n=103 223)**
Ampicillin	na	30.6
Cefadroxil	na	6.0
Cefotaxime	8.0	na
Ceftazidime	7.0	na
Flouroquinolone	18.1	12.3
Gentamicin	6.9	na
Mecillinam	na	3.8
Meropenem	0.0	na
Nitrofurantoin	na	1.0
Piperacillin-tazobactam	2.7	4.1*
Trimetoprim	na	20.9
Trimetoprim-sulphamethoxazole	24.3	na
Resistance to both Cefotaxime/ceftazidime + Gentamicin/tobramycin	2.8	na
Resistance to both Piperacillin-tazobactam + Gentamicin/ tobramycin	0.8	na

*based on selective testing.

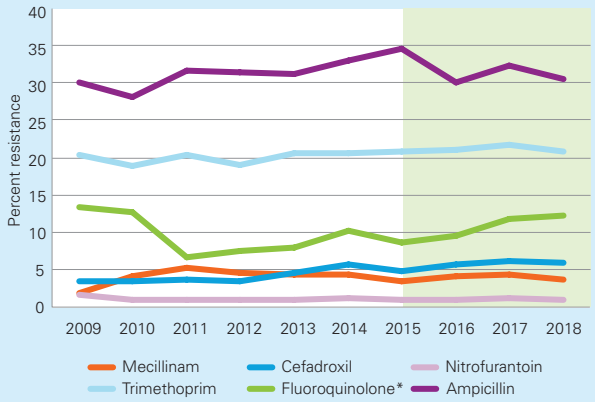
Trends

Figure 3.7. Antibiotic resistance in *E. coli* isolates from bloodstream infections during the years 2009-2018. Number of AST isolates is given in the attached file.



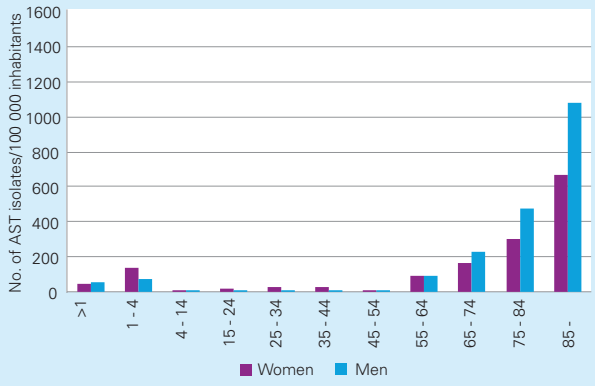
*Prior to 2011, nalidixic acid was used for detection of fluoroquinolone resistance in Enterobacteriaceae. From 2011, ciprofloxacin was used.
Source: The Public Health Agency of Sweden

Figure 3.8. Antibiotic resistance in *E. coli* isolates from urine infections during the years 2009-2018. Number of AST isolates is given in the attached file.



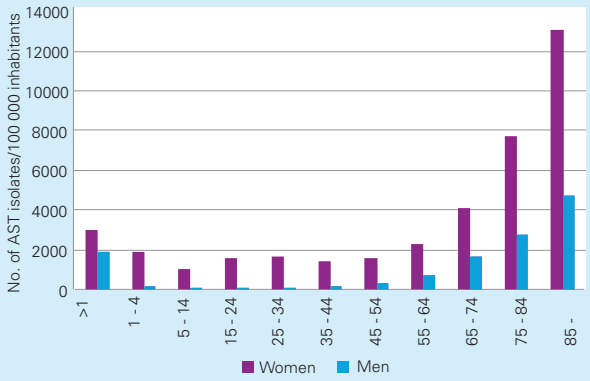
*Prior to 2011, nalidixic acid was used for detection of fluoroquinolone resistance in Enterobacteriaceae. From 2011, ciprofloxacin was used.
Source: The Public Health Agency of Sweden

Figure 3.9. Age distribution among patients with *E. coli* in blood.



Source: The Public Health Agency of Sweden

Figure 3.10. Age distribution among patients with *E. coli* in urine.



Source: The Public Health Agency of Sweden

Comments

The proportion of ESBL producing *E. coli* among invasive isolates has increased continually over the years to the current 8%. The carbapenem resistance is still very low. Combined resistance to cefotaxime/ceftazidime and gentamicin/tobramycin or the combination piperacillin-tazobactam and gentamicin/tobramycin was 2.8% and 0.8% respectively (Table 3.4 and Figure 3.7).

Resistance to commonly prescribed oral antibiotics for treatment of urinary tract infections (UTI) caused by *E. coli* remained stable. Cefadroxil resistance, which can be used as an indicator for production of ESBL, remained at 6% in 2018 (Figure 3.8).

Resistance to fluoroquinolones is still increasing and is now at approximately 18% and 12% for blood and urine isolates respectively (Table 3.4, Figure 3.7 and 3.8). The high increase in flouroquinolone resistance seen during 2016-2017 can mostly be explained by a breakpoint change for ciprofloxacin. These high levels of ciprofloxacin resistance must be considered when choosing empirical treatment for febrile UTI. The age and gender distributions (Figure 3.9 and 3.10) reflects that UTI is more common in women, and that *E. coli* is the most common UTI pathogen.

Klebsiella pneumoniae, from blood and urine cultures

Results from 2018

- Number of reported cases with $ESBL_{CARBA}$-producing *K. pneumoniae*: 48
- Number of reported cases with bloodstream infections caused by $ESBL_{CARBA}$-producing *K. pneumoniae*: 2
- Number of reported cases with ESBL-producing *K. pneumoniae*: 930
- Number of reported cases with bloodstream infections caused by ESBL-producing *K. pneumoniae*: 66

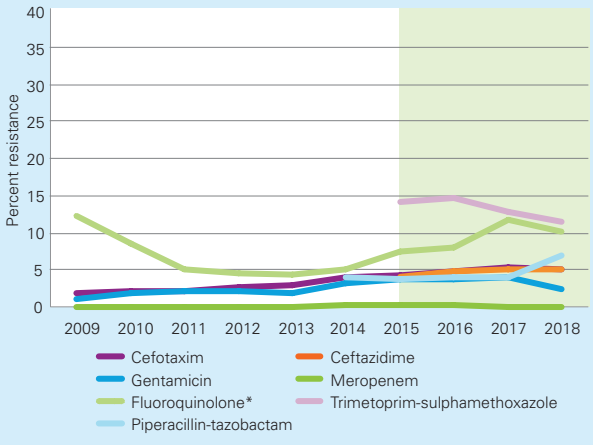
Table 3.5. Proportion (%) of antibiotic resistant *K. pneumoniae* from blood and urine 2018.

Antibiotic	Blood isolates % R (n =1 089)	Urine isolates % R (n=9 901)
Ampicillin	Intrinsic resistance	Intrinsic resistance
Cefadroxil	na	5.4
Cefotaxime	5.0	na
Ceftazidime	5.1	na
Flouroquinolone	10.1	10.7
Gentamicin	2.5	na
Mecillinam	na	8.2
Meropenem	0.1	na
Nitrofurantoin	Intrinsic resistance	Intrinsic resistance
Piperacillin-tazobactam	6.9	11*
Trimetoprim	na	18.6
Trimetoprim-sulphamethoxazole	11.5	na
Resistance to both Cefotaxime/ceftazidime + Gentamicin/tobramycin	2.2	na
Resistance to both Piperacillin-tazobactam + Gentamicin/tobramycin	1.4	na

*based on selective testing.

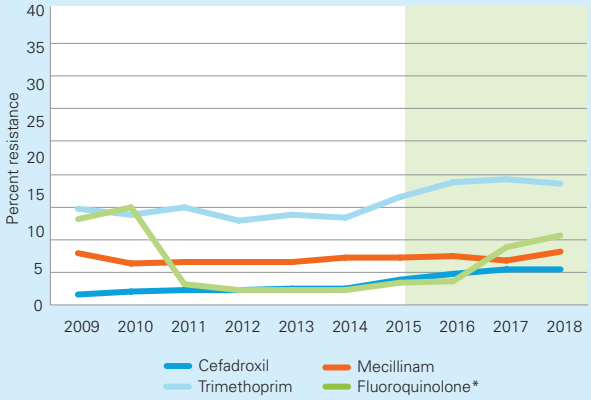
Trends

Figure 3.11. Antibiotic resistance in *K. pneumoniae* isolated from blood during the years 2009-2018. Number of AST isolates is given in the attached file.



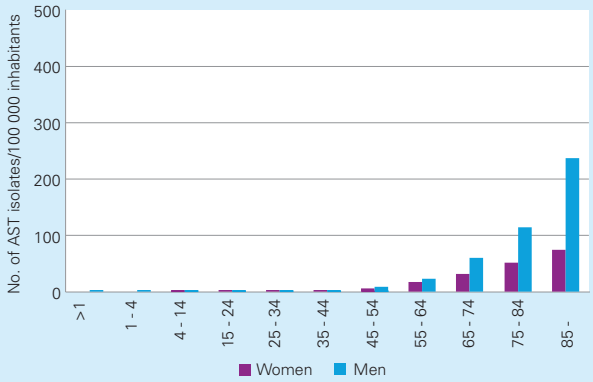
*Prior to 2011, nalidixic acid was used for detection of fluoroquinolone resistance in Enterobacteriaceae. From 2011, ciprofloxacin was used.
Source: The Public Health Agency of Sweden

Figure 3.12. Antibiotic resistance in *K. pneumoniae* isolates from urine during the years 2009-2018. Number of AST isolates is given in the attached file.



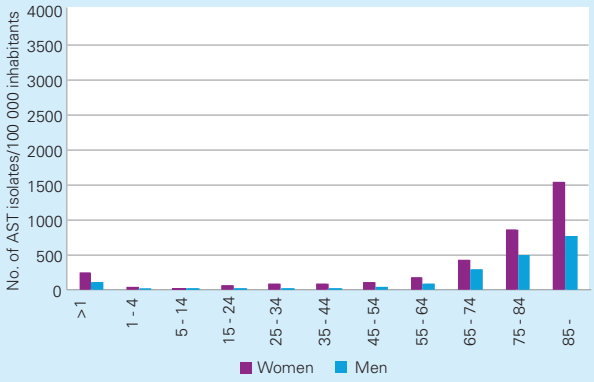
*Prior to 2011, nalidixic acid was used for detection of fluoroquinolone resistance in Enterobacteriaceae. From 2011, ciprofloxacin was used.
Source: The Public Health Agency of Sweden

Figure 3.13. Age distribution among patients with *K. pneumoniae* in blood.



Source: The Public Health Agency of Sweden

Figure 3.14. Age distribution among patients with *K. pneumoniae* in urine.



Source: The Public Health Agency of Sweden

Comments

In 2018, the resistance levels for most antibiotics tested against blood isolates decreased slightly with the exception for piperacillin-tazobactam. Combined resistance to cefotaxime/ceftazidime and gentamicin/tobramycin and the combination piperacillin-tazobactam and gentamicin/tobramy-

cin was 2.2% and 1.4% respectively (Table 3.5 and Figure 3.11). The proportion of ESBL producing *K. pneumoniae* is stable both for isolates from blood and urine (Table 3.5, Figure 3.11 and 3.12).

The mecillinam and fluoroquinolone resistance increased among urine isolates (Figure 3.12). The high increase in flouroquinolone 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.

Characterisation of *E. coli* and *K. pneumoniae* from urine; a national microbial surveillance programme, 2007-2017.

Twenty-five of twenty-six Swedish clinical laboratories contributed to the program collecting consecutive cefadroxil resistant *E. coli* and *K. pneumoniae* from urinary tract infections during one month in 2017. The isolates were characterised genotypically using an amplicon-based sequencing technique.

The results show that even though the number of collected isolates has increased over the years, the percentage of $ESBL_A$, $ESBL_M$ och $ESBL_{CARBA}$ is constant (Figure 3.15). This is also true for the percentage of cefadroxil-resistant *E. coli* that do not carry ESBL-genes. Mcr-mediated resistance was found in only a few isolates and it can be concluded that this is currently not an acute health care problem. The full report can be downloaded from the Public Health Agency of Sweden's website (Folkhälsomyndigheten 2019).

Figure 3.15. A. Distribution of ESBL classes among cefadroxil resistant E. coli between 2007 and 2017. B. Distribution of ESBL classes among cefadroxil resistant *K. pneumoniae* between 2007 and 2017.

Source: The Public Health Agency of Sweden

Staphylococcus aureus including MRSA

Mandatory reporting of methicillin resistant *Staphylococcus aureus*

Results from 2018

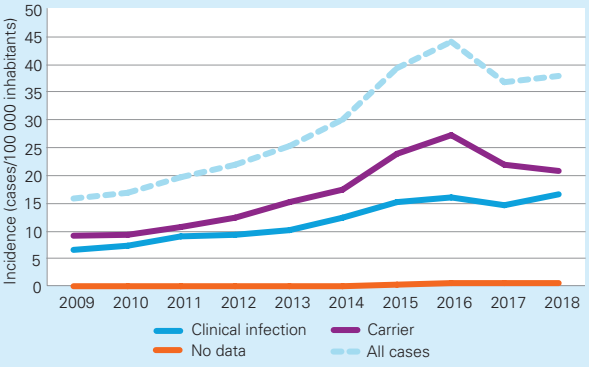
- Number of reported cases: 3 864 (previous year 3 735), relative change +3.5%
- Number of bloodstream infections: 64 (previous year 55), relative change +16%

Trends

In 2018 a total of 3 864 cases of MRSA were notified. The incidence, based on yearly number of cases was 38 cases per 100 000 inhabitants compared to 37 cases per 100 000 inhabitants in 2017, see Figure 3.16. The number of cases reported with clinical infections were 1 688 (44%) while 2 118 cases (55%) were listed as carriers. MRSA-cases were reported from all 21 counties in Sweden. There were variations in incidence, from 24 to 57 cases per 100 000 inhabitants, between the counties. These differences are probably partly explained by different screening and contact tracing practices.

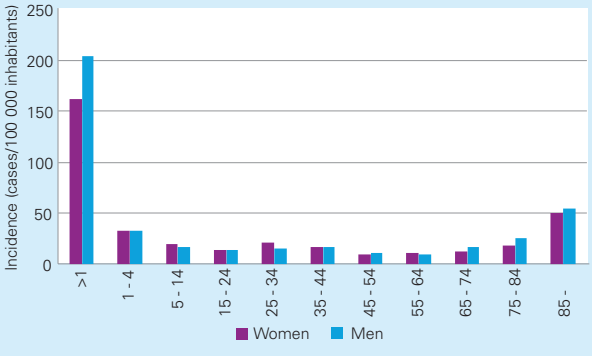
There was a nearly equal distribution between women and men, with 52% (n=2 015) women and 48% (n=1 849) men with a median age of 29 years for women and 30 years for men. Among the domestic MRSA cases (n=1 909), the incidence was highest in the age group <1 year followed by the

Figure 3.16. The incidence (cases/100 000 inhabitants) of cases with MRSA in relation to type of infection, year 2009–2018.



Source: the Public Health Agency of Sweden

Figure 3.17. Incidence (cases/100 000 inhabitants) per age group of cases with MRSA acquired in Sweden 2018.

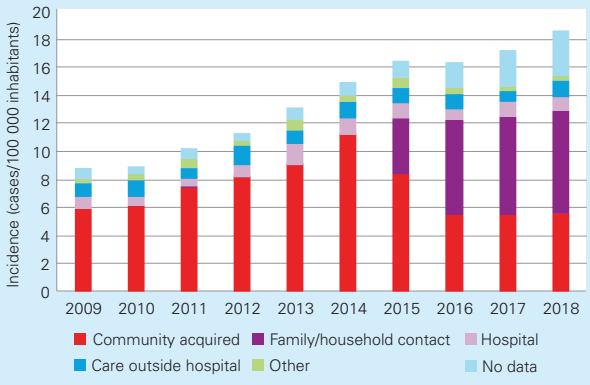


Source: The Public Health Agency of Sweden

age group 85- (Figure 3.17). The high incidence of MRSA among children under one year is likely due to screening practices at neonatal units and in maternal care in combination with contact tracing initiated by new cases.

Community acquired infections continue to be most common among all cases, Figure 3.18. Under 2015 a change in the clinical notification form was made and community acquired infection was divided into family/household contact and community acquired infection. Among cases with MRSA acquired in Sweden, 39% (n=753) were reported under the transmission route family/household contact while 30% (n=573) were reported as community acquired. The proportion of domestic cases with MRSA acquired in hospital as well as healthcare/care outside hospital was low 5% (n=97) and 6% respectively (n=117). Eighteen percent (n=338) of the domestic cases lacked information on acquisition.

Figure 3.18. Epidemiological classification of notified cases with MRSA acquired in Sweden, year 2009-2018. Presented as incidence (cases/100 000 inhabitants).



Source: The Public Health Agency of Sweden

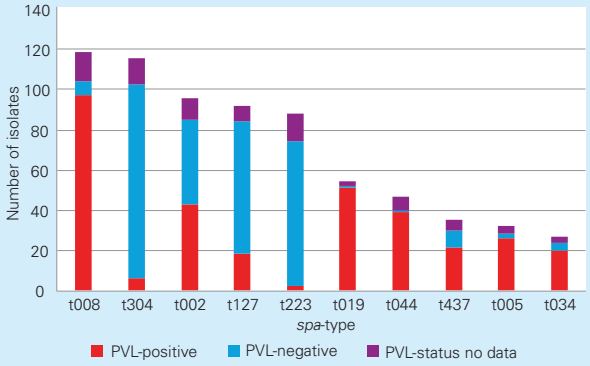
Epidemiological typing of MRSA

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. Typing data were available for isolates from 1 566 (93%) of the clinical cases. In addition to the surveillance program, typing data were reported for 1 256 isolates (59%) from asymptomatic carriers, see Table 3.6. Among the isolates from clinical cases, a total of 308 *spa*-types were identified. The ten most common *spa*-types were seen among 45% of the clinical cases, Figure 3.19.

Table 3.6. Number of typed MRSA isolates 2018 by type of infection.

	Number of notified cases	Number of typed isolates	Proportion of typed isolates, %
Total	3 864	2 850	74
Clinical infection	1 688	1 566	93
Carrrier	2 118	1 256	59
No data	58	28	48

Figure 3.19. The ten most common *spa*-types (with PVL status) for MRSA from clinical infections, 2018.



Source: The Public Health Agency of Sweden

Outbreaks

Thirty minor healthcare related transmissions of MRSA (two to eleven cases) were reported during 2018.

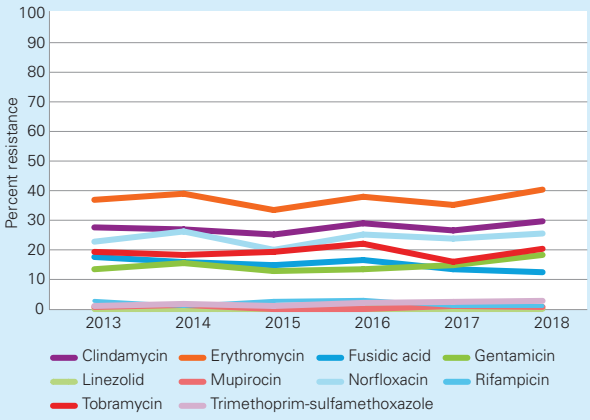
Comments

After many years of increasing numbers of MRSA cases, the number of reported cases declined between 2016 and 2017 and has then remained stable. The decline is most prominent in cases reported as carriers. No major change has been noted in the proportion of domestic cases acquiring MRSA in hospital or care outside hospital. However, 18% of the domestic cases lacked information on way of acquisition.

Antibiotic resistance in voluntary reported clinical isolates of MRSA

Culturing and AST results for *S. aureus* from clinical isolates are presented in Table 3.7 and Figure 3.20. Here, isolates from screening and case finding have been excluded.

Figure 3.20. Antibiotic resistance in clinical isolates of MRSA 2013-2018.



Source: The Public Health Agency of Sweden

Table 3.7. Number of *S.aureus* and MRSA from clinical samples and proportion of MRSA 2013-2018.

	2013	2014	2015	2016	2017	2018
Number of *S.aureus*	72 560	95 444	100 543	105 990	83 362	75 034
Number of MRSA	827	1 099	1 423	1 708	1 355	1 368
Proportion of MRSA	1.1%	1.2%	1.4%	1.6%	1.6%	1.8%

Comments

The proportion of MRSA in clinical samples positive for *S.aureus* were 1.8% in 2018 and has slowly increased since 2013 (Table 3.7). The proportion of resistance in MRSA to other antibiotics remain stable (Figure 3.20).

Staphylococcus aureus, from blood and skin and soft tissue cultures

Results from 2018

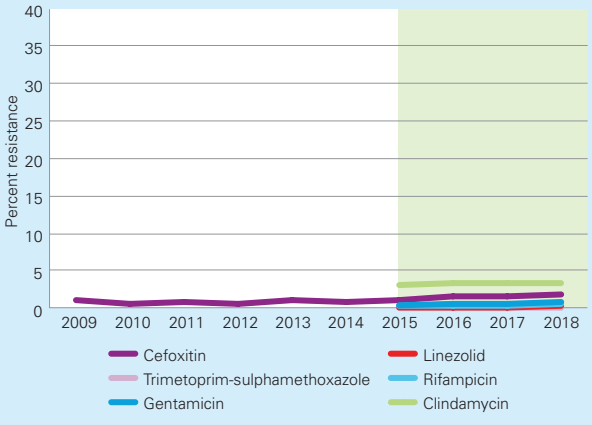
- Number of cases of MRSA reported: 3 864.
- Number of cases with bloodstream infections caused by MRSA reported: 64.

Table 3.8. Proportion (%) of antibiotic resistant *S. aureus* from blood and skin and soft tissue infections 2018.

Antibiotic	Blood isolates, % R (n=3 634)	Skin and soft tissue isolates, % R (n=40 289)
Cefoxitin	1.9	1.9
Clindamycin	3.4	5.4
Erythromycin	na	5.6
Gentamicin	0.9	1.5
Fucidic acid	na	3.4
Linezolid	0.2	na
Rifampicin	0.6	na
Trimetoprim-sulphamethoxazole	0.3	na

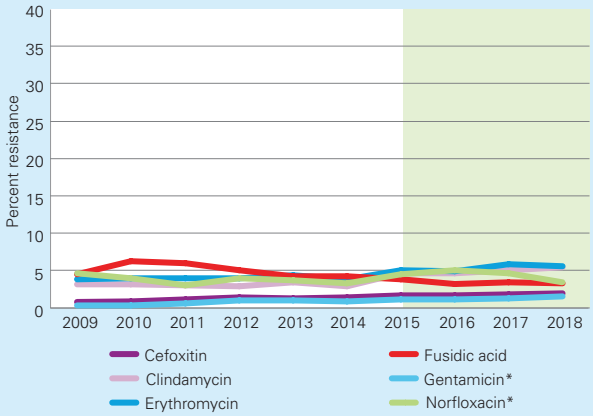
Trends

Figure 3.21. Antibiotic resistance in *S. aureus* from blood during the years 2009-2018. The number of isolates is given in the attached file.



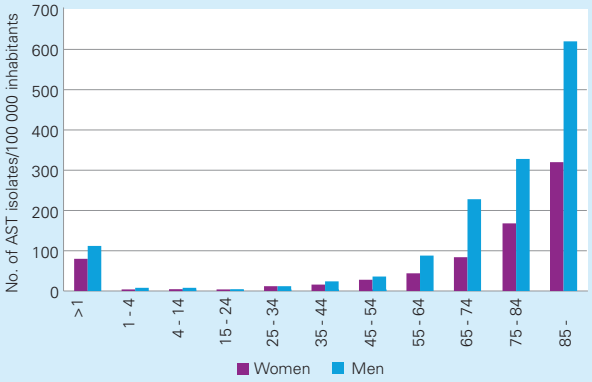
Source: The Public Health Agency of Sweden

Figure 3.22. Antibiotic resistance in *S. aureus* from skin and soft tissue samples 2009-2018. The number of isolates is given in the attached file.



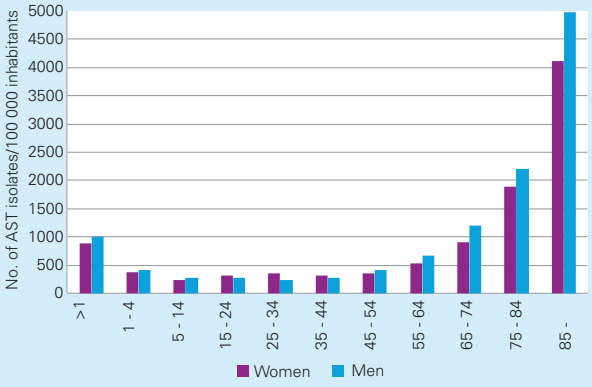
*Resistance based on a selected population.
Source: The Public Health Agency of Sweden

Figure 3.23. Age distribution among patients with *S. aureus* isolated from blood.



Source: The Public Health Agency of Sweden

Figure 3.24. Age distribution among patients with *S. aureus* isolated from skin and soft tissue.



Source: The Public Health Agency of Sweden

Comments

MRSA (indicated by cefoxitin resistance) isolated from blood has slowly increased and is now 1.9% and the same proportion is seen in skin and soft tissue infections (Figure 3.21 and 3.22). Testing of susceptibility to vancomycin is not routinely done on cefoxitin-susceptible *S. aureus*. In 2018, 362 out of 3 634 (10%) isolates were tested for vancomycin resistance with no resistance detected.

Enterococcus faecalis and *Enterococcus faecium* including VRE

Mandatory reporting of vancomycin resistant enterococci

Results from 2018

- Total number of VRE cases reported: 444 (previous year: 244), relative change +82%
- Number of reported cases (*E. faecium*): 438 (previous year: 236), relative change +54%
- Number of reported cases (*E. faecalis*): 6 (previous year: 8)
- Number of bloodstream infections: 9 (previous year: 2)

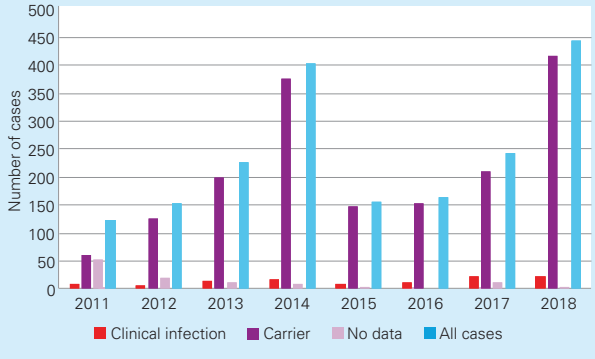
Trends

The national incidence, based on yearly number of cases, increased from 2.4 cases per 100 000 inhabitants to 4.3 cases per 100 000 inhabitants between 2017 and 2018. Nineteen of twentyone counties reported cases of VRE during 2018. Four hundred seventeen (94%) of the cases were healthcare related. Accordingly, a majority of the isolates (n=390, 88%) were from feces, and only 10% from urine, wound or other clinical samples (Figure 3.25). Nine invasive VRE infections were reported in 2018.

In 2018, most cases were reported as acquired in Sweden (81%). Most domestic cases were found through contact tracing (67%) in contrast to cases acquired abroad which were detected through screening (91%) (Figure 3.26).

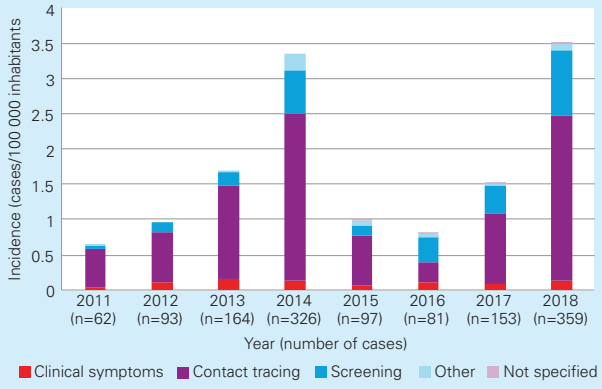
VRE was most common in men, 59%. Median age for men was 61 years and 60 years for women (Figure 3.27). In 2018, 438 *E. faecium* cases and six *E. faecalis* cases were reported. The *vanB* genotype was most commonly found (n=317) (Figure 3.28).

Figure 3.25. Number of cases of reported VRE based on type of infection 2011-2018.



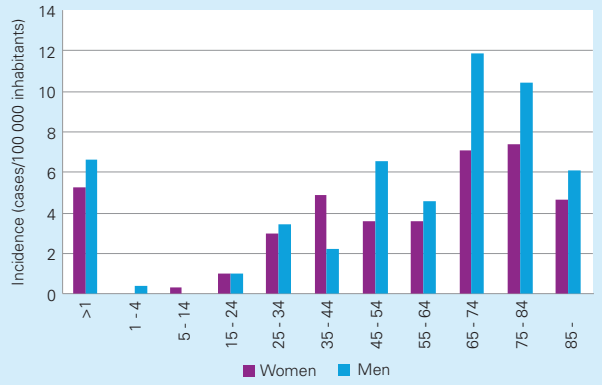
Soure: The Public Health Agency of Sweden

Figure 3.26. Mode of detection of VRE in Sweden during 2011-2018.



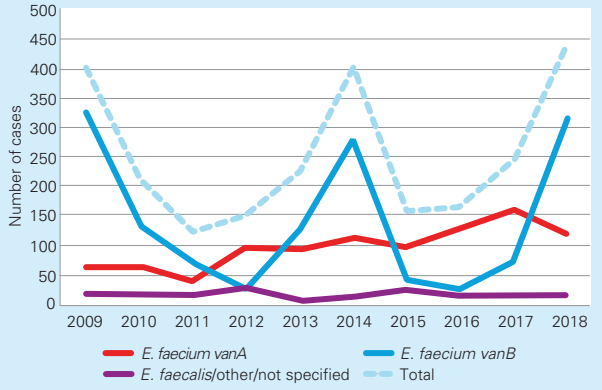
Source: The Public Health Agency of Sweden

Figure 3.27. Incidence (cases/100 000 inhabitants) per age group of notified VRE cases 2018.



Source: The Public Health Agency of Sweden

Figure 3.28. Number of VRE cases and their corresponding *van*-type.



Source: The Public Health Agency of Sweden

Epidemiological typing and outbreaks

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 2018, nineteen hospital-related outbreaks were reported, one large national outbreak with 262 cases, three small outbreaks (5-15 cases), and fifteen small clusters with two to four cases each (Table 3.9). The large outbreak (denoted SE-EfmB-1707) included cases in seven counties where Stockholm (n=98), Västerbotten (n=91), Södermanland (n=38) and Örebro (n=30) reported most cases. In several instances patient transfers were directly linked to spread between hospitals and counties. The outbreak was declared over in the fall/winter 2018. Two of the smaller outbreaks occurred in a hospital in Västra Götaland county (SE-EfmA-1805, n=13 and SE-EfmA-1812, n=7) and the third small outbreak was reported from a neonatal ward and a pediatric surgical ward in two counties (SE-EfmA-1801, n=6) (Table 3.9).

Six out of nine invasive cases were had *E. faecium* harbouring *vanB*. Five belonged to the large outbreak (SE-EfmB-1707) and one was unique. The remaining three cases was casued by *E. faecium* with *vanA* and one of these cases was part of a cluster (SE-EfmA-1813).

Comments

The number of VRE cases increased with over 80% during 2018 due to a large national outbreak. Six out of nine invasive cases were part of outbreaks. 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. Typing results indicating spread are strong motivators, and often necessary to initiate the extensive work needed to stop outbreaks of VRE.

Table 3.9. Epidemiological typing of VRE 2018.

Epidemiological typing	Sequence type (ST)	Number of epidemiological typed VRE
EfmA unique	21 different sequence types	62
EfmB unique	8 different sequence types	33
SE-EfmA-1608	552	3
SE-EfmA-1801	789	6
SE-EfmA-1804	761	2
SE-EfmA-1805	17	14
SE-EfmA-1809	203	3
SE-EfmA-1810	1495	3
SE-EfmA-1811	80	4
SE-EfmA-1812	117	7
SE-EfmA-1813	203	3
SE-EfmA-1814	80	2
SE-EfmA-1815	New	3
SE-EfmB(A)-1612	80	4
SE-EfmB-1707	80	262
SE-EfmB-1802	80	4
SE-EfmB-1803	17	2
SE-EfmB-1805	17	2
SE-EfmB-1806	1495	3
SE-EfmB-1807	New	2
SE-EfmB-1808	80	2
Total number of epidemiological typed VRE	26 different sequence types	**426***

*The total number of isolates is fewer than the number of reported cases since *E. faecalis* is not listed and not all cases are sent to the Public Health Agency of Sweden for epidemiological typing.

Enterococcus faecalis and *Enterococcus faecium*, from blood cultures

Results from 2018

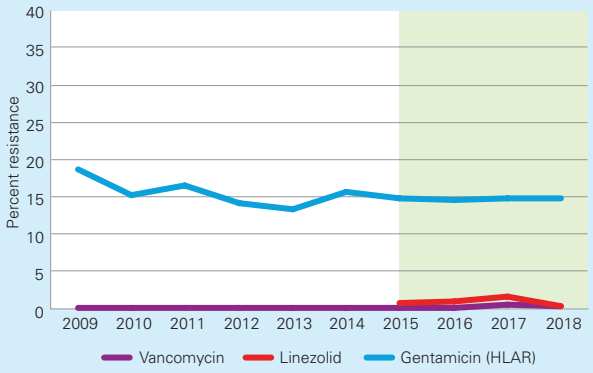
- Total number of VRE cases reported: 444 (previous year: 244), relative change +82%
- Number of reported cases (*E. faecium*): 438 (previous year: 236), relative change +54%
- Number of reported cases (*E. faecalis*): 6 (previous year: 8)
- Number of bloodstream infections caused by VRE: 9 (previous year: 2)

Table 3.10. Proportion (%) of antibiotic resistant *E. faecalis* and *E. faecium* from blood 2018.

Antibiotic	Blood isolates *E. faecalis*, % R (n = 692)	Blood isolates *E. faecium*, % R (n = 433)
Ampicillin	na	83.1
Gentamicin (HLAR)	14.7	18.3
Linezolid	0.3	1.0
Piperacillin-tazobactam	0.0	84.7
Vancomycin	0.3	1.4

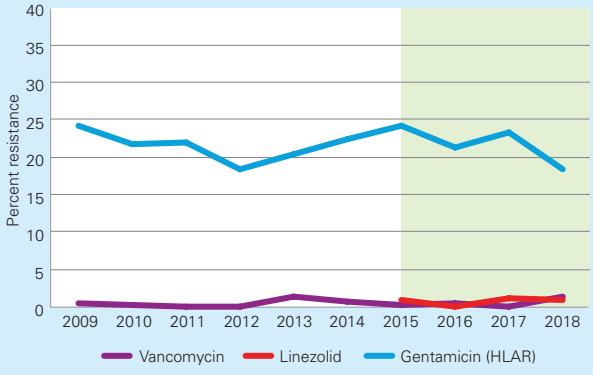
Trends

Figure 3.29. Antibiotic resistance in *E. faecalis* isolated from blood during the years 2009-2018. Number of AST isolates is given in the attached file.



Source: The Public Health Agency of Sweden

Figure 3.30. Antibiotic resistance in *E. faecium* isolated from bloodstream infections during the years 2009-2018. Number of AST isolates is given in the attached file.



Source: The Public Health Agency of Sweden

Comments

The vancomycin resistance among invasive isolates remains low and was 0.3% for *E. faecalis* and 1.4% for *E. faecium* in 2018 (Table 3.10 and Figures 3.29 and 3.30).

Streptococcus pneumoniae including PNSP

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

Results from 2018

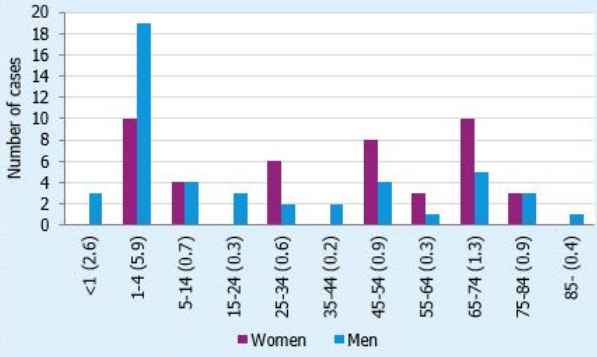
- Number of reported cases: 91 (previous year 61), relative change +50%
- Number of bloodstream infections reported: 3 (previous year 5)

Trends

The incidence increased from 0.6 cases per 100 000 inhabitants to 0.9 cases between 2017 and 2018. PNSP was most common in children up to four years of age (35%). Of all cases 2018, 52% were men and 48% women (Figure 3.31).

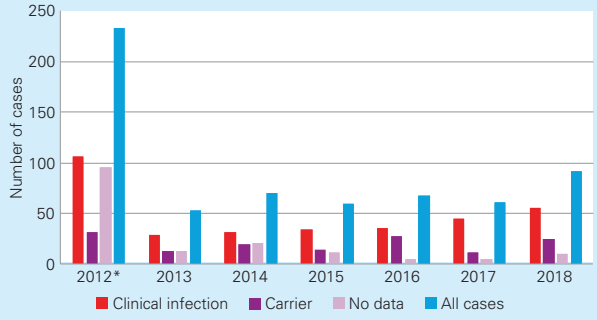
PNSP was most often found in cultures from the nasopharynx (53%). Twenty-six isolates were found in sputum/bronchoalveolar lavage (29%). In 58 cases (64%) the detection of PNSP was due to clinical symptoms and seventeen cases were detected through contact tracing (19%) (Figure 3.32).

Figure 3.31. Incidence per age group and gender for PNSP acquisition 2018.



Source: the Public Health Agency of Sweden

Figure 3.32. Number of cases of reported PNSP based on type of infection 2011-2018.



*The case definition for PNSP was changed in May 2012 from PcG MIC ≥ 0.5 mg/L to PcG MIC > 1 mg/L.
Source: The Public Health Agency of Sweden

Reocurring outbreaks of vancomycin resistant enterococci in Swedish hospitals

Outbreaks of vancomycin resistant enterococci (VRE) is a considerable problem in Swedish hospitals. A large outbreak, encompassing three counties and several hospitals, occurred in 2007, and since then outbreaks have been reported every year. Fortunately VRE has not yet become endemic in any hospital in Sweden. VRE mostly affects vulnerable patient groups, and there tend to be more reported serious infections during years with a high total number of cases. Here we summarize outbreaks since 2007, in addition, experience from handling outbreaks, both from units for communicable disease control and prevention, and from units for infection prevention and control (IPC) is described.

This summer is based on mandatory reported cases and isolates sent for epidemiological typing.

Outbreaks

There have been four larger outbreaks with a hundred or more cases, all of these were caused by *Enterococcus faecium* carrying the van B gene. The first occurred 2007 to 2010, had total of 872 cases, and involved four regions and six hospitals.

The next started in 2010, with around a hundred cases in two hospitals within the same region.

The third outbreak occurred in one hospital during 2013, with 314 cases.

The latest major outbreak started in 2017, and ended last year. It included hospitals in seven regions.

The total number of cases of VRE as well as a summary of outbreaks are given in Table 1.

During the last large outbreak five patients had septicaemia with the outbreak strain. The number cases of septicaemia tend to correlate with the number of cases of VRE in large outbreaks, as well as with the total number of cases. This emphasizes the importance of preventing the spread of VRE.

Regional experience from outbreaks and consequences for healthcare

IPC-units and departments of communicable disease control and prevention from five regions were asked to share their experience from handling outbreaks of VRE. Their viewpoints on effective measures and consequences of VRE outbreaks are summarized below.

Effective measures

There was a high level of agreement between the regions on which measures were important to stop outbreaks of VRE. These measures can be subdivides into the following areas: governance, information, education, concrete IPC-practices, and other measures.

Governance

- Multi-level governance including all levels in the organization is important, including: highest steering level in the healthcare region, clinic head/ clinical center head, head of the ward, individual healthcare workers (HCW).
- Hospital management needs to be engaged, request, and give proper resources for:
- Detection of outbreaks, case finding, and improvement of IPC-measures.
  - Educational activities for personell.

Table 1. Total number of VRE reported per year, number of cases, region, and hospitals in large, medium sized, and small outbreaks.

		2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
	Total number of VRE cases	53	618	402	214	122	152	227	402	157	165	244	444
	Number of cases with VRE isolated from blood	0	11	4	2	0	1	3	7	1	1	2	9
Large outbreaks (>99 cases)	Number of outbreaks	1[a]	1[a]	1[a]	2[a,b]	1[a,b]	1[a]	1[c]	1[c]	1[c]	0	1[d]	1[d]
	Total number of cases	35	500	320	124	45	20	75	254	10	0	3	265
	Total number of hospitals	2	6	6	5	2	1	2	2	2	0	1	6
	Total number of regions	1	4	4	4	2	1	2	2	2	0	1	5
Medium sized outbreaks (>10 and <100 cases)	Number of outbreaks	0	0	0	0	0	2	3	3	2	0	4	1
	Total number of cases	0	0	0	0	0	34	31	45	28	0	143	13
	Total number of hospitals	0	0	0	0	0	3	2	4	3	0	7	1
	Total number of regions	0	0	0	0	0	2	2	3	3	0	6	1
Small outbreaks (<11 cases)	Number of outbreaks	2	0	3	8	8	8	9	12	14	14	5	17
	Total number of cases	6	0	12	35	20	37	36	56	54	63	14	55
	Total number of hospitals	2	0	5	5	5	>7	10	9	>9	>10	5	>10
	Total number of regions	2	0	5	5	5	7	8	8	9	10	5	10

a, b, c and d) The letters indicate different outbreaks, extending over two or more years.

- Assessment and identification of weaknesses in IPC-practices in different parts of the hospital.
- Improvements in working routines, health care processes, and cleaning and disinfection.
- Availability of IPC-expertise for all units in the hospital.
- If necessary close wards and prohibit overcrowding.

- Written routines must be available for:
  - Fromation and remit for an outbreak group.
  - Screening, case finding and care of patients with VRE.
- A national cooperation between IPC-units, with regular teleconferences, is helpful to exchange experience and ask for advice.

Information

- Effective communication internally.
- Active, timely, and open use of public media to inform the public and avoid misinformation.
- Regular feedback to personell on current actions, effects, and results.
- Timely information to carriers and relatives.
- Report carriage and suspected carriage when pateints are transferred.

Education

- Education of HCW personnel led by and IPC doctors and nurses (hands-on, on-site by visits. Cover spread by contact, and persistance of VRE in the hospital environment).
- Patients and relatives should be informed on how to prevent cross infection.

Concrete infection prevention and control practices

- Single-occupancy rooms with a restroom for patients with VRE.
- Improve compliance with basic hygiene routines (hand hygiene, use of personal protective equipment, working clothes regulations).
- Hygiene audits at strategic wards.
- Screening and case-finding
  - Contact tracing and screening in affected wards to identify carriage as early as possible in admitted patients.
  - Case-finding for every newly diagnosed VRE-case.
  - Weekly surveillance cultures on all patients in wards with VRE-carriers admitted. More cases can be detected with an additional sample taken one week after discharge.
- Cleaning and disinfection
  - Responibilities for different personnel needs to be clear, and known by the personnel.
  - Increasing quality of daily cleaning of all patient rooms (ensuring that already existing guidance are adhered to), and restrooms. Cleaning and disinfecting frequently toutched surfaces and seating areas at least once daily.
  - Increased frequency of cleaning all patient restrooms used by multiple patients. From once daily 7 days per week to 3 times daily 7 days per week.
  - Only furniture and equipment that can be disinfected should be used in the hospital.
  - Terminal cleaning of patient rooms performed by professional cleaners.
- Food hygiene
  - Offer alcoholic hand rub to patients, before meals, after visiting the restroom, and when leaving their room.
  - No use of buffets.

Other measures

- Monitoring of antibiotic use, and antibiotic policy.
- Validated, timely method to identify VRE at the local laboratory.

Consequences of VRE-outbreaks

Negative consequences

- Extra work-load for HCW, hospital management and communication department, IPC-unit, cleaning service teams, and laboratory during the outbreak.
- For the patients: some clinical infections, stigmatization of carriers, need for single room care, alerts in patient records, etc.
- Bad publicity for health care providers.
- Worry and increased work load for HCW at department with outbreaks due to added measures.
- Delayed care due to VRE-carriage. Although this should not happen, it can be hard to accomplish.

Positive consequences

- Generally improved IPC-routines, and greater demand for IPC
- Increased focus on good hygiene among HCW, patients, relatives and cleaning personnel.
- The VRE outbreak was an eye-opener for several groups within health care, from management to personnel at words.

Discussion

Fortunately, VRE has not yet become endemic in Swedish hopsitals. In Denmark around 7% of blood stream infections with *E. faecium* are caused by VRE (Danmap 2017). This suggests a rather large spread of VRE within the hospitals. In contrast only 1.4% of blood isolates of E. faecium in Sweden are VRE.

It is important to intensify work to prevent spread of VRE in hospitals as it is a patient safety problem, and outbreaks add to the burden on an already strained health care.

Adopting the effective measures above in a continuous quality improvement work in health care would decrease the risk of future outbreaks of VRE and other bacteria, as well as decrease risks for patients and health care costs.

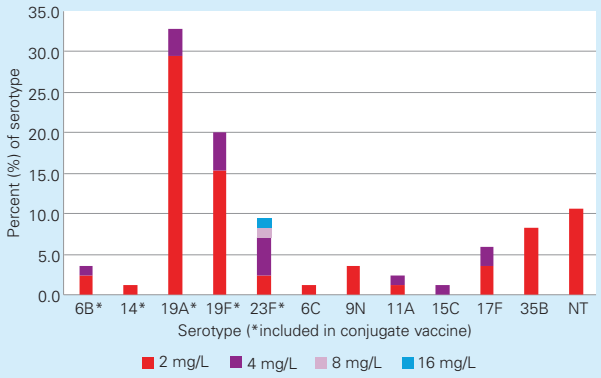
To accomplish this adequate resourses must be assigned for continous quality improvement work to prevent outbreaks, health care associated infection, and promote prudent use of antibiotics.

Epidemiological typing

A total of 85 isolates with PcG MIC > 1 mg/L were sent to the Public Health Agency of Sweden for serotyping during 2018 (93% of notified cases). Of these, 57 isolates (63%) belonged to serotypes included in the conjugate vaccines used for children in the national vaccination programme. Isolates with high PcG MIC-values (n=18) were found in 7 serotypes (Figure 3.33). The three invasive cases were caused by serotype 19A (n=2) and 17F (n=1).

To follow and evaluate the effect of vaccination against pneumococcal disease and to identify spread of antibiotic resistant clones, the Public Health Agency of Sweden collected PNSP isolates with PcG MIC ≥ 0.5 mg/L for serotyping. In 2018, 325 isolates were collected (including the 91 cases of PNSP). The serotype distribution were, in decending order: 19F (19%), NT (15%), 19A (14%), 35B (10%), 23F (6%), 11A (5%), 17B and 6B (4%). Of these, 53 % constituted types included in the conjugate vaccines used for children in the national vaccination programme.

Figure 3.33. Distribution of MICs among PNSP with PcG MIC > 1 mg/L (n=85).



Source: The Public Health Agency of Sweden

Outbreaks

During 2018 there was a spread of multiresistant *S. pneumoniae* of serotype 19A in three children day care centres in Örebro county. Eighteen cases were included, these accounted for one fifth of all reported cases in 2018.

Streptococcus pneumoniae, from blood and nasopharynx cultures

Results from 2018

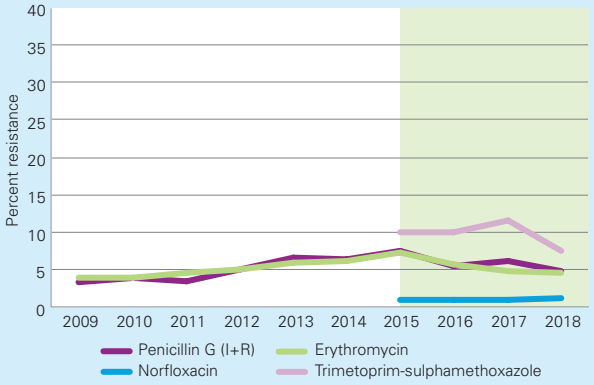
- Number of reported cases of PNSP: 91 cases
- Number of reported cases with bloodstream infections caused by PNSP: 3
- Number of reported cases of cases of invasive pneumococcal disease: 1 408

Table 3.11. Proportion (%) of antibiotic resistant *S. pneumoniae* from blood and nasopharynx 2018.

Antibiotic	Blood isolates, %R **(n=675)**	Nasopharynx isolates, % R **(n=3 194)**
Clindamycin	nd	7.7
Erythromycin	4.6	10.5
Norfloxacin	1.1	nd
Penicillin G (I+R)	4.8	12.6
Penicilln V	nd	14.4
Tetracycline	nd	10.4
Trimetoprim-sulphamethoxazole	7.4	14.3

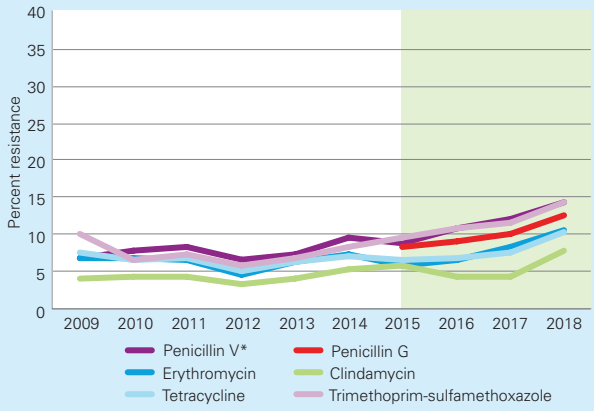
Trends

Figure 3.34. Antibiotic resistance in *S. pneumoniae* isolated from bloodcultures during the years 2009-2018. Number of AST isolates is given in the attached file.



Source: The Public Health Agency of Sweden

Figure 3.35. Antibiotic resistance in *S. pneumoniae* isolated from nasopharynx during the years 2009-2018. Number of AST isolates is given in the attached file.



*Based on susceptibility testing using oxacillin.
Source: The Public Health Agency of Sweden

Comments

Among invasive infections, the proportion of PcG non-susceptible isolates was 4.8% in 2018 and the resistance decreased for all tested antibiotics (Table 3.11 and Figure 3.34). Only one invasive isolate was penicillin resistant (PcG MIC > 2 mg/L). Since 2012, there has been a slow increase in the proportions of resistance for all tested antibiotics for respiratory infections with a higher increase in 2018 (Figure 3.35). Three isolates (< 1%) from nasopharynx were penicillin resistant (PcG MIC > 2 mg/L).

Haemophilus influenzae, from blood and nasopharynx cultures

Results from 2018

- Number of reported cases of invasive *H. influenzae*: 201

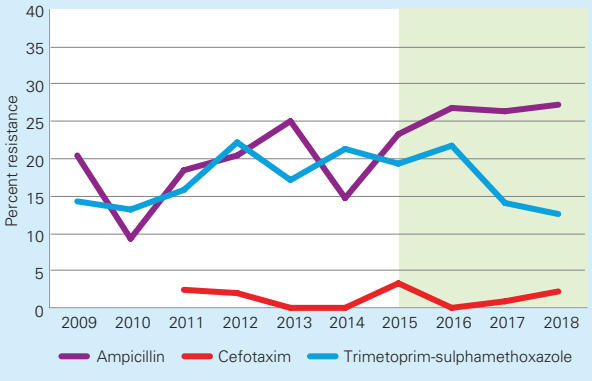
Table 3.12. Proportion (%) of antibiotic resistant *H. influenzae* from blood and nasopharynx 2018.

Antibiotic	Blood isolates, % R (n= 114)	Nasopharynx isolates, % R (n=7 863)
Ampicillin	27.2	na
Cefotaxim	2.2	na
Fluoroquinolones*	nd	1.4
Penicillin G (I+R)	nd	31.8
Tetracycline	nd	0.5
Trimetoprim-sulphamethoxazole	12.6	30.0

*Nalidixic acid was used for detection of fluoroquinolone resistance.

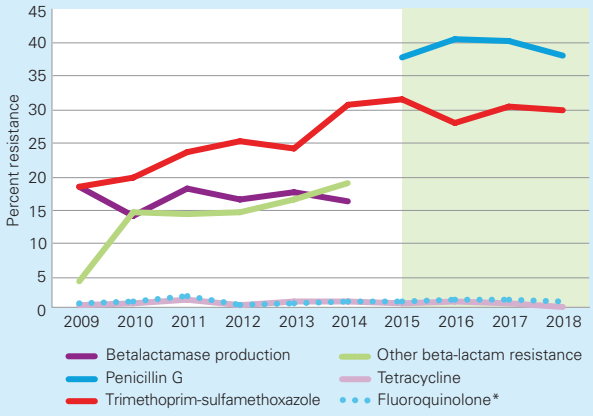
Trends

Figure 3.36. Antibiotic resistance in *H. influenzae* isolated from blood during the years 2009-2018. Number of isolates is given in the attached file.



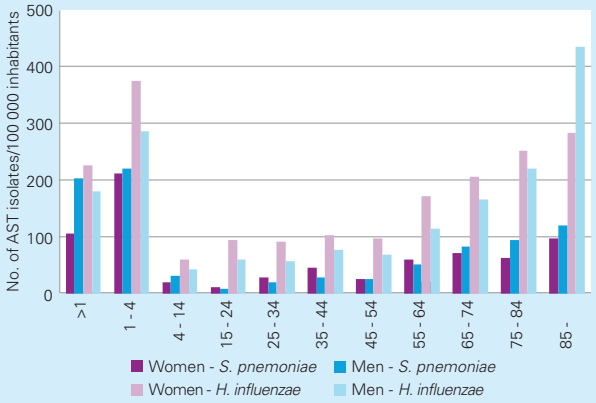
Source: The Public Health Agency of Sweden

Figure 3.37. Antibiotic resistance in *H. influenzae* from nasopharynx during the years 2009-2018. Number of isolates is given in the attached file.



*Nalidixic acid was used for detection of fluoroquinolone resistance.
Source: The Public Health Agency of Sweden

Figure 3.38. Age distribution among patients with *S. pneumoniae* or *H. influenzae* from nasopharynx.



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 and the resistance to trimethoprim-sulfamethoxazole is still decreasing and is now at the levels seen prior to 2011 (Figure 3.36). 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 stable (Figure 3.37).

Pseudomonas aeruginosa, from blood and non-respiratory cultures

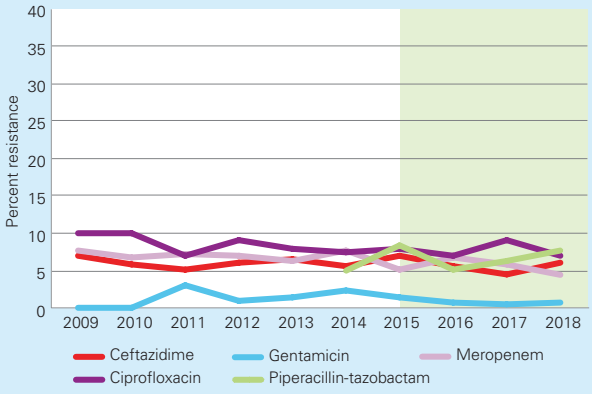
Results from 2018

Table 3.13. Proportion (%) of antibiotic resistant *P. aeruginosa* from blood and non-respiratory specimens 2018.

Antibiotic	Blood isolates, % R (n = 412)	Non-respiratory isolates, % R (n=8 367)
Ceftazidime	6.1	4.7
Ciprofloxacin	7.1	10.1
Gentamicin	0.8	1.4
Tobramycin	nd	0.8
Imipenem	nd	8.2
Meropenem	4.4	4.6
Piperacillin-tazobactam	7.8	5.4

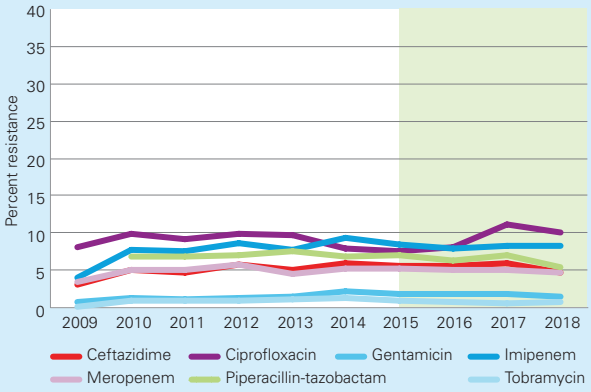
Trends

Figure 3.39. Antibiotic resistance in *P. aeruginosa* from bloodstream infections during the years 2009-2018. Number of isolates is given in the attached file.



Source: The Public Health Agency of Sweden

Figure 3.40. Antibiotic resistance in *P. aeruginosa* from non-respiratory isolates 2009-2018. Number of isolates is given in the attached file.



Source: The Public Health Agency of Sweden

Comments

Resistance to ceftazidime is most often due to efflux pumps and loss of porins, not ESBL production. The resistance for all antibiotics is stable for both blood isolates and non-respiratory isolates (Figure 3.39 and 3.40). Resistance to imipenem continues to be higher (8.2%) than to meropenem (4.6%) in the non-respiratory isolates. The meropenem resistance level is similar in both sample materials (4-5%) (Table 3.13).

Acinetobacter spp, from blood cultures

Results from 2018

TABLE 3.14. Antibiotic resistance in *Acinetobacter* species isolated from blood.

Antibiotic	2014 % R (n=59)	2015 % R (n=41)	2016 % R (n=54)	2017 % R (n=54)	2018 % R (n=55)
Number of AST-tested isolates					
Meropenem	3.4	0	1.9	0	3.7
Ciprofloxacin		0	5.6	0	7.3
Colistin		0	0	0	nd
Gentamicin		0	7	0	6.1
Trimethoprim-sulfamethoxazole		5.1	5.7	0	3.6

Comments

During 2018, a total of 54 isolates of *Acinetobacter* spp. from blood was reported to Svebar. The carbapenem resistance was 3.7% (Table 3.14). Septicemia caused by *Acinetobacter* spp. is still rare in Sweden compared to other countries in Europe where multiresistant *Acinetobacter* is a problem in hospitals.

Streptococcus pyogenes, from blood cultures

Results from 2018

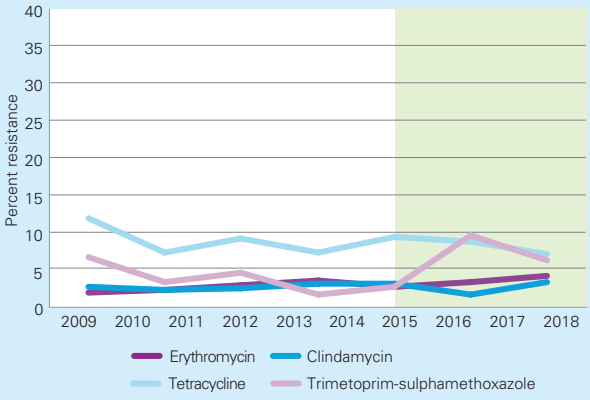
- Number of reported cases of invasive *S. pyogenes*: 823

Table 3.15. Proportion of resistant isolates in *S. pyogenes* from blood 2018.

Antibiotic	Blood isolates, % R (n= 344)
Penicillin G (I+R)	0
Erythromycin	4.1
Clindamycin	3.2
Tetracycline	6.9
Trimetoprim-sulphamethoxazole	6.1

Trends

Figure 3.41. Antibiotic resistance in *S. pyogenes* (iGAS) isolated from blood during the years 2009-2018. Number of isolates is given in the attached file.



Source: The Public Health Agency of Sweden

Comments

Invasive cases of *S. pyogenes* (iGAS) are notifiable according to the Communicable Disease Act and in 2018 a total of 823 cases were reported which is the highest number of cases since it became notifiable. AST results from 344 isolates were available from Svebar (Table 3.15). Some laboratories did not test susceptibility to trimethoprim-sulphamethoxazole and tetracycline. Resistance remained stable, and similar or higher levels of resistance has been reported both in Denmark, Norway and in the US (Figure 3.41).

Streptococcus agalactiae, from blood cultures

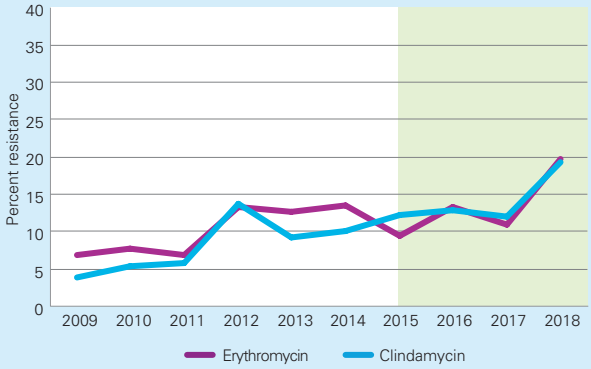
Results from 2018

Table 3.16. Proportion of resistant *S. agalactiae* isolated from blood 2018.

Antibiotic	Blood isolates, % R (n= 311)
Penicillin G (I+R)	0
Erythromycin	19.7
Clindamycin	19.3

Trends

Figure 3.42. Antibiotic resistance in *S. agalactiae* (GBS) from bloodstream infections during the years 2009-2018. Number of AST isolates is given in the attached file.



Source: The Public Health Agency of Sweden

Comments

S. agalactiae is not included in the Communicable Disease Act, but it is an important pathogen in the context of pregnancy and child birth. Resistance to both erythromycin and clindamycin has increased gradually, and is now approximately 20% (Table 3.16 and Figure 3.42). Similar or higher levels of resistance has been reported both in Denmark, Norway and in the US (DANMAP 2017, NORM/NORM-VET 2017 and CDC's Bact Facts Interactive).

Mycobacterium tuberculosis, mandatory reporting

During 2018 a total of 506 cases of tuberculosis (TB) were reported compared to 533 cases during 2017 which is a decrease of 5%. Out of the 506 cases 14 was already on TB treatment when arriving in Sweden.

The number and proportion of culture confirmed cases were 408 (81%) compared to 423 (79%) in 2017. *Mycobacterium bovis* was identified in three cases, *Mycobacterium africanum* in one case and *Mycobacterium tuberculosis* in 404 cases. The proportions of cases diagnosed with MDR-TB increased from 2.6% (11/419) in 2017 to 3.2% (13/404). None of the MDR-cases were 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 66 patients corresponding to 16.3% of the 404 with culture confirmed *M. tuberculosis*, see Figure 3.43. As always the most common resistance found was against isoniazid.

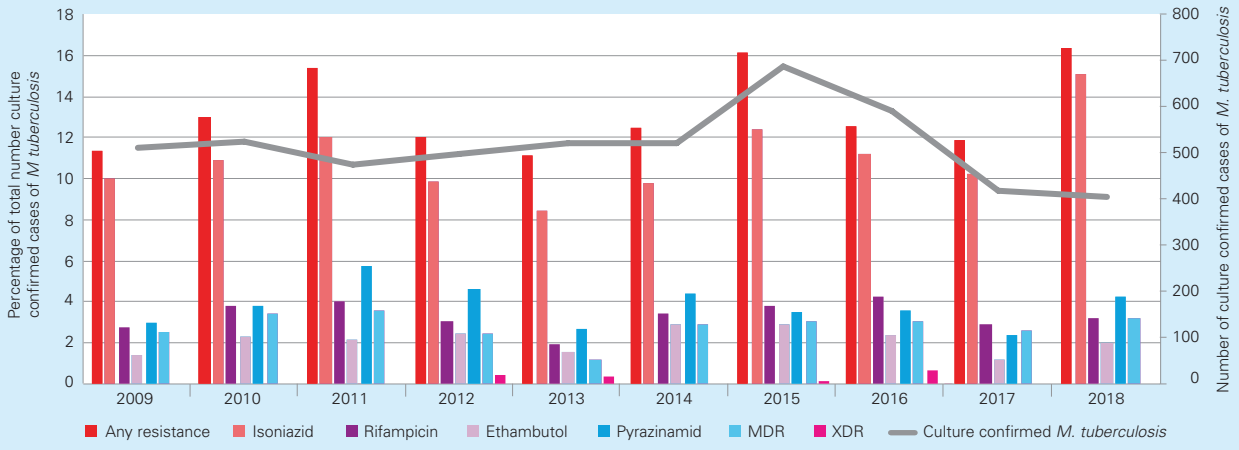
Among the persons born in Sweden 8.9% (5/56) of those with culture confirmed diagnosis had isoniazid resistant TB (no case of *M bovis*) and no other resistance was detected.

Of all the TB cases reported in Sweden 2018, 86% were born in another country. In total 352 in this group had a culture confirmed TB and 64 (18%) had some kind of resistance out of which 13 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 ongoing spread and helps to identify missed opportunities of infection control. Since September 2016 the laboratory at the Public Health Agency of Sweden has changed from MIRU-VNTR to whole genome sequencing, a method that has a higher resolution which reduces the risk of "false" clustering of cases with no connection. Of all the cases 15% (78/506) were considered as infected in Sweden and of the 400 cases analyzed with whole genome sequencing 78% were unique isolates not belonging to any cluster.

The proportion of patients with *M. tuberculosis* resistant against any antibiotics has increased in 2018 including the proportion of MDR-TB but the total number of cases have continued to decrease.

Figure 3.43. Drug resistant *M. tuberculosis* in Sweden 2009-2018.



Neisseria gonorrhoeae, mandatory reporting

Gonorrhoea is a notifiable infection and in 2018, 2 713 cases (26.5 cases per 100 000 inhabitants) of gonococcal infections were reported to the Public Health Agency of Sweden. This is an increase with 7% compared to 2017 (2 531 cases, incidence: 25.0) and an increase with 53% compared to 2016 (1 777 cases, incidence: 17.8). Most of these cases were identified in the three largest counties of Sweden, which comprise the cities Stockholm, Gothenburg, and Malmö, respectively. Clinical isolates are in the present report described from the Swedish Reference Laboratory for Sexually Transmitted Infections (an external body of the Public Health Agency of Sweden), Department of Laboratory Medicine, Clinical Microbiology, Örebro University Hospital, Örebro. Antimicrobial resistance data from Stockholm and Skåne counties are currently not available. In 2018, *N. gonorrhoeae* strains from 580 cases, corresponding to 21% of all reported cases, 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 SIR criteria have been determined by The European Committee on Antimicrobial Susceptibility Testing (EUCAST).

In Table 3.17 the antimicrobial resistance in gonococcal isolates (one isolate per case) cultured in 2018 are compared with those from 2009 to 2017. Briefly, the level of resistance to ciprofloxacin, which previously was used as first-line treatment for gonorrhoea, remains very high, i.e. 57% in 2018. The level of resistance to azithromycin was 5%, using the currently recommended EUCAST azithromycin ECOFF of 1 mg/L. However, using the clinical resistance breakpoint for azithromycin (abandoned by EUCAST in 2019) that was used in 2009-2017. The resistance level was 8%, which represents an increase since 2017 (5%). The resistance to cefixime has substantially decreased since 2012 (10%), and in 2018 it was 1.2%. Nevertheless, this is a minor increase compared to in 2017 when the level of cefixime resistance was only 0.6%, which is the lowest level of cefixime resistance determined any year from 2009 to 2017. Furthermore, as in 2015-2017 no resistance to ceftriaxone was identified. This is exceedingly promising because ceftriaxone is the last remaining option for empirical antimicrobial monotherapy of gonorrhoea. Similar decreases in the resistance to these extended-spectrum cephalosporins (ceftriaxone and cefixime) have been reported in several additional European countries. The reasons for this decline remain unknown, however, most likely the European recommendations to use ceftriaxone (500 mg) plus azithromycin (2 g) in the empiric first-line treatment of gonorrhoea have been effective to eradicate cefixime and ceftriaxone resistant gonococcal strains that have been spreading internationally. No gonococcal isolates resistant to spectinomycin have yet been detected in Sweden. However, the availability of spectinomycin can be limited (in Sweden as in most countries globally), and it is not suitable as monotherapy for pharyngeal gonorrhoea.

TABLE 3.17. Proportion of antibiotic resistance (%) in of Swedish *Neisseria* gonorrhoeae strains 2009-2018.

	2009 (n=384)	2010 (n=618)	2011 (n=805)	2012 (n=877)	2013 (n=967)	2014 (n=384)	2015 (n=462)	2016 (n=601)	2017 (n=528)	2018 (n=580)
Cefixime	5	6	8	10	4	2	2	1	0.6	1.2
Ceftriaxone	0	2	2	1	0.3	0.3	0	0	0	0
Azithromycin	6	12	11	10	13	9	10	3	5	5*
Ciprofloxacin	75	56	55	62	53	60	53	53	47	57
Spectinomycin	0	0	0	0	0	0	0	0	0	0

*Using EUCAST ECOFF of 1 mg/L to distinguish isolates with azithromycin resistance mechanisms.

Neisseria meningitidis, mandatory reporting

Invasive meningococcal disease is a notifiable disease, and in 2018 a total of 56 clinical cases (0.5 cases per 100,000 inhabitants) of the disease were reported. In total, 56 clinical invasive isolates from blood, cerebrospinal fluid or puncture (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.

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. Production of β-lactamase was examined by nitrocefin discs.

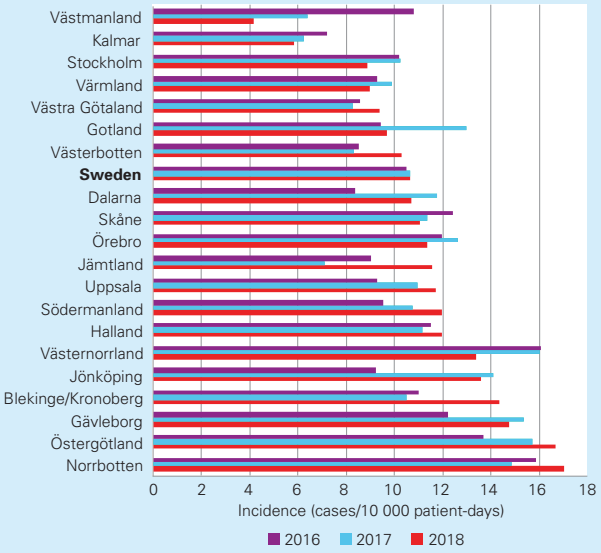
Ten (18%) isolates had an intermediate susceptibility to penicillin G (MIC>0.064 mg/L), and one of these isolates was resistant (MIC>0.25 mg/L). All isolates (100%) were susceptible to cefotaxime (MIC values of <0.002-0.023 mg/L), meropenem (MICs: 0.004-0.016 mg/L), chloramphenicol (MICs: 0.38-2 mg/L), ciprofloxacin (0.002-0.006 mg/L), and rifampicin (MICs: 0.003-0.125 mg/L). None of the isolates obtained in 2018 produced β-lactamase, and in fact no β-lactamase-producing meningococcal isolate has ever been identified in Sweden.

Clostridioides difficile

Incidence of *Clostridioides difficile* (CDI) infections

In 2018, 6 475 new CDI cases were reported corresponding to an incidence of 63 cases per 100 000 inhabitants. The incidence of new CDI cases per 10 000 patient-days for 2018 was 11 cases/10 000 patient-days (patient-days data are from 2017) (Figure 3.44). The incidence has decreased by 25% between 2009 and 2016 and has since remained stable.

Figure 3.44. Incidence of new cases of CDI (cases per 10 000 patient-days) distributed per Swedish counties 2016-2018. (Incidence of cases 2018 is calculated using patient-days for 2017).

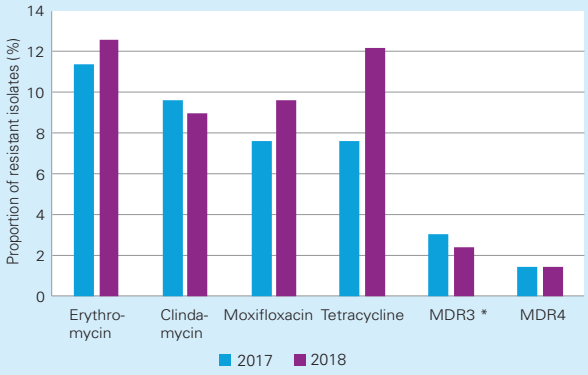


Source: The Public Health Agency of Sweden

Antibiotic resistance in *Clostridioides difficile* isolates 2018

In 2018, susceptibility to four indicator antibiotics (erythromycin, tetracycline, moxifloxacin and clindamycin) and two antibiotics used for treatment of CDI (metronidazole and vancomycin) were tested in 615 isolates. Resistance to indicator antibiotics is often associated with outbreak prone types and increased rate of recurrent CDI. Tetracycline resistance increased by 60% in 2018 compared to 2017 (Figure 3.45), this occurred mainly in PCR ribotype 078/126.

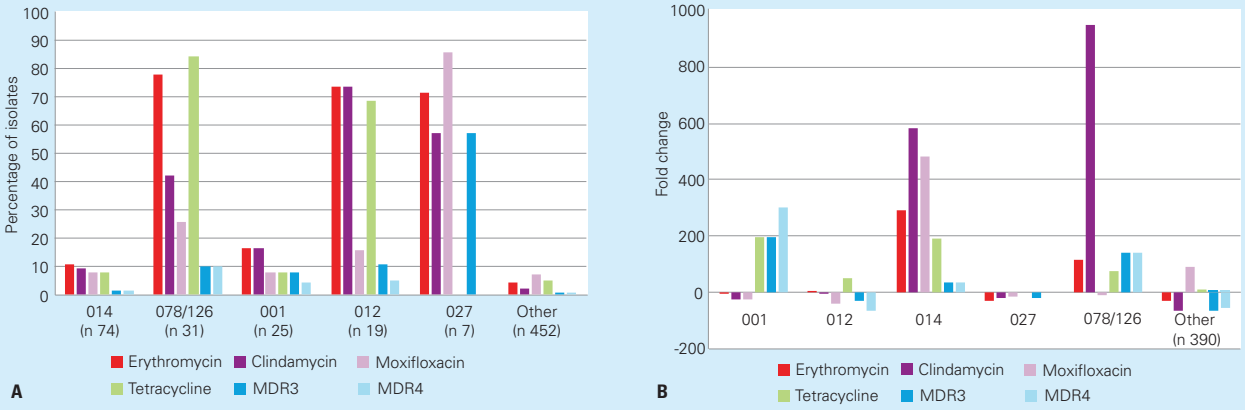
Figure 3.45. Proportion of isolates resistant to erythromycin, clindamycin, moxifloxacin and tetracycline.



*MDR3 are isolates resistant to erythromycin, clindamycin and moxifloxacin and MDR4 are isolates resistant to all four tested antibiotics.
Source: The Public Health Agency of Sweden

Increased resistance to all indicator antibiotics was seen in PCR ribotype 014. A cluster of isolates of ribotype 014 resistant to both erythromycin and clindamycin was found in one county. Resistance to indicator antibiotics was most frequently found in the ribotypes 027, 012, 078/126, 001 and 014 (Figure 3.46. A). The largest changes in resistance between 2017 and 2018 occurred within ribotypes 014, 078/126 and 001 (Figure 3.46 B). The changes observed could be be caused by a clonal spread of resistant isolates All isolates tested were susceptible to metronidazol and vancomycin.

Figure 3.46 A, B. Proportion of isolates resistant to indicator antibiotics for the most common resistant PCR ribotypes 2018 (A). Fold change of resistance 2018 compared to 2017 for the most common resistant PCR ribotypes (B).



Source: The Public Health Agency of Sweden

Zoonotic pathogens: *Campylobacter* and *Salmonella*

Campylobacter spp., from faecal samples

Infection with *Campylobacter* spp. is a notifiable disease in Sweden and a total of 8 132 cases were reported in 2018. Less than half of all notified cases (45%) were acquired in Sweden. In the national surveillance program, isolates from domestic cases are collected twice during the year (week 11 and 34). The focus of the epidemiological typing, with whole-genome sequencing, is species identification and cluster analysis to identify potential outbreaks.

Antibiotic susceptibility data collected from Svebar were published in Swedres 2017 for the first time. For 2018, a total of 4 004 *Campylobacter* species isolates were reported. The majority were found in feacal samples (97%) where the combination *C. jejuni/C. coli* were most frequent reported. They constituted two-thirds of all reported isolates, but less than one percent of these isolates had an AST. The *C. jejuni* isolates constituted almost one-third of the *Campylobacter* spp. isolats and, here, more than 40% of the isolates had an AST (Table 3.18).

TABLE 3.18. Antibiotic resistance in *Campylobacter jejuni* from faecal samples 2017-2018.

	2017 (n=1 809)			2018 (n=1 205)		
Antimicrobial	Resistance (%)	Number of isolates with AST	Data from number of laboratories	Resistance (%)	Number of isolates with AST	Data from number of laboratories
Ciprofloxacin	37	700	6	50	506	5
Erythromycin	< 1	687	6	1	506	5
Tetracycline	28	701	5	31	492	5

Salmonella sp., from faecal and urine samples

Infection with *Salmonella* is a notifiable diseases in Sweden and a total of 2 040 cases were reported in 2018. Approximately one third of all cases were acquired in Sweden. The national surveillance program focus on epidemiological typing to identify potential outbreaks. Isolates from domestic cases are continuously sent to the Public Health Agency of Sweden for species identification, serotyping and for S. Typhimurium, monophasic *S.* Typhimurium och S. Enteritidis multiple-locus variable number tandem repeat analysis is performed.

A total of 1 401 *Salmonella enterica* isolates were reported (*Salmonella* Typhi and *Salmonella* Paratyphi A excluded). Over 90% were from faeces and urine sampling. Approximately half of these isolates had an AST (Table 3.19).

Comments

The proportion of isolates with reported AST-results is 40-50 % for *Campylobacter* and *Salmonella*. In addition, there is a variability in tested isolates between laboratories. The proportion of tested isolates varies from 10% to over 80% of all isolates.

For *C.jejuni* the resistance for ciprofloxacin was 50% and 31% for tetracycline in 2018. One percent were resistant to erythromycin (Table 3.18).

For *Salmonella* sp, the highest resistance were for the quinolones, 22%, in 2018. Resistance to cefotaxime and ceftazidime was higher compared to 2017. No meropenem resistance was found (Table 3.19).

Most *Salmonella* and *Campylobacter* infections, 65% and 55% respectively, were acquired abroad. The data on antibiotic resistance cannot be separated according to origin of infection.

TABLE 3.19. Antibiotic resistance in *Salmonella enterica* (n=1 226) from faecal and urine samples 2017-2018.

	2017 (n=1 401)			2018 (n=1 226)		
Antimicrobial	Resistance (%)	Number of isolates with AST	Data from number of laboratories	Resistance (%)	Number of isolates with AST	Data from number of laboratories
Azitromycin	3	335	4	1	348	5
Cefotaxim	< 1	656	10	2	613	9
Ceftazidim	< 1	599	9	2	552	9
Meropenem	0	546	7	0	457	8
Fluoroquinolone	26	605	10	22	604	9
Piperacillin-tazobactam	1	482	6	1	403	8
Trimethoprim-sulfamethoxazole	6	652	10	3	608	9

Antibiotic resistance in animals

Notifiable diseases

In Sweden, findings of $ESBL_{CARBA}$-producing Enterobacteriaceae and methicillin-resistant coagulase-positive staphylococci in animals are notifiable (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 also Enterobacteriaceae producing $ESBL_A$ or $ESBL_M$ are notifiable when detected in humans, specific attention is also paid to these bacteria in animals.

ESBL-producing Enterobacteriaceae

Farm animals

In Sweden, carbapenemase-producing Enterobacteriaceae ($ESBL_{CARBA}$) in animals are notifiable but not classical ESBLs ($ESBL_A$) or plasmid-mediated AmpC ($ESBL_M$). In Svarm, active screening for *E. coli* resistant to ESCs in healthy farm animals using samples collected at slaughter has been performed since 2008. The proportions of faecal samples positive for *E. coli* with $ESBL_A$ or $ESBL_M$ in screenings of healthy animals and of meat in Sweden are shown in Table 4.1.

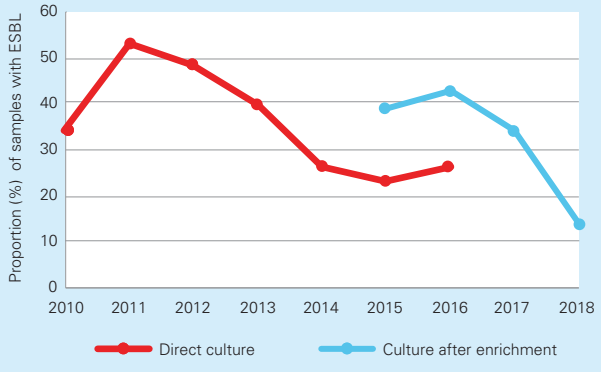
During 2018, samples of intestinal contents from healthy broilers (n=300) and healthy turkeys (n=72) as well as samples of chicken meat (n=288) at retail were screened for *E. coli* resistant to ESCs and carbapenems using selective media. The meat samples comprised fresh meat originating both from Sweden (n=242) and other countries (n=46). Furthermore, during 2017 and 2018, samples of intestinal contents from healthy cattle under one year (n=67) were screened for *E. coli* resistant to ESCs and carbapenems using selective media. Finally, in a special study performed in collaboration between SVA and the Swedish National Food Agency, samples of frozen meat from sheep/lamb were screened for *E. coli* resistant to ESCs and carbapenems using selective media (see In Focus ESBL-producing *E. coli* in meat from lamb on the Swedish market). 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).

Escherichia coli with ESC-resistance was isolated from 42 (14%) of the samples of intestinal contents from broilers and a transferable gene coding for ESC resistance was detected in 38 isolates, i.e. 13% of the samples. The majority of these were $ESBL_M$ and carried the genes bla_{CMY-2} (n=24). The isolates with $ESBL_A$ carried $bla_{CTX-M-1}$ (n=13), or bla_{SHV-12} (n=1). Carbapenem resistant *E. coli* was not isolated from any sample.

Apart from resistance against beta-lactams, including ESCs, 8 (19%) of the investigated isolates were also resistant to at least two other antibiotics, i.e. they were multiresistant. All of these were resistant to sulphonamides and tetracycline and one of the isolates was also resistant to gentamicin.

Due to differences in methodology during 2010-2018, 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 $ESBL_M$ between 2018 and 2017 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.

FIGURE 4.1. Proportion (%) of samples from broilers positive for *E. coli* with $ESBL_A$ or $ESBL_M$ from 2010 to 2018. The number of samples each year varies (n=100-302, 2018 n=300).



Escherichia coli with ESC-resistance was isolated from 43 (15%) of the samples of chicken meat and a transferable gene coding for ESC resistance was detected in 36 isolates, i.e. 13% of the samples. The majority of these were $ESBL_M$ and carried the genes bla_{CMY-2} (n=21). The isolates with $ESBL_A$ carried $bla_{CTX-M-1}$ (n=13), bla_{TEM-52} (n=1), or $bla_{CTX-M-1}$ plus bla_{TEM-52} (n=1). Separated by origin, $ESBL_A$ or $ESBL_M$ were detected in 28 (12%) of the samples from broiler meat originating from Sweden and 8 (17%) of the samples from broiler meat originating from other countries. Carbapenem resistant *E. coli* was not isolated from any sample.

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

							Beta-lactamase (No. isolates)								
Animal species	**Matrix**	**Year**	**No. of samples**	**No. samples with ESC resist-ance**	**No. samples with $ESBL_A$ or $ESBL_M$**	**% samples with $ESBL_A$ or $ESBL_M$**	**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	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[e]	Intestine	2017-18	67	3	2	3	1			1					
Cattle	Meat	2017	249	3	2	<1				1	1				
Cattle[e]	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	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	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	Faeces	2012	84	6	1	1									1[d]
Horses	Faeces	2010	431	9	6	1								6	

[a]CTX-M-1-group, ten caecal and four meat isolates were sequenced and possessed the gene blaCTX-M-1. [b]CIT-group, five caecal and three meat isolates were sequenced and possessed the gene blaCMY-2. [c]One isolate carried both an $ESBL_A$ 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 blaCMY-2. [e]Cattle under 1 year, in 2012 calves 1-4 weeks of age.

TABLE 4.2 Clinical isolates of different bacterial species of Enterobacteriaceae, producing $ESBL_A$ or $ESBL_M$, from companion animals and horses, 2008-2018.

Beta-lactamase group	gene	Bacterial species	Animal species	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
All	All	Enterobacteriaceae	Cats		1	3	3			1	2	2	5	3
All	All	Enterobacteriaceae	Dogs	1	3	4	18	12	14	22	24	31	17	22
All	All	Enterobacteriaceae	Horses	2	5	24	16	6	9	8	14	18	31	22
CIT	CMY-16	*Escherichia coli*	Cat							1				
	CMY-2	*Escherichia coli*	Cat		1[a]	1						1	1[b]	1[b]
		Escherichia coli	Dog			1	9	4	5	5	6	5	5[b]	9
		Klebsiella pneumoniae	Dog								1			
		Proteus mirabillis	Dog				1				2	2		
CTX-M-1	CTX-M-1	*Enterobacter cloacae* group	Dog							4				
		Escherichia coli	Dog			1		1	1	3			3	2
		Enterobacter cloacae group	Horse								1		2	
		Enterobacter spp.	Horse						1					
		Escherichia coli	Horse		2	9	8	3	3	2	3	5	13	6
		Klebsiella oxytoca	Horse							1				
		Serratia odorifera	Horse			1								
	CTX-M-3	*Escherichia coli*	Cat										1	
		Enterobacter spp.	Dog						1					
		Escherichia coli	Dog						2		1	2		
	CTX-M-15	*Enterobacter cloacae* group	Cat								1			
		Escherichia coli	Cat			1						1	2	1
		Klebsiella pneumoniae	Cat			1	1							
		Enterobacter cloacae group	Dog								2	2	1	1
		Enterobacter spp.	Dog		1	2	1	2	1	6				
		Escherichia coli	Dog	1			2	3	2		2	7	1	6
		Morganella morganii	Dog									1		
		Klebsiella pneumoniae	Dog		1						1	2		
		Escherichia coli	Horse		1	1						1		
		Klebsiella pneumoniae	Horse		1						3			1
	CTX-M-55	*Escherichia coli*	Dog								1	1		
	CTX-M-57	*Escherichia coli*	Dog								1			
CTX-M-2	CTX-M-2	*Escherichia coli*	Dog				1							
CTX-M-9	CTX-M-9	*Escherichia coli*	Dog				1	2	1	1				
		Escherichia coli	Horse							1				
	CTX-M-14	*Kluyvera* sp.	Cat				1							
		Escherichia coli	Cat											1
		Escherichia coli	Dog								5	5	2	1
		Klebsiella pneumoniae	Dog								1			1
		Escherichia coli	Horse				1				1			
	CTX-M-27	*Escherichia coli*	Dog				3		1	1	1	1	4[b]	
	CTX-M-65	*Escherichia coli*	Cat										1[b]	1[b]
DHA	DHA-1	*Escherichia coli*	Dog											1
SHV	SHV-12	*Escherichia coli*	Cat										1	
		Escherichia coli	Dog							2		3	2	
		Citrobacter braakii	Horse			1								
		Citrobacter spp.	Horse											1
		Enterobacter aerogenes	Horse									1		
		Enterobacter amnigenus	Horse							1				
		Enterobacter cloacae group	Horse							1	2	5	8	8
		Enterobacter spp.	Horse		1	3	5	3	3					
		Escherichia coli	Horse	2		2	2					3	5	6
		Escherichia hermanii	Horse			1								
		Klebsiella oxytoca	Horse						2		1	1	3	
		Klebsiella pneumoniae	Horse							1				
		Leclercia adecarboxylata	Horse									1		
		Pantoea agglomerans	Horse									1		
TEM	TEM-52	*Escherichia coli*	Cat								1			
	TEM-52-like	*Escherichia coli*	Dog											1
unknown	unknown	*Escherichia coli*	Cat				1							
unknown	unknown	*Escherichia coli*	Dog		1	1								
unknown	unknown	*Enterobacter cloacae* group	Horse							1	3			
unknown	unknown	*Escherichia coli*	Horse			1								
unknown	unknown	*Klebsiella pneumoniae*	Horse			5								

[a]The gene belongs to the CIT-group, but it has not been sequenced and it is therefore uncertain if the enzyme is blaCMY-2. [b]The isolates carries both an $ESBL_A$ and an $ESBL_M$ gene.

ESBL-producing *E. coli* in meat from lamb on the Swedish market

Escherichia coli producing ESBL ($ESBL_A$), plasmid-mediated AmpC (pAmpC; $ESBL_M$), or both, have emerged as a significant human health problem in many countries, including Sweden. Their presence is increasingly reported in beef, pork and chicken meat and such food. Chicken meat in particular is a potential source of human exposure to these resistant bacteria (Börjesson et al., 2016).

The demand for meat from lamb has increased in Sweden during the last years. In Svarm 2008, antimicrobial resistance in *E. coli* from healthy sheep was rare, and none of the isolates tested were resistant to third-generation cephalosporins. Those samples were however not screened for *E. coli* resistant to extended spectrum cephalosporins (ESCs) using selective culture. Such data are scarce in the literature, both in sheep and meat thereof. The occurrence of *E. coli* resistant to ESCs in lamb was recently investigated by the Swedish National Food Agency. The study was part of a project mapping various foodborne bacteria in such meat at retail in Sweden, for use in risk assessment and future risk management strategies.

Method

The occurrence of *E. coli* resistant to ESCs was investigated in 95 samples of Swedish meat from lamb, 149 samples of imported meat from lamb and 59 samples of meat from lamb from other EU-countries. Samples were collected fresh or frozen from September 2017 to May 2018 at retail, from stores accounting for 94 percent of the retail market share in Sweden (Dagligvarukartan™, 2017). The samples were screened for *E. coli* resistant to ESCs and carbapenems by culture on MacConkey agar (Oxoid) with cefotaxime (1 mg/L) or ChromID Carba (CC) agar (bioMérieux) and ChromID OXA 48 (CO) agar (bioMérieux), respectively, with prior enrichment in buffered peptone water (BPW). Briefly, 25 g of surface meat or minced meat was homogenized in 225 mL BPW and incubated at 37°C overnight. From the BPW homogenizate 10 µL were spread onto each agar plate and incubated overnight at 44°C (MacConkey agar) or 37°C (CC, CO agar). Up to three lactose positive colonies with morphology typical for *E. coli* from each plate were sub-cultured on horse-blood agar (5% v/v), after which species identity was confirmed by testing the isolates for production of tryptophanase (indole).

Production of beta-lactamases and carbapenemases in *E. coli* was verified by Etest®ESBL (CT/CTL and TZ/TZL) or Etest®AmpC and Etest®MBL or Etest®Meropenem, respectively (bioMérieux, Sweden). Isolates were further characterised at the National Veterinary Institute (SVA). Phenotypic antibiotic susceptibility testing was performed using Sensititre EUVSEC and EUVSEC2 microdilution panels and interpreted according to ECOFFs from EUCAST (www.eucast.org). Determination of transferable genes encoding resistance to ESCs, other resistance genes, plasmid replicon types and MLST types was performed by whole genome sequencing. DNA from confirmed isolates was extracted from overnight cultures on horse-blood agar using Qiagen EZ1 DNA tissue kit according to the recommendations of the manufacturer. DNA-concentrations were determined using Qubit HS DNA-kit (Life technologies). DNA was then sent to Sci-life clinical genomics (Solna, Sweden) for library preparation and paired-end sequencing using Illumina technologies. The specific ESBL-gene was determined using "Antimicrobial Resistance Identification By Assembly" (ARIBA; Hunt et al., 2017) against the Resfinder (https://cge.cbs.dtu.dk/services/ResFinder/) and CARD (https://card.mcmaster.ca/) databases. Reads were trimmed with Trimmomatic 0.36 and genome assembly was performed with SPAdes v.3.9.1 with the careful parameter, followed by Pilon v1.21 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).

Results and comments

Escherichia coli resistant to third generation cephalosporins were isolated from 3 (1 percent) out of 303 meat samples tested and a transferable gene coding for ESC resistance was detected in two of those isolates. Both positive meat samples were of EU-origin (Table). One sample contained *E. coli* ST58 with the bla_{CTXM-1} gene ($ESBL_A$) and the other sample contained *E. coli* ST1485 with the bla_{CMY-2} gene ($ESBL_M$). Both isolates were multidrug resistant. Resistance to tetracycline, trimethoprim, sulphamethoxazole and certain aminoglycosides were shared traits (based on phenotypic and genotypic data; genotypic data shown in Table). None of the isolates was resistant to carbapenems.

Escherichia coli with transferable resistance to ESCs was isolated for the first time in lamb at retail in Sweden. The bacteria were absent in Swedish meat and the overall occurrence was low, possibly reflecting the generally low usage of antibiotics in sheep compared to other food producing animals (Davies et al., 2017; Santman-Berends et al., 2014). Thus, such meat is currently at maximum a very limited contributor to the prevalence of *E. coli* with transferable resistance to ESCs within the human health-care sector.

Table. Characteristics of *E. coli* with transferable resistance to ESCs in meat from lamb on the Swedish market.

Sample type	Origin	Beta-lactamase phenotype	MLST type	Plasmid replicon type(s)	ESBL-gene	Other resistance genes
Sirloin	EU	$ESBL_M$	1485	IncQ1	bla_{CMY-2}	ant(3'')-Ia, aph(3'')-Ib, aph(6)-Id, dfrA, mdt, sul1, sul2, tetA
Sirloin	EU	$ESBL_A$	58	IncQ1, IncFIB, IncFII, IncI1	$bla_{CTX-M-1}$	aac(3'')-IV,aadA1, aph(3'')-Ib, aph(6)-Id, dfrA, mdfA, sul1, sul2, tetA

In focus

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The difference in the proportion of samples of chicken meat of Swedish origin positive for *E. coli* with $ESBL_A$ or $ESBL_M$ between 2018 and 2016 is statistically significant ($p<0.01$, X^2). This is in concordance with the decreased occurrence in broiler caecal samples.

Apart from resistance against beta-lactams, including ESCs, 10 (23%) of the investigated isolates were also resistant to at least two other antibiotics, i.e. they were multiresistant. Three of these isolates were of Swedish origin and seven from other countries. All were resistant to sulphonamides and tetracycline. Among the non-domestic isolates, one was also resistant to trimethoprim and quinolones, and four were also resistant to trimethoprim, quinolones and chloramphenicol.

Escherichia coli with ESC-resistance was not isolated from any of the samples from healthy turkeys. In concordance, carbapenem resistant *E. coli* was not isolated from any sample either.

Escherichia coli with ESC-resistance was isolated from 3 (4%) of the samples of intestinal contents from cattle under one year and a transferable gene coding for ESC resistance was detected in 2 isolates, i.e. 3% of the samples. These two isolates carried the genes $bla_{CTX\text{-}M\text{-}1}$ and $bla_{CTX\text{-}M\text{-}15}$ (both $ESBL_A$) respectively. Carbapenem resistant *E. coli* was not isolated from any sample.

Apart from resistance against beta-lactams, including ESCs, one of the three investigated isolates was also resistant to at least two other antibiotics, i.e. it was multiresistant. This isolate was resistant to sulphonamides, trimethoprim and quinolones.

Companion animals and horses

In Svarm, there are no recurring active screenings for ESBL-producing Enterobacteriaceae in healthy companion animals or horses. However, the results of the screenings for ESC resistant *E. coli* that have been performed are shown in Table 4.1.

Furthermore, for a number of years, funding from the Swedish Board of Agriculture has enabled SVA to perform confirmation of suspected ESC-resistance in isolates of Enterobacteriaceae free of charge for referring laboratories. During 2018, 47 submitted isolates of 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=3), dogs (n=22) and horses (n=22). This is comparable with the number of ESBL-producing Enterobacteriaceae confirmed in 2017.

Apart from resistance against beta-lactams, including ESCs, 73% of the investigated isolates were also resistant to at least two other antibiotics, i.e. they were multiresistant. The most common resistances were against streptomycin (64%), trimethoprim-sulphonamides (64%), gentamicin (52%), tetracycline (52%) and enrofloxacin (38%).

Methicillin-resistant *Staphylococcus aureus* (MRSA)

In Sweden, MRSA in animals was first verified in 2006 and was made notifiable in 2008. Since then, most cases in domesticated animals have been detected in passive monitoring when animals with clinical infections were sampled. From such samples, isolates of *S. aureus* with resistance to oxacillin or cefoxitin were 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 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 about 1200 isolates have been tested up to and including 2018. The monitoring is performed on isolates with anonymized origin. In this monitoring, PVL-negative MRSA with *mecC* was detected four times in 2010-2011 (Unnerstad et al., 2013), and once in 2013 and 2015, respectively. PVL-positive MRSA with *mecA* was detected in 2012 and PVL-negative MRSA with *mecA* in 2014 and 2017. No MRSA was detected during 2018. In addition, active monitoring was performed in 40 bovine dairy herds in Kalmar County in 2012. Samples were taken from bulk milk, from five cows and five unweaned calves in each herd. MRSA was not found. However, also in 2012, PVL-positive MRSA with *mecA* was isolated from several animals in a dairy herd (Unnerstad et al., 2018).

In 2016 and early 2017 there was an outbreak of MRSA with *mecC* among goats and sheep connected to a zoo. MRSA was found in samples from 20 goats and 6 sheep. Some of the animals had symtoms of dermatitis around the nostrils and some were without clinical symtoms. There was an epidemiological link through direct or indirect contact between all positive animals. 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.

Companion animals and horses

Up to and including 2018, a total of 112 cases of MRSA in companion animals and horses have been confirmed. These include 48 dogs, 20 cats, 1 rabbit and 43 horses. In these species, there is currently no regular active monitoring of MRSA but screenings in dogs were performed in 2006 and 2012 without detection of MRSA. Screening studies in horses have been performed twice, in 2007 and 2010, with only one positive sample in 2007.

TABLE 4.3. Large animals. Isolates of methicillin-resistant *Staphylococcus aureus* (MRSA) in Swedish horses, pigs, cows, goats and sheep up to and including 2018. All isolates were positive for the *mecA* or *mecC* and nuc 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	2	R	≤0.12-0.25	0,5	>16	≤0.5	>16	8	>32	8	2	t011	*A*
Pig	2010	1	R	0.5	1	64	0.5	>64	0.25	>32	16		t011	*A*
Pig	2010	1	R	≤0.25	≤0.25	≤0.5	≤0.25	0.5	0.5	0.5	4	2	t373	*C*
Cow	2010	2	R	≤0.25	≤0.25-0.5	≤0.5	0.25-0.5	≤0.5	0.25-0.5	1-2	4-8		t524	*C*
Cow	2010	1	R	≤0.25	0.5	≤0.5	0.25	≤0.5	0.5	2	8		t524	*C*
Cow	2011	1	R	≤0.25	0.5	≤0.5	0.12	≤0.5	0.25	1	8		t9111	*C*
Cow	2012	2	R	≤0.25	0.5-1	≤0.5	0.25-0.5	≤0.5-1	0.25-0.5	2	8		t002	*A*
Cow	2013	1	R	≤0.25	1	≤0.5	0.5	≤0.5	0.5	2	8		t843	*C*
Cow	2014	1	R	≤0.25	>32	16	0.25	≤0.5	0.25	2	8		t127	*A*
Cow	2015	1	R	≤0.25	≤0.25	≤0.5	0.12	≤0.5	0.25	1	8		t843	*C*
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*
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 2018. All isolates were positive for the *mecA* or *mecC* and *nuc* genes. Shaded areas indicate MIC above EUCAST ECOFF. One isolate from a cat, in 2013, and two from dogs, in 2017 and 2018 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*
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*
Rabbit	2017	1	R	≤0.25	≤0.25	≤0.5	4	0.5	0.25	0.5	4	≤1	t132	*A*

In 2018, MRSA was detected in clinical samples, mostly from wound infections, from four dogs and five 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). Two of the MRSA-positive cats were from the same household and were screened for MRSA as a rabbit in the same family previously was diagnosed with MRSA.

In 2018, MRSA was isolated from four horses, two with wound infections, one from a uterine sample and one of unknown origin (Table 4.3). In isolates from horses, *spa*-type t011, clonal complex 398, has dominated historically. In 2018, all four isolates were also of *spa*-type t011.

Wild animals

A screening study in hedgehogs was performed in 2015 and MRSA was isolated from 35 out of 55 sampled animals. MRSA has also been detected in four samples from hedgehogs before this study and in one sample during 2016. In addition, as part of an ongoing research project there are nine reported cases of MRSA during 2018. All isolates from hedgehogs have been MRSA with *mecC*. For more information on MRSA in hedgehogs, see Swedres-Svarm 2016.

Methicillin-resistant *Staphylococcus pseudintermedius* (MRSP)

In 2018, there were 57 MRSP cases (56 dogs and 1 cat) reported to the Swedish Board of Agriculture (Figure 4.2). This number is about the same level as in the last years. Isolates from 47 cases were available for genome sequencing and susceptibility testing. Two additional isolates were susceptibility tested only, and nine isolates were not available for further typing. Information on the sampling site was available for 52 cases; skin (including external ear canal) 25 cases, wounds (including surgical wounds) 17 cases and the remaining 10 were isolated from various other sites. All but two isolates were defined as multi-resistant. For resistance phenotypes, see Table 4.5.

FIGURE 4.2. Number of cases of methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) in Sweden notified to the Swedish Board of Agriculture 2008-2018. In 2006-2007 the numbers represent the isolates that were sent to SVA and confirmed as *mecA*-positive.

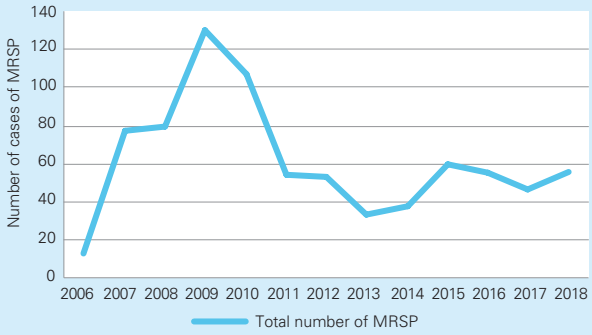


TABLE 4.5. Resistance phenotypes (beta-lactams excluded) and multilocus sequence types of isolates of methicillin resistant *Staphylococcus pseudintermedius* (MRSP) in 2018. All isolates were positive for the *mecA* gene. Shaded areas indicate resistance.

Antibiotic MIC (mg/L)									MLST								
Beta-lac-tams	Ery	Cli	Tsu	Tet	Enr	Fus	Gen	Nit	ST45	ST258	ST265	ST551	ST1331	Single ST:s[a]	Not yet d esignated	Not determined	Sum
R	>2	>2	>4	>4	>1	≤0.5	4->4	≤16				11		5	2	1	19
R	>2	>2	2>4	>4	≤0.25	≤0.5-1	>4	≤16			2			3			5
R	>2	>2	>4	>4	≤0.25-0.5	≤0.5	≤1	≤16		1				2	1		4
R	>2	>2	0.5-1	>4	>1	≤0.5	4->4	≤16	2						1	1	4
R	>2	>2	≤0.25-0.5	≤0.25	≤0.25-0.5	>2	≤1	≤16					2	1			3
R	>2	2->2	0.5-1	≤0.25	≤0.25	≤0.5	≤1-2	≤16						1	2		3
R	>2	>2	≤0.25-0.5	>4	≤0.25-0.5	≤0.5-1	>4	≤16						2			2
R	≤0.5	≤0.5	0.5	≤0.25	≤0.25-0.5	≤0.5	≤1	≤16							2		2
R	>2	>2	>4	≤0.25	≤0.25	>2	2	≤16						1			1
R	>2	>2	1	>4	≤0.25	>2	≤1	≤16						1			1
R	>2	≤0.5	≤0.25	>4	≤0.25	≤0.5	4	≤16							1		1
R	>2	≤0.5	0.5	≤0.25	≤0.25	>2	≤1	≤16							1		1
R	≤0.5	≤0.5	2	≤0.25	≤0.25	2	≤1	≤16						1			1
R	≤0.5	≤0.5	0.5	>4	>1	≤0.5	>4	≤16						1			1
R	≤0.5	≤0.5	0.5	>4	≤0.25	>2	≤1	≤16		1				1			1
								Sum	**2**	**2**	**2**	**11**	**2**	**18**	**10**	**2**	**49**

[a]Single ST:s include ST71, ST118, ST181, ST261, ST305, ST386, ST498, ST555, ST649, ST730, ST825, ST934, ST1095, ST1332, ST1333, ST1334, ST1336, ST1338, ST1384, ST1385, ST1386, ST1387, ST1388, ST1383, ST1389, ST1390, ST1391, and ST1392.

The results of the genome sequencing divided the isolates into 33 different multi-locus sequence types, of which ST551 was the most common type with 11 isolates (10 from dogs and 1 from a cat; Table 4.5.). In earlier years, ST71 (a sequence type spread in Europe and described by Perreten et al. 2010), was dominating among Swedish isolates. In 2018, only 1 out of 47 isolates was of this type. Now the epidemiology of MRSP is more diverse with several sequence types occurring.

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. 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 passerine birds during the winter season, while *Salmonella* from cats most likely are cases when cats have eaten these birds lying dead or diseased on the ground. Such isolates are almost invariably *S.* Typhimurium, which are susceptible to all tested antibiotics. Therefore, only the first 5 and 25 index cases of *Salmonella* from passerines and cats, respectively, and thereafter every eighth case are serotyped. For details on methodology see Materials and methods, resistance in bacteria from animals.

All animals 2018

A total of 92 *Salmonella* isolates were tested in 2018, all belonging to the species *S. enterica* and with two subspecies represented, subsp. *enterica* (75 isolates) and subsp. *diarizonae* (17 isolates). The isolates were shared into 19 different serovars with *S.* Typhimurium as the most dominant type with 48 isolates (Table 4.6).

Two isolates belonged to the monophasic type 4,[5],12:i:-, which however is a well known variant of *S.* Typhimurium and they are in this context therefore counted as such. Three antigenic formulae, *S. enterica* subsp. *enterica* 4:a:-, *S. enterica* subsp. *enterica* 4:b:-, and *S. enterica* subsp. *enterica* 6,7:-:1,5 are not included in the latest list of recognized *Salmonella* serovars. They may therefore represent new serovars or monophasic variants of other, known serovars. Distributions of MICs and resistance for all isolates are presented in Table 4.7 and for the subset *S.* Typhimurium in Table 4.8. It is noteworthy that 16 of the isolates were categorized as resistant to colistin, having a MIC of 4 mg/L. This has not previously been reported, and therefore, these isolates were tested by PCR for presence of *mcr-1* to *mcr-5* genes, which are known to confer resistance to colistin, but all isolates were negative for these genes. Three of the isolates were *S.* Dublin which is a serovar known to have slightly higher MIC and one isolate was *S.* Konstanz. The remaining 12 were *S.* Typhimurium from cats, a dog, and a bird. At this point it is not possible

TABLE 4.6. Serovar distribution and number of *Salmonella* isolates tested for antibiotic susceptibility, 2018.

Serovar	Cat	Sheep	Dog	Wild birds	Wild mammals	Cattle	Poultry	Horse	Pigeon	Pig	Total
S. Agona			1								**1**
S. Cerro							1				**1**
S. Dublin						4					**4**
S. Duesseldorf						1					**1**
S. enterica subsp. *diarizonae* 38:r:z	1										**1**
S. enterica subsp. *diarizonae* 42:r:z							1				**1**
S. enterica subsp. *diarizonae* 61:-:1,5		15									**15**
S. enterica subsp. *enterica* 4:a:-										2	**2**
S. enterica subsp. *enterica* 4:b:-						1					**1**
S. enterica subsp. *enterica* 6,7:-:1,5					1						**1**
S. Enteritidis					1						**1**
S. Hessarek	1									1	**2**
S. Infantis			2			1		1			**4**
S. Konstanz	1										**1**
S. London			3								**3**
S. Mbandaka							3				**3**
S. Mikawasima						1					**1**
S. Szentes						1					**1**
S. Typhimurium	12		9	11		4	4		2	4	**46**
S. Typhimurium monophasic 4,[5],12:i:-			1					1			**2**
Total	**15**	**15**	**16**	**11**	**2**	**13**	**9**	**2**	**2**	**7**	**92**
% of total	**16**	**16**	**17**	**12**	**2**	**14**	**10**	**2**	**2**	**8**	

TABLE 4.7. Distribution of MICs and resistance (%) in *Salmonella enterica* (n=92) from all animals, 2018.

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	7							91.3	2.2						6.5				
Azithromycin	NA[a]									55.4	41.3	3.3							
Cefotaxime	0					100													
Ceftazidime	0						100												
Chloramphenicol	1										98.9				1.1				
Ciprofloxacin	0	63.0	37.0																
Colistin	17							67.4	15.2	17.4									
Gentamicin	0						83.7	16.3											
Meropenem	0		100																
Nalidixic acid	0									100									
Sulphamethoxazole	7										2.2	6.5	25.0	52.2	7.6				6.5
Tetracycline	4								95.6				1.1		3.3				
Tigecycline	0					98.9	1.1												
Trimethoprim	2					75.0	22.8							2.2					

[a]No approved breakpoints exist for *Salmonella*.

TABLE 4.8. Distribution of MICs and resistance (%) in *Salmonella* Typhimurium, including two monophasic variants (n=48) from all animals, 2018.

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	8							91.7							8.3				
Azithromycin	NA[a]									83.3	14.6	2.1							
Cefotaxime	0					100													
Ceftazidime	0						100												
Chloramphenicol	2										97.9					2.1			
Ciprofloxacin	0	56.3	43.7																
Colistin	25							50.0	25.0	25.0									
Gentamicin	0						75.0	25.0											
Meropenem	0		100																
Nalidixic acid	0									100									
Sulphamethoxazole	8										4.2	2.1	20.8	52.1	12.5				8.3
Tetracycline	8								91.7				2.1		6.2				
Tigecycline	0					97.9	2.1												
Trimethoprim	0					68.8	31.2												

[a]No approved breakpoints exist for *Salmonella*.

to conclude whether it may be a methodological phenomenon or alternatively a particular variant of *S.* Typhimurium. Further investigation using WGS may reveal the reason for the increased MICs of colistin. All 16 colistin resistant isolates were susceptible to all other compounds. Most of the isolates (70 of 92; 76%) were susceptible to all antibiotics tested. Twenty-two isolates showed resistance to one or more compounds, and six of these isolates were multiresistant with resistance to 3 or 4 compounds (Table 4.9). All six multiresistant isolates were resistant to both ampicillin (aminopenicillins) and sulphamethoxazole (sulphonamides) (Table 4.9). Notably, four of the multiresistant isolates originated from dogs, while the remaining two were from one cattle and one horse, respectively. Two of the dog isolates were *S.* London, which is a rare serovar. The isolates were from different dogs and timepoints and from different places in Sweden, but whether the isolates may still have been related, e.g. from a common, commercial food item, is not known.

In the subset of *S.* Typhimurium, resistance was overall low in 2018 but has varied over the years (Figure 4.3). The variation is largely due to differences in occurrence of multiresistant strains between the years. The two monophasic *S.* Typhimurium isolates from a dog and a horse, respectively, had the same multiresistance profile as has been described from other countries. This type has spread over the last decade in many European countries and become one of the most prevalent strains. The same resistance profile was found in a *S.* Typhimurium from a dog. The last multiresistant isolate was from cattle but, in addition to resistance to ampicillin, tetracycline and sulphonamides, it was resistant to chloramphenicol. This was the typical profile of the *S.* Typhimurium phage type DT104, which was widespread during the 1990'ies but now is less prevalent. The present isolate was not investigated further to determine whether it was indeed a DT104.

FIGURE 4.3. Resistance (%) to ampicillin, chloramphenicol, sulphamethoxazole, and tetracycline in *Salmonella* Typhimurium from all animals, 2000-2018.

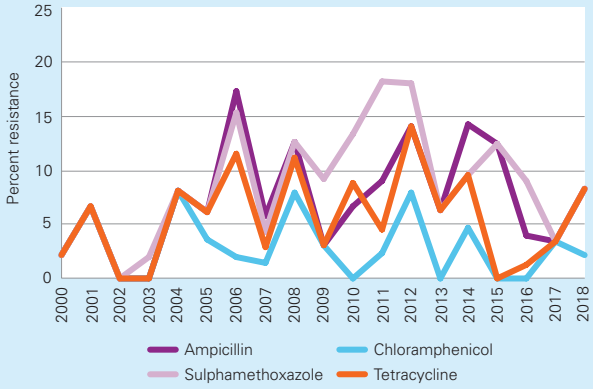


TABLE 4.9. MICs (mg/L) in the isolates of *Salmonella enterica* resistant to one or more antibiotic, 2018. Shaded fields indicate resistance.

Source	Serovar	Sul	Tmp	Cip	Tet	Mer	Azt	Nal	Ctx	Chl	Tgc	Caz	Col	Amp	Gen
Dog	London	>1024	>32	≤ 0.015	≤ 2.	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	≤ 1	>64	≤ 0.5
Cattle	Typhimurium	>1024	0.5	≤ 0.015	32	≤ 0.03	8	≤ 4	≤ 0.25	128	≤ 0.25	≤ 0.5	≤ 1	>64	1
Dog	London	>1024	>32	≤ 0.015	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	≤ 1	>64	≤ 0.5
Dog	Typhimurium	>1024	≤ 0.25	≤ 0.015	>64	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	0.5	≤ 0.5	≤ 1	>64	≤ 0.5
Dog	Monophasic	>1024	≤ 0.25	0.03	>64	≤ 0.03	8	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	≤ 1	>64	1
Horse	Monophasic	>1024	≤ 0.25	0.03	>64	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	≤ 1	>64	≤ 0.5
Cat	Typhimurium	64	≤ 0.25	≤ 0.015	< 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Cat	Typhimurium	64	0.5	≤ 0.015	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Dog	Typhimurium	64	≤ 0.25	≤ 0.015	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Cat	Typhimurium	64	≤ 0.25	0.03	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Cat	Typhimurium	64	0.5	≤ 0.015	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Cat	Typhimurium	64	0.5	≤ 0.015	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Cat	Typhimurium	128	0.5	≤ 0.015	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Cat	Typhimurium	64	≤ 0.25	≤ 0.015	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Cattle	Typhimurium	128	≤ 0.25	0.03	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Dog	Typhimurium	64	≤ 0.25	0.03	≤ 2	≤ 0.03	8	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Cattle	Dublin	32	≤ 0.25	≤ 0.015	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Cattle	Dublin	32	≤ 0.25	≤ 0.015	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Cat	Typhimurium	128	0.5	0.03	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Cat	Konstanz	32	≤ 0.25	≤ 0.015	≤ 2	≤ 0.03	16	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Cattle	Dublin	32	≤ 0.25	≤ 0.015	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Wild bird	Typhimurium	128	0.5	≤ 0.015	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5

The two *Salmonella* isolates from wild mammals were a *S.* Enteritidis from a hedgehog and a *S. enterica* subsp. *enterica* 6,7:-:1,5 from a wild boar. Hedgehogs have in other countries been shown to often carry a host adapted type of *S.* Enteritidis phage type 9a or 11, but no further investigations were made on the present isolate.

The subspecies *diarizonae* is usually associated with reptiles, but here this subspecies was found in a cat and a duck. However, both animals may have been in contact with reptiles. Fifteen *S. enterica* subsp. *diarizonae* 61:-:1,5 were found in sheep. This particular serovar has also been reported in sheep from several other countries, e.g. 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. All isolates of this serovar were susceptible to all antibiotics tested.

Farm animals 2000-2018

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 2000-2018, isolates from the vast majority of notified incidents in major farm animals were tested in

TABLE 4.10. Resistance phenotypes of *Salmonella* Typhimurium (n=355) from notified incidents in farm animals, 2000-2018.

		Phagetype																					
Phenotype	**Source**	**1**	**7**	**9**	**10**	**12**	**15a**	**39**	**40**	**41**	**99**	**104**	**110b**	**120**	**125**	**126**	**146**	**193**	**195**	**NST**	**NT**	**Monophasic**	**Not typed**	**Sum**
AmpStrSulTetNalChlFlf	**Pigs**											1												1
AmpStrSulTetChlFlfGen	**Cattle**																						1	1
AmpStrSulTetChlFlf	**Cattle**											6		1									3	10
AmpStrSulTetChlFlf	**Pigs**											4											2	6
AmpStrSulTetChlFlf	**Sheep**											1												1
AmpStrSulTetChl	**Cattle**											1												1
AmpStrSulTetNal	**Cattle**																						3	3
AmpStrSulTet	**Cattle**													1							2	2		5
AmpStrSulTet	**Pigs**																					1		1
AmpStrSulTet	**Poultry**																				1	2		3
AmpStrSulTm	**Cattle**																						2	2
AmpSulTetChl	**Cattle**																						1	1
AmpStrSul	**Cattle**													1								1	1	3
StrSulTet	**Cattle**																			1				1
AmpSul	**Cattle**											2												2
AmpSul	**Pigs**											1												1
StrGen	**Cattle**									1														1
StrGen	**Pigs**								1															1
StrGen	**Poultry**									1														1
StrSul	**Pigs**																					2		2
StrSul	**Poultry**						2																	2
SulTm	**Cattle**																1			1			1	3
SulTm	**Pigs**																						1	1
Amp	**Poultry**																			2				2
Gen	**Poultry**																			1				1
Nal	**Pigs**					1																		1
Str	**Cattle**											1		1		1				4			1	8
Str	**Pigs**								4	3		2		1						4	1		2	17
Str	**Poultry**									2										3				5
Tet	**Pigs**																						1	1
Col	**Cattle**																						1	1
Susceptible	**Sheep**	1																					3	4
Susceptible	**Cattle**	4			2		1	1	1	6		2		5	1	1				27	1	1	15	68
Susceptible	**Pigs**	1	1			2			33	5	1	1		8					1	18	2		21	94
Susceptible	**Poultry**	1		1		1			5	1			1	2				1	1	43	4		28	89
Sum		**7**	**1**	**1**	**2**	**4**	**3**	**1**	**44**	**19**	**1**	**22**	**1**	**20**	**1**	**2**	**1**	**1**	**2**	**104**	**11**	**9**	**87**	**344**

Svarm, in total 725 isolates. About half of the isolates, 354 (47%), were *S.* Typhimurium and of these 37% were from pigs, 32% from cattle, 30% from poultry and 1% from sheep.

The majority (75%) of *S.* Typhimurium isolates from farm animal incidents were susceptible to all antibiotics tested while 39 isolates (11%) were multiresistant, i.e. resistant to three or more compounds. All phenotypic resistance combinations for *S.* Typhimurium are shown in Table 4.10. Only one multiresistant *S.* Typhimurium isolate was found in farm animals in 2018. This was an isolate from cattle, which was found resistant to ampicillin, sulphonamides, tetracycline and chloramphenicol. It should be noted that in 2018, the isolates were not tested for streptomycin or florfenicol, so this isolate may also have been resistant to these compounds, which is often the case for isolates with this resistance combination. The most common traits were resistance to ampicillin, streptomycin, tetracycline, sulphonamide, chloramphenicol and florfenicol. Resistance to third generation cephalosporins was not found and resistance to ciprofloxacin was found in isolates from only five incidents. None of them were from 2018.

The 39 multiresistant isolates of *S.* Typhimurium in the period 2000-2018 were from 38 separate notified incidents of which 25 involved cattle, 8 pigs, 2 poultry and 1 incident involved both pigs and cattle. Of the two remaining incidents, one was in sheep and one in ducks in a hobby flock. Three incidents in 2004 and two in 2015 involved cattle and were epidemiologically linked through trade of calves. An epidemiological link was also suspected between four incidents 2007-2008 involving cattle, pigs and sheep. There were no known links between the other incidents.

In 2018 none of the notified incidents in farm animals involved monophasic *S.* Typhimurium I (O 4,5,12:i- / O 4,12:i:- /O 4,5:i:- / O 4:i:-). Since this variant was first found in 2006, eight incidents of monophasic *S.* Typhimurium have been confirmed in farm animals in Sweden. Three incidents involved only cattle, three only pigs, one only ducks, and one incident involved both cattle and poultry. In six of the incidents the isolates were multiresistant. However, monophasic *S.* Typhimurium has also been found in other animal species, i.e. from five dogs, two wild birds and a horse, of which a case from a dog and the one from the horse was from 2018. All five isolates from dogs and the horse isolate were multiresistant whereas the isolates from wild birds were susceptible to all antibiotics tested. Epidemiological links were confirmed between some of the incidents of monophasic *Salmonella*.

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 2018. For details on methodology see Materials and methods, resistance in bacteria from animals.

Of the 170 isolates tested, 127 (75%) were susceptible to all six antibiotics. Resistance to quinolones only (ciprofloxacin and nalidixic acid) was the most common phenotype (22%) (Table 4.11). Three isolates (2%) were resistant to both quinolones and tetracycline.

In 2016 resistance to tetracycline was more common than in previous years (16%) but this year only 2% were resistant to tetracycline (Figure 4.4). The probable explanation for the tetracycline resistance peak and for the increase in quinolone resistance this year is 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 4.4. Ciprofloxacin, nalidixic acid and tetracycline resistance (%) in *Campylobacter jejuni* from broilers. In years 2001-2002 enrofloxacin was tested instead of ciprofloxacin. The number of isolates per year has varied (n=50-170).

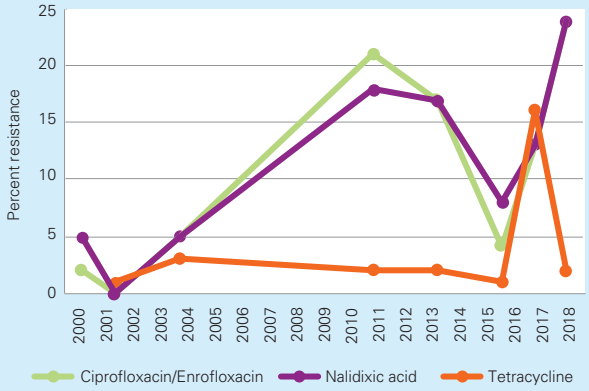


TABLE 4.11. Distribution of MICs and resistance (%) for *Campylobacter jejuni* from broilers, 2018.

Antibiotic	Resistance (%) n=170	Distribution (%) of MICs (mg/L)											
		≤0.12	0.25	0.5	1	2	4	8	16	32	64	128	>128
Ciprofloxacin	24	72.4	2.9	0.6				14.7	9.4				
Erythromycin	0				97.6	2.4							
Gentamicin	0	0.6	14.7	82.9	1.2	0.6							
Nalidixic acid	24					4.1	57.1	14.7				24.1	
Streptomycin	<1		0.6	7.1	70.0	2.6	1.2				0.6		
Tetracycline	2			95.9	1.8				0.6	1.8			

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. It is likely that in some cases there are more than one animal sampled from the same herd. Regarding horses, dogs and cats, duplicates based on animal identity have 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. During the latest years, the number of samples submitted has decreased and the sampling strategy has probably changed to some extent. This may influence the proportion of resistant isolates. Some of 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. However, isolates may be susceptibility tested regardless of presence of virulence factors.

As in previous years, resistance to ampicillin, streptomycin, tetracycline and trimethoprim-sulphamethoxazole were the most common resistance traits (Table 4.12). Resistance to ampicillin and to trimethoprim-sulphamethoxazole has increased considerably over the years. The increase levelled off in 2015-2017, but in 2018 the figures have increased again (Figure 4.5).

According to a national regulation from 2013 (SJVFS 2013:42), susceptibility testing is generally required before ordination of fluoroquinolones for animals. Due to this, sampling may be biased towards isolates from herds with therapeutic failure with trimethoprim-sulphonamides, since fluoroquinolones may be an alternative for treatment of *E. coli* diarrhoea. Co-resistance between trimethoprim-sulphonamides and other antibiotics is common.

A project with randomized (i.e. non-biased) sampling was carried out during 2016-2017. The results showed no major difference in resistance compared to the material from clinical submissions (see 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 for routine diagnostics.

Multiresistance occurred in 31% (16/52) of the isolates in 2018 and has varied over the years (20% in 2017, 25% in 2016 and 2015, 42% in 2014 and 38% in 2013). Resistance phenotypes are shown in Table 4.13.

FIGURE 4.5. Resistance (%) in *Escherichia coli* from pigs 1995-2018. 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, 2018 n=52).

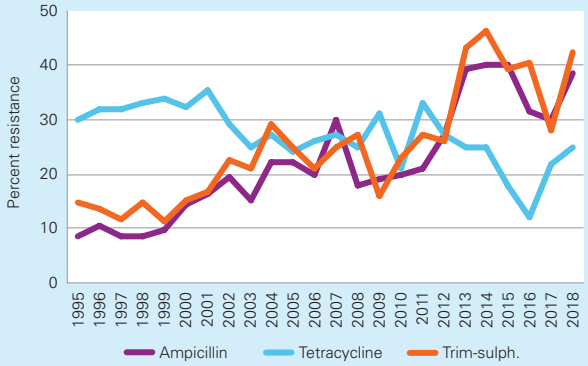


TABLE 4.12. Distribution of MICs and resistance (%) in *Escherichia coli* from pigs 2018. Clinical isolates from faecal samples or from samples taken post mortem from the gastro-intestinal tract.

Antibiotic	Resistance (%) 2018 n=52	≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	38					57.7	3.8			38.5		
Cefotaxime	0		100									
Colistin	2[b]				96.2	1.9			1.9			
Enrofloxacin	6	94.2		3.8			1.9					
Gentamicin	0					100						
Neomycin	4						96.2			1.9	1.9	
Nitrofurantoin	0							19.2	69.2	9.6	1.4	
Streptomycin	29							63.5	7.7	5.8	5.8	17.3
Tetracycline	25					75.0			1.9	23.1		
Trim-Sulph.[a]	42			57.7		1.9		40.4				

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphamethoxazole); [b]The isolate with MIC >8 mg/L was negative for *mcr-1* to *mcr-5* genes with PCR. .

TABLE 4.13. Resistance phenotypes of isolates of *Escherichia coli* from pigs 2018. Shaded areas with "R" indicate resistance.

Resistance phenotypes										Number of isolates
Amp	Tsu	Str	Tet	Enr	Neo	Col	Gen	Ctx	Nit	
R	R	R	R	R	R					1
R	R	R	R		R					1
R	R	R	R							3
R	R	R								7
R	R		R	R						1
R	R		R							3
R	R									3
R										1
	R	R								2
	R									1
		R								1
			R							4
				R		R				1
										23
									Sum	**52**

Brachyspira hyodysenteriae

Isolates of *Brachyspira hyodysenteriae* are from clinical submissions of faecal samples. Only the first isolate from each herd each year is tested for antibiotic susceptibility. In routine diagnostics at SVA clinical breakpoints at >2 mg/L for tiamulin and >16 mg/L for tylosin are used. These breakpoints were also used in Svarm until 2011. Analysis of antibiotic susceptibility data from isolates of *B. hyodysenteriae* from Sweden 1990-2010 has resulted in a proposal for wild type cut-off values (Pringle et al., 2012). In Table 4.14 these cut-off values are used on all data. With the suggested wild type cut-off value >0.25 mg/L for tiamulin, resistance is detected throughout the period. However, during 2016, isolates with MICs above the clinical breakpoint (>2 mg/L) were detected for the first time from Swedish pigs. Therapeutic failure was also observed. Five isolates from 2016 and 2017 are classified as clinically resistant.

The cut-off value for tylosin (>16 mg/L) has not been changed compared to previous years. Tylosin resistance has decreased over the years. Mutations in the 23S rRNA gene of *Brachyspira* spp. that increase tylosin MICs also affects tylvalosin MICs. However, with the cut-off values used in this material, the proportion of resistance to tylvalosin is generally higher than to tylosin. This could indicate that the cut-off value for tylvalosin is too low.

TABLE 4.14. Resistance (%) in *Brachyspira hyodysenteriae* from pigs 2005-2018 and distribution of MICs for isolates from 2016-2018 (2018 n=5). Clinical isolates from faecal samples.

Antibiotic	Resistance (%)					Distribution (%) of MICs (mg/L)													
	2005-06	2007-08	2009-11	2012-15	2016-18	≤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=29	n=31														
Doxycycline	9	3	5	0	0			22.6	67.7	9.7									
Tiamulin	7	18	8	3	29[b]		35.5	9.7	25.8	3.2	9.7		3.2		12.9				
Tylosin	81	76	60	55	32							29.0	29.0	6.5	3.2				32.3
Tylvalosin	NA[a]	93	55	79	45				3.2	19.4	32.3	12.9		9.7	19.4		3.2		
Valnemulin	0	18	3	3	42	41.9	16.1		9.7	3.2	9.7	3.2	3.2	12.9					

[a]Not analysed [b]All isolates with MICs above 2 mg/L are from a defined outbreak.

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, a clinical breakpoint for tiamulin of >2 mg/L and for tylosin of >16 mg/L are used at SVA. With these breakpoints, 11% of the isolates were resistant to tiamulin and 54% to tylosin (Table 4.15). If the same wild type cut-off value as for *B. hyodysenteriae* is used, 27% of the isolates were resistant to tiamulin.

Actinobacillus pleuropneumoniae

Isolates of *Actinobacillus pleuropneumoniae* are from post mortem investigations of lungs or from lung samples taken at slaughterhouses within the monitoring programme SvarmPat. The resistance situation is favourable and almost no resistance was detected (Table 4.16). However, 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.

TABLE 4.15. Distribution of MICs for *Brachyspira pilosicoli* from pigs 2005-2018, n=356. Clinical isolates from faecal samples. The number of isolates each year varies (n=7-67, 2018 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			40.2	49.2	3.9	2.5	3.7	0.6						
Tiamulin		38.8	22.8	11.5	8.7	5.3	1.7	0.6	2.2	8.4				
Tylosin							7.3	18.3	16.9	3.9	4.5	3.9	5.9	39.3
Tylvalosin[a]				0.5	13.0	26.4	26.9	7.8	1.6	3.1	9.8	10.9		
Valnemulin	49.7	16.9	5.1	10.7	7.3	4.2	2.0	1.1	3.1					

[a]193 isolates tested.

TABLE 4.16. Distribution of MICs and resistance (%) in *Actinobacillus pleuropneumoniae* from pigs 2011-2018. Clinical isolates from post mortem investigations of lungs. The number of isolates each year varies (n=16-57, 2018 n=16).

Antibiotic	Resistance (%) 2011-2018	Distribution (%) of MICs (mg/L)														
	n=253	≤0.008	0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	>128
Ampicillin	0								100								
Chloramphenicol	0[a]									100							
Ciprofloxacin	0[a]	0.4	17.7	40.9	40.9												
Florfenicol	<1										99.6		0.4				
Gentamicin	<1									15.4	69.2	15.0	0.4				
Nalidixic acid	0[a]								4.6	72.2	22.8	0.4					
Penicillin	0				2.0	12.3	40.3	45.5									
Streptomycin	NR[a,b]											3.8	37.1	57.0	2.1		
Tetracycline	0								100								
Trimethoprim	0[a]					31.6	46.8	19.4	1.3	0.8							

[a]237 isolates tested; [b]Not relevant since the genus has inherently low susceptibility to streptomycin.

Pasteurella spp.

Most isolates of *Pasteurella* spp. are from post mortem investigations of lungs or from lung samples taken at slaughterhouses within the monitoring programme SvarmPat. Some isolates are also from nasal swabs collected within a control programme for atrophic rhinitis in nucleus and multiplying herds. Isolates from the control programme are likely from healthy pigs, whereas isolates from lung samples are most likely from pigs with respiratory disease. Antibiotic resistance is rare among isolates of *Pasteurella* spp. (Table 4.17).

Isolates from 2013-2018 (n=148) 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 *P. multocida*, but species identification of some isolates is uncertain. Cut-off values for *P. multocida* (Table 6.12) are used for all isolates in Table 4.17.

TABLE 4.17. Distribution of MICs and resistance (%) in *Pasteurella* spp. from pigs 2005-2018. Clinical isolates from the respiratory tract, isolated from nasal swabs or from post mortem investigations of lungs. The number of isolates each year varies (n=7-95, 2018 n=9).

Antibiotic	Resistance (%) 2005-2018 n=286	Distribution (%) of MICs (mg/L)															
		≤0.008	0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	>128
Ampicillin	0								100								
Chloramphenicol	0[a]									100							
Ciprofloxacin	0[b]	21.6	58.8	18.6	1.0												
Enrofloxacin	0[c]					98.9	1.1										
Florfenicol	1[d]										98.9	1.1					
Gentamicin	<1									73.8	20.6	4.9	0.3	0.3			
Nalidixic acid	0[b]								50.5	40.2	8.2		1.0				
Penicillin	0					54.2	41.6	4.2									
Streptomycin	NR[e]										2.8	44.4	35.3	12.2	5.2		
Tetracycline	0								98.6	1.4							
Trim-Sulph	1[f]							96.5	0.6	1.2	0.6	1.2					

[a]104 isolates tested; [b]97 isolates tested; [c]189 isolates tested; [d]282 isolates tested; [e]Not relevant since the genus has inherently low susceptibility to streptomycin; [f]172 isolates tested, concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphamethoxazole).

Cattle

Escherichia coli from faecal samples

Isolates of *E. coli* are from the gastro-intestinal tract of calves. Most of the isolates are probably from calves no more than a few weeks old, i.e. during a period when resistance in enteric bacteria often is high in cattle. Resistance was high to ampicillin, streptomycin and tetracycline (Table 4.18 and Figure 4.6), as in previous years. Multiresistance occurred in 51% (23/45) of the isolates from 2017-2018, compared to 32% in 2016, 56% in 2015, 76% in 2014 and 70% in 2013. For resistance phenotypes in multiresistant isolates in 2017-2018, see Table 4.19.

FIGURE 4.6. Resistance (%) in *Escherichia coli* from calves 2007-2018. 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, 2017-18 n=45).

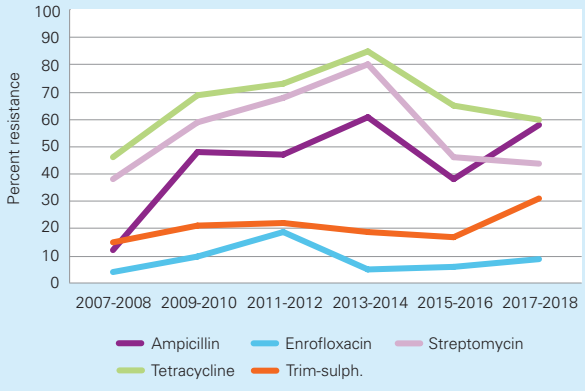


TABLE 4.18. Distributions of MICs and resistance (%) in *Escherichia coli* from calves 2017-18. Clinical isolates from faecal samples or from samples taken post mortem from the gastro-intestinal tract.

Antibiotic	Resistance (%) 2017-18 n=45	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	58					40.0	2.2			57.9		
Cefotaxime	2[b]		97.8	2.2								
Colistin	0				93.3	6.7						
Enrofloxacin	9	91.1		8.9								
Gentamicin	2					97.8	2.2					
Neomycin	20						75.6	4.4	2.2	6.7	11.1	
Nitrofurantoin	0							44.4	53.3	2.2		
Streptomycin	44							51.1	4.4		6.7	37.8
Tetracycline	60					40.0				60.0		
Trim-Sulph.[a]	31			68.9				31.1				

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphamethoxazole); [b]The isolate with MIC 0.5 mg/L had an MIC below ECOFF on further testing.

TABLE 4.19. Resistance phenotypes of isolates of *Escherichia coli* from calves 2017-18. Shaded areas with "R" indicate resistance.

Resistance phenotypes Amp	Tet	Str	Tsu	Neo	Enr	Ctx	Gen	Col	Nit	Number of isolates
R	R	R	R	R						1
R	R	R	R		R					1
R	R	R	R							6
R	R	R		R						1
R	R	R								4
R	R				R					2
R	R									1
R		R	R	R						1
R		R	R		R					1
R		R	R							3
R		R								2
R										3
	R		R	R						1
	R			R						5
	R									5
										8
									Sum	**45**

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. According to a national regulation from 2013 (SJVFS 2013:42), susceptibility testing is generally required before ordination of fluoroquinolones for use in animals. As a consequence, the number of isolates of *E. coli* from milk samples that were susceptibility tested increased in 2013 and the number of susceptibility tested isolates each year is still higher than before the regulation. Although antibiotic treatment may not be indicated for *E. coli* mastitis, fluoroquinolones may be the clinically most effective group of antibiotics if treatment is required.

In the material from 2018, 28% (28/100) of the isolates were resistant to at least one antibiotic. Resistance to ampicillin, streptomycin, tetracycline or trimethoprim-sulphamethoxazole was most common as in previous years (Table 4.20). Multiresistance occurred in 15% (15/100) of all isolates.

Klebsiella pneumoniae from milk samples

Isolates of *Klebsiella pneumoniae* are from clinical submissions of milk samples from dairy cows. Resistance was uncommon and 79% (41/52) of isolates was susceptible to all tested antibiotics, excluding ampicillin. Multiresistance did not occur in isolates from 2018.

TABLE 4.20. Resistance (%) in *Escherichia coli* from dairy cows 2015-2018. Distribution of MICs from 2018. Clinical isolates from milk.

Antibiotic	Resistance (%)				Distribution (%) of MICs (mg/L)										
	2015 n=113	2016 n=74	2017 n=79	2018 n=100	≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	20	27	15	24					54.0	21.0	1.0		24.0		
Cefotaxime	3[b]	1[d]	0	0		100									
Colistin	<1[c]	0	4[e]	0				89.0	11.0						
Enrofloxacin	2	4	3	1	99.0						1.0				
Gentamicin	0	1	0	1					99.0	1.0					
Neomycin	<1	0	4	5						95.0		1.0	2.0	2.0	
Nitrofurantoin	0	0	0	0							33.0	63.0	3.0	1.0	
Streptomycin	20	26	14	20							69.0	11.0	1.0	1.0	18.0
Tetracycline	11	16	9	8					92.0				8.0		
Trim-Sulph.[a]	12	22	9	14			85.0	1.0		1.0	13.0				

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphamethoxazole); [b]The isolates with MICs 1 and 2 were further tested with PCR but genes conferring transferable ESC resistance were not detected. The isolate with MIC 0.5 mg/L was further tested and did not show an ESBL or AmpC phenotype; [c]The isolate was not available for PCR detection of mcr genes; [d]The 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; [e]The three isolates with MIC 4 mg/L were negative for *mcr-1* to *mcr-5* genes with PCR.

TABLE 4.21. Resistance (%) in *Klebsiella pneumoniae* from dairy cows 2015-2018. Distributions of MICs from 2018. Clinical isolates from milk.

Antibiotic	Resistance (%)				Distribution (%) of MICs (mg/L)										
	2015 n=41	2016 n=36	2017 n=34	2018 n=52	≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	NR[b]	NR	NR	NR								5.8	94.2		
Cefotaxime	0	0	0	0		100									
Colistin	0	3[c]	9[d]	0				90.4	9.6						
Enrofloxacin	2	14	3	8	92.3	3.8	1.9		1.9						
Gentamicin	0	0	0	0					100						
Neomycin	0	0	0	0						100					
Nitrofurantoin	NR	NR	NR	NR							3.8	3.8	34.6	57.7	
Streptomycin	15	3	3	13							82.7	3.8	7.7	1.9	3.8
Tetracycline	10	6	12	8					88.5	3.8		1.9	5.8		
Trim-Sulph.[a]	0	6	0	0			100								

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

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 2013-2018 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 6.12) are used for all isolates in Table 4.22.

Antibiotic resistance was generally rare among isolates of *Pasteurella* spp. (Table 4.22), but beta-lactamase producing *P. multocida* has occurred occasionally in samples from calves in 2016, 2017 and 2018. In addition, isolates of beta-lactamase producing *P. multocida* have been confirmed in 2003 and beta-lactamase producing *Mannheimia haemolytica* in 2010 and 2015. Penicillin is considered the antibiotic of choice for treatment of pneumonia in cattle in Sweden. Sampling and susceptibility testing are of importance for early detection of resistance, especially if therapeutic failure is seen.

TABLE 4.22. Distribution of MICs and resistance (%) in *Pasteurella* spp. from calves 2005-2018. Clinical isolates from the respiratory tract, isolated from nasal swabs or from post mortem investigations of lungs.

Antibiotic	Resistance (%) 2005-2015 n=239	2016 n=104	2017 n=86	2018 n=79	Distribution (%) of MICs (mg/L) ≤0.06	0.12	0.25	0.5	1	2	4	8	16	>16
Ampicillin	0	13	2	5				22.8	72.2			5.1		
Enrofloxacin	0[b]	0	0	0		100								
Florfenicol	0	0	0	0						100				
Penicillin	0	13	2	5	3.8	87.3	3.8		5.1					
Tetracycline	0	0	0	0					100					
Trim-Sulph[a]	0	0	1	0				100						

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

Laying hens

Escherichia coli

Isolates of *E. coli* are from various locations and isolated at post mortems of laying hens in production (23 – 81 weeks of age). Occurrence of resistance was particularly high to enrofloxacin but resistance to ampicillin and tetracycline were also common traits (Table 4.23). Use of antibiotics in egg production in Sweden is very limited and quinolones have, over the years, only been used on rare occasions. Furthermore, according to a national regulation from 2013 (SJVFS 2013:42), susceptibility testing is generally required before ordination of fluoroquinolones for use in animals. One isolate was resistant to cefotaxime (MIC >4 mg/L) and a bla_{CMY-2}-gene was detected in this isolate. Multiresistance occurred in 2% (2/100) of the isolates. One of these isolates was resistant to four antibiotics (ampicillin, enrofloxacin, streptomycin and tetracycline) and the other to seven antibiotics (ampicillin, colistin, enrofloxacin, gentamicin, streptomycin, tetracycline and trimethoprim-sulphametoxazole). The latter isolate was investigated, but was negative, for *mcr-1* to *mcr-5* genes with PCR.

TABLE 4.23. Distributions of MICs and resistance (%) in *Escherichia coli* from laying hens 2017-2018. Clinical isolates from samples taken at post mortems.

Antibiotic	Resistance (%) 2017-2018 n=100	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	11					80.0	9.0			11.0		
Cefotaxime	1[b]		99.0				1.0					
Colistin	1[c]				93.0	6.0			1.0			
Enrofloxacin	39	61.0	5.0	32.0		1.0		1.0				
Gentamicin	1					99.0				1.0		
Neomycin	0						100					
Nitrofurantoin	0							39.0	59.0	1.0	1.0	
Streptomycin	3							93.0	4.0	1.0	1.0	1.0
Tetracycline	13					86.0		1.0		13.0		
Trim-Sulph.[a]	3			97.0				3.0				

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

Farmed fish

Flavobacterium psycrophilum

Isolates of *Flavobacterium psycrophilum* are from clinical submissions of farmed fish. Data from 2015-2018 are compiled and presented as distributions of MICs in Table 4.24. Most isolates are from rainbow trout. Smith et al. (2014) have proposed epidemiological cut-offs for florfenicol, oxolinic acid and oxytetracycline for *F. psycrophilum*. These are used in the distributions in Table 4.24. Resistance to oxolinic acid and oxytetracycline was high in this material.

In Figure 4.7. resistance to tetracycline and quinolones (nalidixic acid or oxolinic acid) in *F. psycrophilum* 2005-2018 is shown. A three-year moving average is used. There is a marked increase in resistance to these antibiotics over the years. There is a limited therapeutic use of oxolinic acid as well as of tetracycline in aquaculture in Sweden. The antibiotic mostly used is florfenicol (Svarm 2011). 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 in the absence of relevant selective pressure (Söderlund et al., 2018).

FIGURE 4.7. Resistance (%) in *Flavobacterium psycrophilum* from farmed fish 2005-2018 with a three-year moving average. The number of isolates each year varies (n=12-32, 2018 n=21).

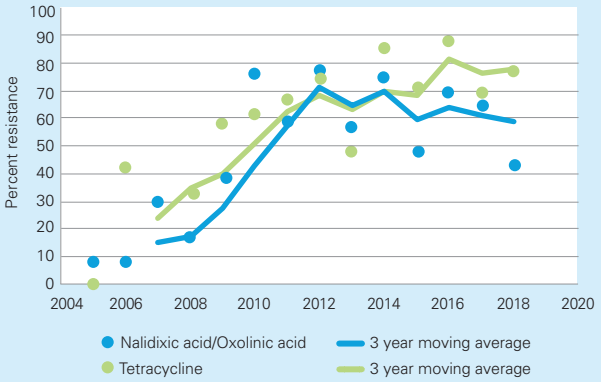


TABLE 4.24. Distributions of MICs and resistance (%) in *Flavobacterium psycrophilum* from farmed fish 2015-2018. The number of isolates each year varies (n=16-31, 2018 n=21).

Antibiotic	Resistance (%) 2015-2018	Distribution (%) of MICs (mg/L)											
	n=94	≤0.008	0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	>8
Florfenicol	0					5.3	12.8	46.8	30.9	4.3			
Oxolinic acid	55	1.1			5.3	33.0	5.3	1.1	2.1	52.1			
Oxytetracycline	76			1.1	22.3	1.1	2.1	2.1	13.8	24.5	28.7	4.3	

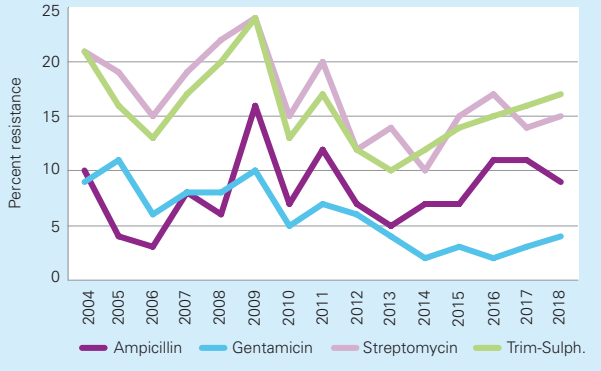
Horses

Escherichia coli

Isolates of *Escherichia coli* are from clinical submissions of the genital tract of mares. As in previous years, resistance to trimethoprim-sulphamethoxazole and streptomycin was most common in 2018 (Table 4.25 and Figure 4.8). The resistance to trimethoprim-sulphamethoxazole have gradually increased from 10 to 17% between 2013 and 2018 (Figure 4.8). 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-seven percent (237/309) of the isolates were susceptible to all the tested antibiotics. Multiresistance was detected in 6% (20/309) of the isolates, which is less than in 2016 (10%) but about the same as in 2017 (7%) (see previous Swedres-Svarm reports). Eight of the twenty multiresistant isolates were resistant to three antibiotics; seven to four; three to five; one to six and one to seven antibiotics. The most common phenotype was resistance to ampicillin, streptomycin and trimethoprim-sulphamethoxazole, representing 70% (14/20) of all the multiresistant isolates. This phenotype was also the most common in *E. coli* isolated from dogs (68%) and cats (63%). Six of the seven isolates resistant to four antibiotics had the common phenotype and were in addition resistant to gentamicin (3/7) or tetracycline (3/7). The three isolates resistant to five antibiotics had the com-

FIGURE 4.8. Resistance (%) in clinical isolates of *Escherichia coli* from horses 2004-2018. Isolates are from clinical sampling of the genital tract of mares. The number of isolates each year varies (n=124-324, 2018 n=309).



mon phenotype and were in addition resistant to cefotaxime and gentamicin. The two isolates resistant to six and seven antibiotics had the common phenotype, and resistance to cefotaxime, gentamicin and tetracycline, and for the isolate resistant to seven antibiotics also neomycin. A single isolate was resistant to enrofloxacin.

Five isolates were resistant to cefotaxime (MIC >0.25mg/L). Genes conferring transferable ESC resistance were detected in all these isolates. For more information, see Notifiable diseases, ESBL-producing Enterobacteriaceae.

Three isolates were resistant to colistin (MIC >2mg/L). The isolates were available for PCR detection of the *mcr-1* to *mcr-5* genes, and all were negative.

Streptococcus equi ssp. *zooepidemicus*

Isolates of *Streptococcus equi* ssp. *zooepidemicus* are from clinical submissions, and mainly from the respiratory tract (88%). The material from 2018 included two isolates with high MIC to penicillin (0.12 and 0.25). As the isolates were not available for further analyses, the results were invalidated. 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 12% in 2015-2018 and for trimethoprim-sulphamethoxazole 5-18% in 2015-2018 (Table 4.26 and previous Swedres-Svarm reports).

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

TABLE 4.25. Distributions of MICs and resistance (%) in *Escherichia coli* from horses, 2018. Clinical isolates from the genital tract of mares.

Antibiotic	Resistance (%) 2018 n=309	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	9					61.5	28.2	1.6		8.7		
Cefotaxime	2		98.4			0.3	1.3					
Colistin	1				85.1	13.9	1.0					
Enrofloxacin	<1	99.7				0.3						
Gentamicin	4					96.4	0.6			2.9		
Neomycin	<1						98.4	1.0	0.3	0.3		
Nitrofurantoin	1							44.7	52.8	1.6		1.0
Streptomycin	15							77.3	7.4	3.2	1.6	10.3
Tetracycline	4					95.8	0.3	0.3		3.6		
Trim-Sulph.[a]	17			81.9	0.6	0.3	0.3	16.8				

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

TABLE 4.26. Distribution of MICs and resistance (%) in *Streptococcus equi* ssp. *zooepidemicus* isolated from horses, 2018. Clinical isolates mainly from the respiratory tract.

Antibiotic	Resistance (%) 2018 n=97	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						99.0	1.0						
Clindamycin	11					88.7	11.3							
Erythromycin	0					100								
Gentamicin	NR[b]								13.4	86.6				
Nitrofurantoin	0										100			
Penicillin	0	100												
Tetracycline	NR[b]					1.0	10.3	51.5	33.0	4.1				
Trim-Sulph.[a]	18				66.0	16.5	10.3	3.1		4.1				

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

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 over the last ten years are shown in Figure 4.27. Resistance to penicillin due to penicillinase-production has been the most common trait over the years, but the figures have declined from 36% in 2008-2009 to 18% in 2018 (Figure 4.9 and Table 4.27). The number of isolates with penicillinase production of *S. aureus* in horses was low compared to *S. pseudintermedius* isolated from dogs (70-77%, Table 4.29), comparable to *S. felis* from cats (19%, Table 4.34) and high compared to *S. schleiferi* from dogs (3%, Table 4.30). Resistance to fusidic acid in the tested isolates has increased from 2017 (9%) to 17% in 2018 and is almost at the same level as penicillin (Table 4.27).

Fifty-five percent (65/118) of the isolates were susceptible to all the tested antibiotics. Multiresistance was not detected among the isolates.

MRSA was not detected among the tested isolates. For more information on MRSA isolated from horses in Sweden, see Notifiable diseases, Methicillin resistant *Staphylococcus aureus* (MRSA).

Fusobacterium spp.

Isolates of *Fusobacterium* spp. are from clinical submissions of samples from various locations in years 2014-2018. Of in total 40 isolates, the most common species were *F. necrophorum* (60%) and *F. equinum* (20%). For the beta-lactam antibiotics and tetracycline, the MICs were low for all isolates (penicillin MIC ≤0,12-0,25 and tetracycline MIC ≤1). Published data regarding antibiotic susceptibility of *Fusobacterium* spp. in horses are scarce and no established breakpoints for either microbiological or clinical resistance are available. To our knowledge there are no reports on beta-lactam resistance in *Fusobacterium* spp. from animals.

FIGURE 4.9. Resistance (%) in clinical isolates of *Staphylococcus aureus* 2008-2018 from skin of horses. The number of isolates each year varies (n=75-145, 2018 n=118).

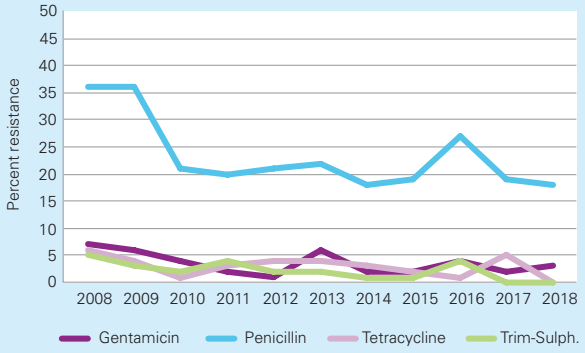


TABLE 4.27. Distribution of MICs and resistance (%) in *Staphylococcus aureus* isolated from horses, 2018. Clinical isolates from the skin.

Antibiotic	Resistance (%) 2018 n=118	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Cefoxitin	0		1.7			55.9	42.4					
Cephalotin	9				91.5		8.5					
Clindamycin	3			97.5	1.7		0.8					
Enrofloxacin	2		94.1	4.2	0.8	0.8						
Erythromycin	<1			93.2	5.9		0.8					
Fusidic acid	17			83.1	14.4	1.7	0.8					
Gentamicin	3				93.2	4.2	1.7	0.8				
Nitrofurantoin	0								95.8	4.2		
Penicillin [a]	18											
Tetracycline	0		68.6	30.5	0.8							
Trim-Sulph.[b]	0		92.4	7.6								

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

Dogs

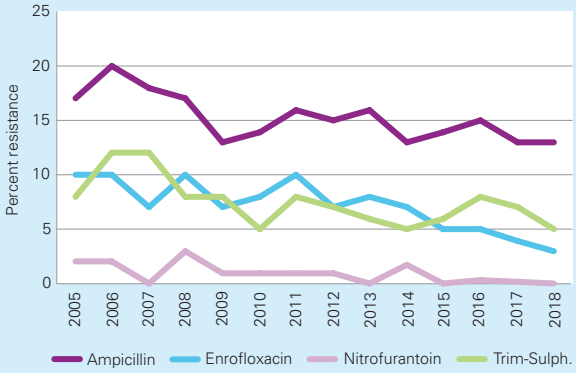
Escherichia coli

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 2018 (Table 4.28 and Figure 4.10). The proportion of resistance in the tested isolates has differed somewhat throughout the years, but the trend of declining figures continues in 2018 (Figure 4.10).

Eighty-two percent (885/1082) of the isolates were susceptible to all the tested antibiotics. Multiresistance was detected in 6% (60/1082) of the isolates, a slightly lower figure compared to 2015-2017 (7-9%) (see previous Swedres-Svarm reports).

Seventy-three percent (44/60) of the multiresistant isolates were resistant to three antibiotics; 15% (9/60) to four; 8% (5/60) to five and 3% (2/60) to six. The most common phenotype, resistance to ampicillin, streptomycin and trimethoprim-sulphamethoxazole, was detected in 68% (41/60) of the multiresistant isolates. The same phenotype was also the most common in *E. coli* isolated from horses (70%) and cats (63%). Of the sixteen isolates resistant to four or more antibiotics twelve were of the common phenotype, and commonly also resistant to tetracycline (10/12).

FIGURE 4.10. Resistance (%) in clinical isolates of *Escherichia coli* from dog urine 2005-2018. The number of isolates each year varies (n=304-1162, 2018 n=1082).



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

Eight (<1%) of the isolates were resistant to colistin (MIC >2mg/L). Five of the isolates were available for PCR detection of the *mcr-1* to *mcr-5* genes, and all were negative.

TABLE 4.28. Distribution of MICs and resistance (%) in *Escherichia coli* from dogs, 2018. Clinical isolates from urine.

Antibiotic	Resistance (%) 2018 n=1082	Distribution (%) of MICs (mg/L)										
		≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	13					62.5	23.8	1.0		12.7		
Cefotaxime	<1		99.4	0.2		0.1	0.3					
Colistin	<1				87.5	11.7	0.6		0.1			
Enrofloxacin	3	96.8	1.3	1.3	0.4			0.3				
Gentamicin	<1					99.4	0.4	0.1	0.2			
Neomycin	<1						99.2	0.3	0.1	0.2	0.3	
Nitrofurantoin	<1							42.1	56.4	0.7	0.6	0.1
Streptomycin	8							87.8	4.4	2.2	1.5	4.1
Tetracycline	4					95.6	0.4		0.1	4.0		
Trim-Sulph.[a]	5			94.1	0.7	0.3	0.2	4.7				

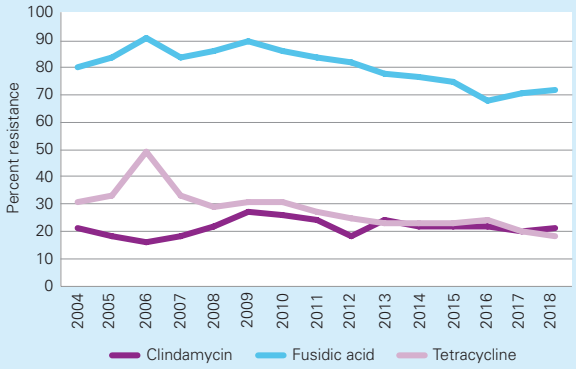
[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphamethoxazole).

Staphylococcus pseudintermedius

In Swedres-Svarm 2018 (and Swedres-Svarm 2017) three different sample collections of *Staphylococcus pseudintermedius* from clinical submission are compared. *Staphylococcus pseudintermedius* from skin lesions (S1), from wounds (S2) and from the external ear canal (S3). Data for S1, S2 and S3 from 2018 are presented in Table 4.29. The S1 collection is compared to earlier data in Figure 4.11.

Resistance to penicillin due to penicillinase-production dominates for all sample collections (70-77%, Table 4.29). Although the figures have differed somewhat through the years the resistance to penicillin for sample collection S1 has declined since 2009 (90%). Resistance to clindamycin, fusidic acid and tetracycline for S1 has differed somewhat over the years but, compared to penicillin, remains at lower levels (Figure 4.11).

FIGURE 4.11. Resistance (%) in clinical isolates of *Staphylococcus pseudintermedius* from skin (sample collection S1) of dogs 2007-2018. The number of isolates each year varies (n=220-566, 2018 n=515).



Twenty-four percent (124/515) of the isolates in sample collection S1, 18% (182/1005) in S2 and 22% (169/784) in S3 were susceptible to all the tested antibiotics. The figures are low compared to other staphylococci isolated from animals, as *S. schleiferi* from dogs (81%), *S. aureus* from horses (55%) and *S. felis* from cats (73%).

The proportion of multiresistance for the S1 collection has varied from 26 to 36% between 2009 and 2017 (see previous Swedres-Svarm reports). In 2018 the corresponding figure was 25% (128/515). The proportion of multiresistance in sample collection S2 and S3 was 20% (153/784 and 201/1005). This is high compared to the figures in isolates of other staphylococci reported in Swedres-Svarm, as *S. schleiferi* isolated from dogs (2%), *S. aureus* from horses (0%) and *S. felis* from cats (7%). Twenty-two percent (28/128) of the S1-multiresistant isolates were resistant to five or more antibiotics, similar to 2017 (21%) but less compared to 2016 when one-third of the multiresistant isolates were resistant to five or more antibiotics. Resistance to penicillin, clindamycin and erythromycin was the most common phenotype for all three sample collections, S1 70% (90/128); S2 and S3 58% (118/203 and 89/153). Of the S1-isolates resistant to four or more antibiotics 85% (69/81) has the common phenotype combined with resistance to fusidic acid 55% (38/69), tetracycline 42% (29/69), and/or trimethoprim/sulphamethoxazole 30% (21/69). Resistance to penicillin, clindamycin and erythromycin was also the most common multiresistant trait in isolates of *S. felis* (77%, 17/22).

Twelve (S1 and S2) and nine (S3) isolates were resistant to oxacillin (MIC >0.5 mg/L). All isolates were available for PCR detection of the *mecA* and *mecC* genes. Nine isolates were found to be MRSP in each sample collection S1 and S2

TABLE 4.29. Distribution of MICs and resistance (%) in *Staphylococcus pseudintermedius* from dogs 2018. Clinical isolates from skin (S1), wounds (S2) and external ear canals (S3).

Antibiotic	Resistance (%)			Distribution (%) of MICs (mg/L) S1 = skin sample										
	2018 n=784 S3	2018 n=1005 S2	2018 n=515 S1	≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Cephalothin	2	2	4				96.1	3.9						
Cefoxitin [a]					78.7	19.0	1.4	0.6	0.4					
Clindamycin	13	14	21			79.5	2.5	0.6	17.4					
Enrofloxacin	<1	1	3		92.8	4.7	1.0	1.6						
Erythromycin	16	17	22			78.1	1.4	0.4	20.2					
Fusidic acid	21	15	18			76.0	6.4	1.2	16.5					
Gentamicin	3	2	4				93.6	2.7	1.6	2.1				
Nitrofurantoin	<1	0	<1								98.1	1.6	0.2	0.2
Oxacillin	1	2	3		84.3	13.0	1.6	1.2						
Penicillin [b]	70	77	72											
Tetracycline	22	20	18		80.0	2.3		0.2	0.2	17.2				
Trim-Sulph. [c]	8	8	9		53.7	36.8	6.0			3.5				

[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)

and 4/9 in S3. 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 (66%), skin (15%) or wounds (11%).

The proportion of resistance in isolates of *S. schleiferi* (Table 4.30) was lower for most antibiotics compared to isolates of the more common staphylococci isolated from dogs, *S. pseudintermedius* (Table 4.29). Three percent of the tested *S. schleiferi* isolates were penicillinase producing and comparable to figures between 2014 and 2017 (<1-4%) (see previous Swedres-Svarm reports). The proportion of isolates with penicillinase production was low also compared to other staphylococci from animals, 70-77% in *S. pseudintermedius* (Table 4.29), 18% in *S. aureus* from horses (Table 4.27) and 19% in *S. felis* from cats (Table 34). Between 2016 and 2018 the proportion of resistance to enrofloxacin has declined from 20% to 3% and to fusidic acid from 14 % to 6%, while for the other tested antibiotics there is no difference (see Table 4.30 and previous Swedres-Svarm reports).

Eighty-one percent (195/240) of the *S. schleiferi* isolates were susceptible to all the tested antibiotics. Multiresistance was detected in 2% (4/240), which is the same as in 2017. This is low compared to *S. pseudintermedius* isolated from dogs (20-25%) and *S. felis* from cats (7%), but slightly higher compared to *S. aureus* from horses (0%). All four multiresistant *S. schleiferi* isolates were resistant to three of the tested antibiotics. No specific phenotype was noticed.

Pseudomonas aeruginosa

Isolates of *Pseudomonas aeruginosa* are from clinical submissions of 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 earlier tested for polymyxin B susceptibility but the substance was replaced by the equivalent colistin in 2014. All tested isolates have been sensitive to polymyxin B throughout the years (see previous Swedres-Svarm reports). Since 2014 to 2018, 1% or less of the tested isolates have been resistant to colistin, but the isolates have not been available for further analyses for presence of transferable genes.

The proportion of resistance to enrofloxacin has gradually declined from 25% in 2009 to 8% in 2018 and the figures for gentamicin have stabilized to about 1-2% over the recent years (see Table 4.31 and previous Swedres-Svarm reports). None of the isolates were resistant to all three antibiotics, but one isolate was resistant to both enrofloxacin and gentamicin and one to colistin and gentamicin.

TABLE 4.30. Distribution of MICs and resistance (%) in *Staphylococcus schleiferi* from dogs, 2018. Clinical isolates from various locations.

Antibiotic	Resistance (%) 2018 n=240	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Cephalothin	3				97.5	2.5						
Cefoxitin [a]			37.9	59.2	1.7	1.3						
Clindamycin	4			95.8	1.7	0.8	1.7					
Enrofloxacin	3		88.8	7.9	2.1	1.3						
Erythromycin	3			96.7	1.3		2.1					
Fusidic acid	6			84.2	10.0	3.8	2.1					
Gentamicin	0				97.9	2.1						
Nitrofurantoin	<1								97.5	2.1	0.4	
Oxacillin	0		98.3	1.7								
Penicillin [b]	3											
Tetracycline	3		90.0	5.8	1.3	0.4	0.4	2.1				
Trim-Sulph.[c]	<1		95.8	3.8	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)

TABLE 4.31. Distribution of MICs and resistance (%) in *Pseudomonas aeruginosa* from dogs, 2018. Clinical isolates from the external ear canal.

Antibiotic	Resistance (%) 2018 n=366	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	32
Enrofloxacin	8	1.9	3.8	22.4	43.2	21.0	3.0	4.6		
Colistin[a]	1				77.9	16.7	4.4	0.3	0.8	
Gentamicin	2					83.9	11.7	1.9	1.1	1.4

[a]Colistin is equivalent to polymyxin B

Pasteurella canis

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

The most commonly detected *Pasteurella* sp. in the material was *P. canis* (n=232). The *P. canis* isolates were susceptible to all the tested antibiotics, with the exception of three isolates resistant to enrofloxacine (MIC 0.5) (Table 4.32). *Pasteurella dagmatis* (n=29), *P. multocida* (n=18) and *P. stomatis* (n=11) were less common and were susceptible to all the tested antibiotics (data not shown). The same cut-off values were used for all *Pasteurella* spp. tested.

TABLE 4.32. Distribution of MICs and resistance (%) in *Pasteurella canis* from dogs, 2018. Clinical isolates from various locations.

Antibiotic	Resistance (%) 2018 n=232	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	32
Ampicillin	0				100					
Enrofloxacin	1	98.7		1.3						
Gentamicin	0					98.3	1.7			
Penicillin	0	100								
Tetracycline	0				100					
Trim-Sulph.[a]	0			99.6		0.4				

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

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 4.28), resistance to ampicillin was the most common trait in 2018 (Table 4.33 and Figure 4.12). In comparison, in *E. coli* from the genital tract of mares (horses) resistance to ampicillin came in third place after resistance to trimethoprim-sulphamethoxazole and streptomycin (Table 4.25 and Figure 4.8). The proportions of resistance in the *E. coli* isolated from cats have differed somewhat over the years as shown in Figure 4.12.

Seventy-three percent (396/545) of the *E. coli* isolates were susceptible to all the tested antibiotics. Multiresistance was detected in 3% (19/545) of the isolates, and comparable to figures between 2010 and 2017 (2-5%) (see previous Swedres-Svarm reports). Seven of the isolates were resistant to three antibiotics; six to four and six to five antibiotics. The

FIGURE 4.12. Resistance (%) in clinical isolates of *Escherichia coli* from urine of cats, 2007-2018. The number of isolates each year varies (n=131-545, 2018 n=545).

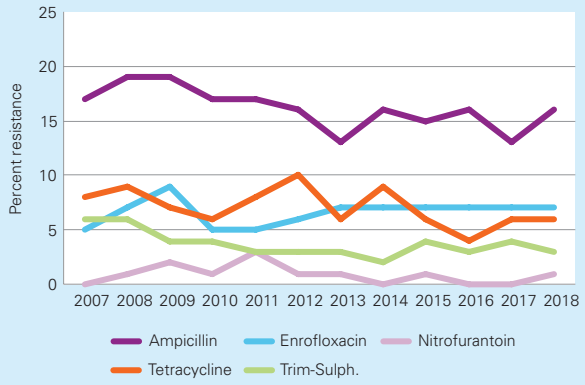


TABLE 4.33. Distribution of MICs and resistance (%) in *Escherichia coli* isolated from cats, 2018. Clinical isolates from urine.

Antibiotic	Resistance (%) 2018 n=545	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	16					71.4	12.1	0.9	0.7	14.9		
Cefotaxime	<1		99.4	0.6								
Colistin	<1				89.2	9.9	0.7		0.2			
Enrofloxacin	7	92.5	2.6	4.2	0.6			0.2				
Gentamicin	<1					99.4	0.6					
Neomycin	<1						98.9	0.4		0.4	0.4	
Nitrofurantoin	1							43.7	54.3	0.7	0.2	1.1
Streptomycin	6							89.5	4.8	1.5	0.7	3.5
Tetracycline	6				93.8		0.6		0.2	5.5		
Trim-Sulph.[a]	3			96.3	0.6	0.2		2.9				

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

most common phenotype was the same as for *E. coli* from dogs, resistance to ampicillin, streptomycin and trimethoprim-sulphamethoxazole with 63% (12/19). Eight of 12 isolates with the common phenotype were also resistant to tetracycline.

Three of the *E. coli* isolates were resistant to cefotaxime (MIC >0.25 mg/L). Genes conferring transferable ESC resistance were not detected in the three isolates. For more information of ESBL isolated from cats in Sweden, see Notifiable diseases, ESBL-producing Enterobacteriaceae.

Five isolates were resistant to colistin (MIC >2mg/L). Three of the isolates were available for PCR detection of the *mcr-1* to *mcr-5* genes, and all three were negative.

Staphylococcus felis

Isolates of *Staphylococcus felis* are from clinical submissions of samples from various locations, but mainly the external ear canal (33%), abscesses and wounds (32%), and urine (17%). The proportion of resistance to the tested antibiotics in isolates of *S. felis* (Table 4.34) are less compared to *S. pseudintermedius* in dogs (Table 4.29). For example, resistance to penicillin due to penicillinase production was 19% in *S. felis*, but 70-77% in *S. pseudintermedius*.

Seventy-three percent (227/310) of the *S. felis* isolates were susceptible to all the tested antibiotics. Multiresistance was detected in 7% (22/310) of the isolates. This is the same figure as in 2017, but slightly higher compared to the figures in 2015 and 2016 (4-5%), as well as in *S. aureus* from horses (0%) and *S. schleiferi* from dogs (2%), but less than in *S. pseudintermedius* (20-25%). Ninety-one percent (20/22) of the multiresistant isolates were resistant to three antibiotics and the two remaining to five antibiotics. The most common phenotype was resistance to penicillin, clindamycin and erythromycin (77% or 17/22). The two isolates resistant to five antibiotics had the common phenotype and in addition resistance to gentamicin and tetracycline.

Pasteurella multocida

Isolates of *Pasteurella* spp. are from clinical submissions of samples from various locations, but mainly from wounds or skin lesions (49%), abscesses (18%) and the external ear canal (16%).

Pasteurella multocida (n=392) was the most common *Pasteurella* sp. isolated in samples from cats. The proportion of resistance to antibiotics was low in the tested isolates (Table 4.35). *Pasteurella dagmatis* (n=18), *P. stomatis* (n=12) and *P. canis* (n=2) were also detected in the studied material. All those isolates, except for one isolate of *P. stomatis* (enrofloxacin, MIC 0.5 mg/L, data not shown), were susceptible to all the tested antibiotics. The same cut-off values were used for all *Pasteurella* spp. tested.

TABLE 4.34. Distribution of MICs and resistance (%) in *Staphylococcus felis* from cats, 2018. Clinical isolates from various locations.

Antibiotic	Resistance (%) 2018 n=310	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Cephalothin	2				98.4	1.6						
Cefoxitin [a]			94.5	4.5	0.6		0.3					
Clindamycin	7			93.2	0.6		6.1					
Enrofloxacin	<1		98.4	1.3	0.3							
Erythromycin	11			89.4	1.9		8.7					
Fusidic acid	3			93.9	3.5	2.3	0.3					
Gentamicin	<1				97.4	1.9	0.6					
Nitrofurantoin	0								99.4	0.6		
Oxacillin	0		97.7	2.3								
Penicillin [b]	19											
Tetracycline	2		95.5	2.3				2.3				
Trim-Sulph.[c]	0		97.7	2.3								

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

TABLE 4.35. Distribution of MICs and resistance (%) in *Pasteurella multocida* from cats. Clinical isolates from various locations.

Antibiotic	Resistance (%) 2018 n=392	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	32
Ampicillin	0				100					
Enrofloxacin	<1	99.2	0.5	0.3						
Gentamicin	<1					77.8	18.6	3.1	0.5	
Penicillin	0	90.1	8.9	1.0						
Tetracycline	<1				99.0	0.5	0.3	0.3		
Trim-Sulph [a].	<1			98.5	0.5	0.5		0.5		

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

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 from the flora 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 causing infections in animals or humans. Resistance in indicator bacteria contaminating meat indicates the potential exposure of humans to such reservoirs among farm animals through the food chain.

In 2018, indicator bacteria from broilers and turkeys were studied. Samples of intestinal contents were collected at slaughter and cultured for *E. coli*. Samples from broilers and turkeys 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 178 (99%) of 179 samples cultured. The majority of the isolates (69%) was susceptible to all antibiotics tested (Table 4.36). Resistance to ampicillin (16%), sulphonamides (15%), tetracycline (13%) and trimethoprim (11%) were the most common traits (Table 4.36 and 4.37). Nineteen isolates (11%) were multiresistant, i.e. resistant to three or more antibiotics. All but one had resistance to sulphonamides in their phenotype and all but three also had resistance to ampicillin and trimethoprim in their phenotype.

Levels of resistance in *E. coli* from broilers are low in an international perspective. This favourable situation is likely due to the limited use of antibiotics in broiler production in Sweden (see Sales of antibiotics for animals). This is the first occasion since the start of the monitoring in year 2000, that resistance to any specific antibiotic tested is above 15%. Resistance to sulphonamides, tetracycline, ampicillin and trimethoprim has gradually increased since 2007 while resistance to quinolones has decreased again after an increase in previous years (Fig 4.13). The reasons for these changes are not known but introduction and spread of multiresistant clones and/or plasmids are potential explanations.

One isolate was resistant to cefotaxime and ceftazidime and carried a bla_{CMY-2} gene. Using selective culture, ESC resistant *E. coli* was isolated from 42 (14%) of 300 samples of intestinal content from broilers and in thirty-eight (13%), a transferable gene conferring the ESC-resistance was detected. Twenty-four isolates carried the gene bla_{CMY-2}, 13 carried the gene $bla_{CTX-M-1}$, and 1 carried the gene bla_{SHV-12}. For more details and comments see section Antibiotic resistance in animals, Notifiable diseases.

Turkeys

Escherichia coli was isolated from 66 (92%) of 72 samples cultured. The majority of the isolates (80%) was susceptible to all antibiotics tested (Table 4.36). Resistance to ampicillin (9%) and tetracycline (6%) were the most common traits (Table 4.36 and 4.37). Multiresistance was not detected in any of the isolates.

Resistance has for most substances been stable for the four years since 2013 that *E. coli* from turkeys have been studied in Svarm. For ampicillin, sulphonamides and tetracycline there has however been a substantial decrease in the proportion of resistant isolates (Fig 4.14). The total number of isolates

FIGURE 4.13. Percent resistance in *Escherichia coli* from broilers 2000-2018. The number of isolates each year varies (n=140-390, 2018 n=178).

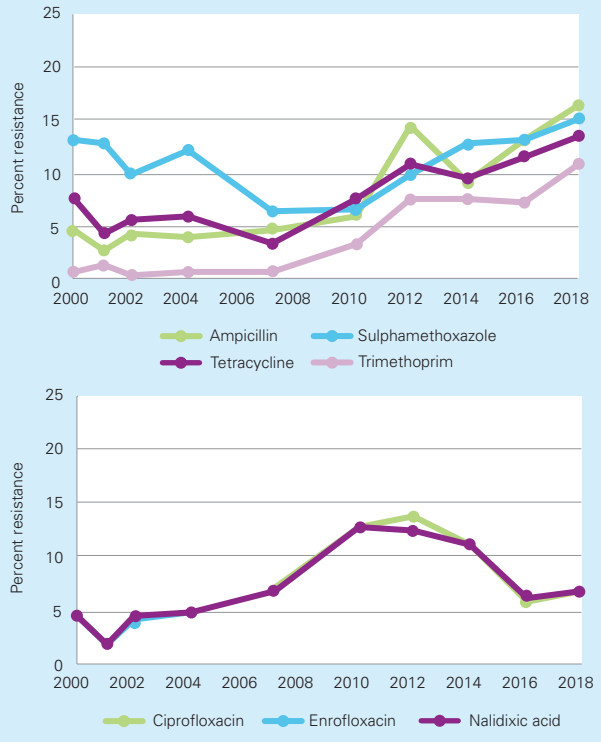
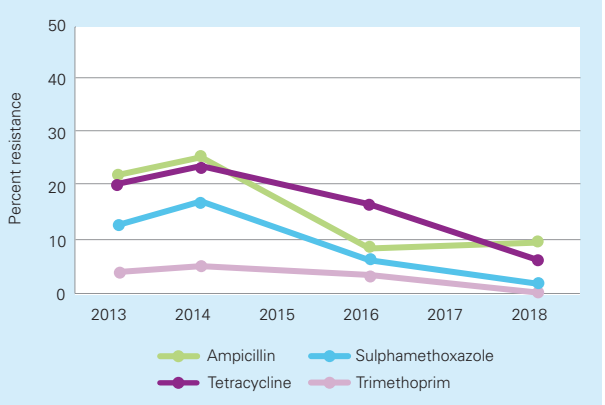


FIGURE 4.14. Percent resistance in *Escherichia coli* from turkeys 2013-2018. The number of isolates each year varies (n=55-85, 2018 n=66).



tested is small and the results should therefore be interpreted with caution. Resistance in *E. coli* from turkeys is about as prevalent as among isolates from broilers and involves the same antibiotics.

The samples from turkeys were also screened for ESC resistant *E. coli* using selective culture, but no such isolates were detected. For details and comments see section Antibiotic resistance in animals, Notifiable diseases.

TABLE 4.36. Resistance (%) and multiresistance (%) in indicator *Escherichia coli* from broilers and turkeys, 2018. Data on indicator *E. coli* from previous Svarm-reports are given for comparison.

Antibiotic	ECOFF (mg/L)	Resistance (%)									
		Broilers	Broiler meat	Cattle	Laying hens	Pigs	Pig meat	Sheep	Turkeys	Dogs	Horses
		2018	2012	2015	2012	2017	2011	2006-09	2018	2012	2010-11
		n=178	n=92	n=101	n=61	n=140	n=20	n=115	n=66	n=74	n=274
Ampicillin	>8	16	18	1	3	19	30	2	9	9	2
Azithromycin	16	0	-	1	-	0	-	-	0	-	-
Cefotaxime	>0.25	1	0	0	2	0	0	0	0	1	0
Ceftazidime	>0.5	1	-	0	-	0	-	-	0	-	-
Chloramphenicol	>16	0	0	0	0	6	0	0	2	0	<1
Ciprofloxacin	>0.06	7	4	0	5	0	10	<1	3	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	>16	7	4	0	5	0	0	0	3	0	<1
Sulphamethoxazole	>64	15	16	2	8	21	10	7	2	4	15
Tetracycline	>8	13	14	1	13	9	0	<1	6	8	2
Tigecycline	>0.5	0	-	0	-	0	-	-	0	-	-
Trimethoprim	>2	11	7	0	5	15	10	2	0	1	16
Multiresistance[a]											
Susceptible to all above		69	66	96	80	71	70	89	80	84	83
Resistant to 1		15	18	2	7	9	10	9	18	8	2
Resistant to 2		6	7	2	7	6	5	2	2	7	12
Resistant to 3		7	3		7	7	15	<1			2
Resistant to >3		4	5			6				<1	<1

[a]Ciprofloxacin and nalidixic acid as well as cefotaxime and ceftazidime were considered as one antibiotic class.

TABLE 4.37. Distribution of MICs and resistance (%) in *Escherichia coli* from intestinal content from broilers (n=178) and turkeys (n=66), 2018.

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	16							5.1	39.9	37.6	1.1				16.3				
	Turkeys	9							9.1	56.1	25.8					9.1				
Azithromycin	Broilers	0								0.6	29.2	62.9	7.3							
	Turkeys	0									30.3	62.1	7.6							
Cefotaxime	Broilers	1					99.4				0.6									
	Turkeys	0					100													
Ceftazidime	Broilers	1						99.4				0.6								
	Turkeys	0						100												
Chloramphenicol	Broilers	0										99.4	0.6							
	Turkeys	2										97.0	1.5				1.5			
Ciprofloxacin	Broilers	7	82.6	10.7		3.4	3.4													
	Turkeys	3	84.8	12.1			1.5						1.5							
Colistin	Broilers	0							97.8	2.2										
	Turkeys	0							100											
Gentamicin	Broilers	1						78.1	19.7	1.7	0.6									
	Turkeys	0						81.8	12.1	6.1										
Meropenem	Broilers	0		100																
	Turkeys	0		100																
Nalidixic acid	Broilers	7									93.3				3.9	2.2	0.6			
	Turkeys	3									97.0				1.5		1.5			
Sulphamethoxazole	Broilers	15										10.7	48.9	24.2	1.7					14.6
	Turkeys	2										16.7	53.0	27.3	1.5					1.5
Tetracycline	Broilers	13								86.5					5.1	8.4				
	Turkeys	6								93.9					3	3				
Tigecycline	Broilers	0					99.4	0.6												
	Turkeys	0					100													
Trimethoprim	Broilers	11					23.6	53.9	10.7	1.1					10.7					
	Turkeys	0					54.5	45.5												
			≤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 consumption in human and veterinary medicine

Data included and calculations

The figures on total amount of antibiotics consumed for systemic use of antibiotics to humans (ATC group J01 excluding methenamine, and JA07AA oral glycopeptides; sales to hospitals and on prescriptions to individuals; ATC/DDD index version 2019) were retrieved as defined daily doses and calculated to kg active substance. Figures on sales of antibiotics for use in animals (QJ01, QA07AA, and QJ51; total sales) are those presented in Sales of antibiotics for animals. For technical reasons products for intramammary use (QJ51) were included, resulting in not fully harmonised inclusion criteria. However the total sales of this type of products is only around 50 kg, this does not influence any conclusions. Sales for aquaculture were not included, nor were sales of drugs authorized for human use but sold for animals. The contribution of such sales to the total volume 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. For animal body mass, the data on population correction unit for 2016, excluding fish, was used as a proxy for 2018 (EMA, 2018). This unit roughly corresponds to the total biomass of major animal populations, excluding dogs and cats.

Comparison of consumption in tonnes active substance

In 2018, a total of 59.5 and 10.0 tonnes of antibiotics in included ATC classes were consumed in human and veterinary medicine, respectively. Figure 5.1 displays the consumption of beta-lactam antibiotics. These substances are by far the most commonly prescribed antibiotics in both human and veterinary medicine and also represent the largest amounts measured as kilograms. Penicillins (J01C and QJ01C) represent most of the amount in kg active substance of antibiotics for both humans and animals; 70 and 58%, respectively. The substances 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 2018 are included. Of these, the only class where consumption in animals outweighs human consumption is trimethoprim-sulphonamides, of which more than half are products only authorised for use in horses.

FIGURE 5.1. Consumption of beta-lactam antibiotics in human and veterinary medicine, kg active substance, 2018. Please note the difference in indexation of the x-axis between Figures 5.1 and 5.2.

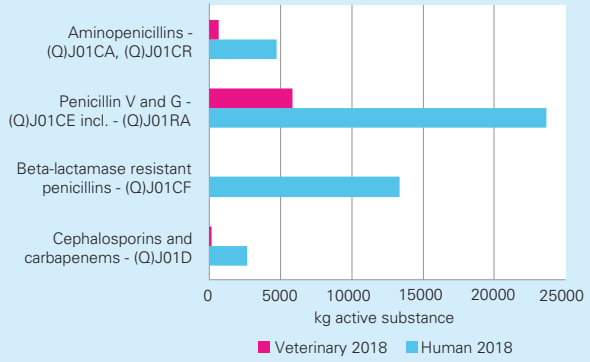
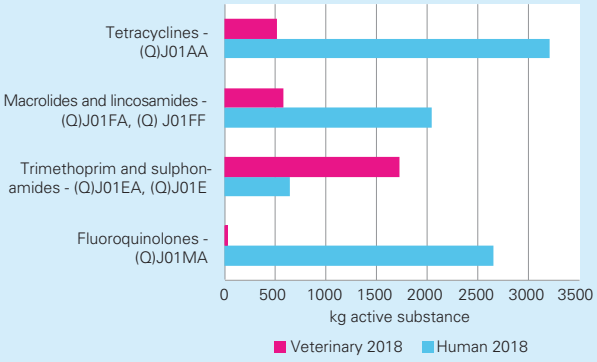


FIGURE 5.2. Consumption of fluoroquinolones, macrolides, lincosamides, trimethoprim and sulphonamides, and tetracyclines in human and veterinary medicine, kg active substance, 2018. Please note the difference in indexation of the x-axis between Figure 5.1 and 5.2.

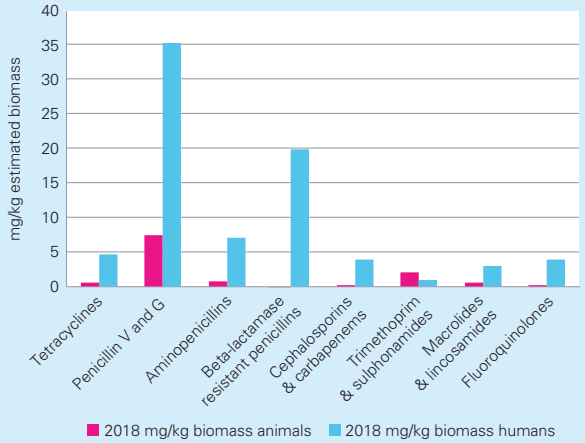


Comparison of consumption expressed as mg per kg estimated biomass

In 2018, the consumption was 88.6 and 12.7 mg active substance per kg estimated biomass in human and veterinary medicine, respectively. In Figure 5.3, a comparison of consumption of antibiotics for use in humans and animals are shown expressed as mg per estimated kg biomass. Data on the total consumption do not take the heterogeneity of the likelihood of exposure within the population into account. This is especially true for data on consumption 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

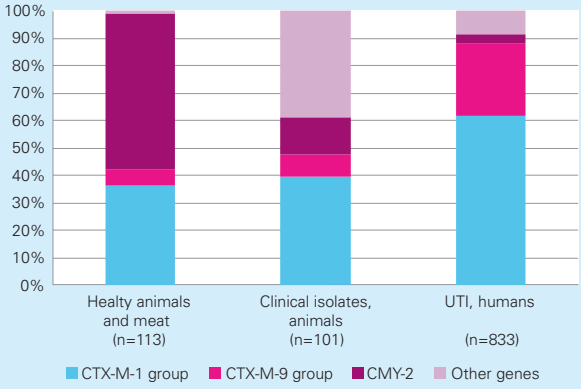
particular animal species) can be far larger than in the total population. Nevertheless, in Figure 5.3 the largest differences are noted for beta-lactamase resistant penicillins where consumption by animals is negligible (only sold as products for intramammary use), and for the fluoroquinolones where consumption by humans is 108 times higher than in animals.

FIGURE 5.3. Consumption of antibiotics in humans and animals expressed as mg active substance per estimated kg biomass in 2018. Only classes where the total consumption exceeded 1 000 kg active substance are shown.



clear difference in the dominating gene groups. Due to an increased occurrence of $bla_{CTX\text{-}M\text{-}1}$ among *E. coli* from broilers in the last years, this difference is now less clear. Still, nothing indicates a need to revise the previous 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 Enterobacteriaceae in animals is warranted.

FIGURE 5.4. Proportion of different gene groups conferring ESBL-resistance occurring in isolates from healthy animals and food (2017-18), clinical isolates from animals (2017-18), and isolates from urinary tract infections (UTI) in humans, 2017.



Comparison of antibiotic resistance in human and veterinary medicine

ESBL-producing Enterobacteriaceae

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, except for broilers where *E. coli* with $ESBL_A$ or $ESBL_M$ resistance have been found in a large proportion of birds. However, the occurrence in broilers has decreased compared to previous years. Moreover, in a majority of the broiler samples, the $ESBL_A$- or $ESBL_M$-producing *E. coli* only constitute a small part of all the *E. coli* in the intestinal flora.

In Figure 5.4, the gene groups conferring ESBL-resistance occurring in samples from animals, food and humans are compared. Data regarding sick animals, healthy animals and food are from Swedres-Svarm 2017 and 2018 whereas data regarding urinary tract infections in humans are from consecutive isolates of cefadroxil resistant *E. coli* and *K. pneumoniae* collected in 2017. Previously, it has been clear that the majority of isolates from humans in Sweden is not of the same types of $ESBL_A$ or $ESBL_M$ as in broilers, as there has been a

MRSA

Zoonotic transmission of MRSA occurs by direct or indirect contact. 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. Mostly this concerns pigs but also in veal calves, broilers and dairy cows, due to spread of livestock-associated MRSA, and mostly clonal complex (CC) 398.

The latest screening of pigs in Sweden was in nucleus and multiplying pig herds in 2014. MRSA was not detected, indicating a favourable situation. However, MRSA CC398 occurs among horses and *spa*-type t011, belonging to CC398, is by far the most common type. Consequently, all four cases of MRSA in horses in 2018 were of this type.

In humans, cases of domestically acquired MRSA CC398 is uncommon. In 2018, there were six cases and the isolates were of *spa*-types t011 (n=2), t034 (n=3), and t3933 (n=1). The epidemiological information concerning possible animal contacts 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).

Throuout the years, MRSA with *mecC* has been isolated from a number of 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, as part of an ongoing research project there were nine cases of MRSA with *mecC* from hedgehogs.

In humans, cases of domestically acquired MRSA with *mecC* are also uncommon. In 2018, there were 13 cases and the isolates were of *spa*-types t373 (n=6), t528 (n=1), t843 (n=2), t1736 (n=1), t6594 (n=1), t9111 (n=1) and t9716 (n=1). The epidemiological information concerning possible animal contacts is scarce but some of the *spa*-types in cases from humans have also been found in cases from animals. However, even if there would be zoonotic transfer it is currently not considered a public heath 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). Once the animal is contaminated by, or carrying, MRSA it may serve as vector for transmission to other humans. 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 anonymized 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, infection prevention and control measures in animal health care is needed to prevent nosocomial spread 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, genotypically related isolates from broilers and humans have not been found. Hence, 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. Notably, transferable resistance to extended spectrum cephalosporins has never been found and resistance to fluoroquinolones (e.g. ciprofloxacin) is rare. 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. In 2018, a number of isolates from animals had MIC of 4 mg/L for colistin and therefore should be considered resistant. This has not been observed before and needs to be investigated further.

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 (22%) 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

Data from feacal isolates of *Campylobacter jejuni* from humans were available 2018 and of these, half were resistant to fluoroquinolones, 31% to tetracycline and 1% to erythromycin. This year, 170 isolates of *C. jejuni* from broilers were tested.

The resistance percentages were lower than the data for humans 2018; fluoroquinolones (24%), tetracycline (2%) and erythromycin (0%).

The explanation of the higher resistance among the human isolates is probably that most sources of infections were foreign.

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

Clinical resistance in *Escherichia coli*

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 interpretation 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 presented in antibiotic resistance in 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 this comparison, some data sets for bacteria from animals presented in Swedres-Svarm have been interpretated using clinical breakpoints for humans (Table 5.1). Resistance was 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 bloodstream 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 com-

TABLE 5.1. Resistance (%) in *Escherichia coli* from various sample types from humans and different animal categories interpreted with clinical break-points (in brackets, mg/L) according to NordicAST v. 8.0 if not indicated by foot-notes that other interpretive criteria were used.

Category	Sample type	Year	Number of isolates	Amp (>8)	Cip (>0.5)	Ctx (>2)	Gen (>4)	Mer (>8)	Nit (>64)	Tmp (>4)
Dog (UTI)	Urinary	2018	1 082	12.7	0.3[a]	0.3	0.3		0.1	4.7[b]
Cat (UTI)	Urinary	2018	545	15.6	0.2[a]	0	0		1.1	2.9[b]
Horse (e.g. endometritis)	Genital tract	2018	309	8.7	0.3[a]	1.3	2.9		1.0	16.8[b]
Dairy cow (mastitis)	Milk	2016-18	79	22.1	0.4[a]	0	0		0	14.6[b]
Calf (enteritis)	Faeces/Post mortem	2016-18	74	35.1	0[a]	0	0		0	23.0[b]
Calf (healthy)	Faeces	2017	85	23.6	0	0	0			4.7
Pig (enteritis)	Faeces/Post mortem	2016-18	183	32.7	1.1a	0	0		0	36.1[b]
Pig (healthy)	Intestinal content	2017	143	18.2	0	0	0	0		14.7
Turkey (healthy)	Intestinal content	2018	66	9.1	1.5	0	0	0		0
Broiler (healthy)	Intestinal content	2018	178	16.3	0	0.6	0	0		10.7
Laying hens (e.g. salpingitis)	Post mortem	2018	100	11.0	2.0[a]	0	1.0			3.0[b]
Humans (UTI)	Urinary	2018	103 223	30.6	12.3				1.0	20.9
Humans (bloodstream inf.)	Blood	2018	5 383		18.1	8.0	6.9[c]	0		24.3[b]

[a]Enrofloxacin tested, BP >2mg/L except for horses (>0.25) and laying hens (>1) (CLSI 2018b); [b]Trim-Sulpha tested, BP >4 mg/L, NordicAST v. 8.0.

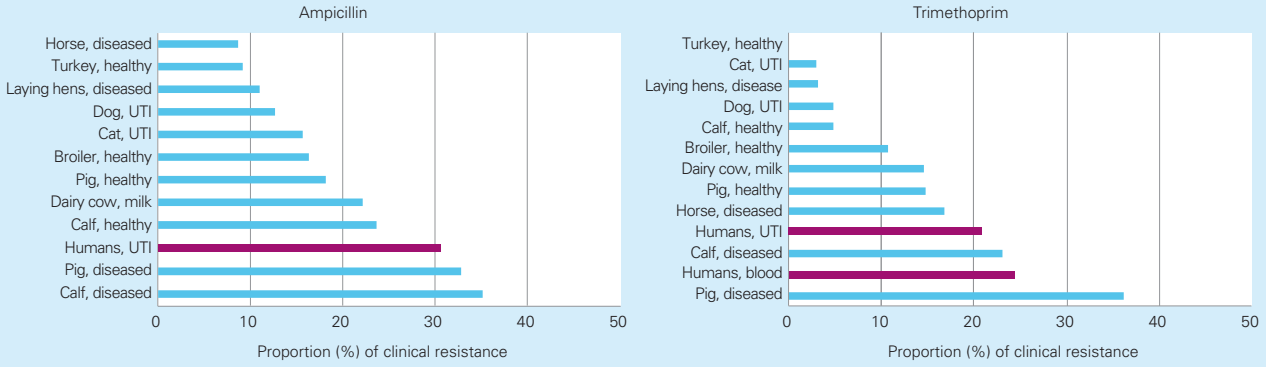
mon in some categories of diseased and healthy animals (See Antibiotic resistance in animals). Possibly, the selection pressure from fluoroquinolone use in animal populations is not sufficient to select for further mutations to clinical resistance in isolates with reduced susceptibility.

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 5.5). 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 is 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.

Moreove, 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 5.5. Proportion of clinical resistance to ampicillin and trimethoprim in *Escherichia coli* from humans and animals. For details see Table 5.1.



Background data, material, methods and references

Demographics and denominator data

Humans

TABLE 6.1. Inhabitants in Sweden per region, per age, 2018.

	0-6 years	7-19 years	20-64 years	65-79 years	80 years and older	All ages
Blekinge	12 187	23 575	86 279	27 370	9 960	159 371
Dalarna	22 276	41 315	153 856	51 266	17 452	286 165
Gotland	4 102	7 856	31 950	11 106	3 581	58 595
Gävleborg	21 608	41 111	155 557	50 461	16 900	285 637
Halland	26 658	50 462	177 743	51 769	18 193	324 825
Jämtland	10 088	18 513	71 231	22 297	7 677	129 806
Jönköping	30 569	55 111	197 836	53 623	20 098	357 237
Kalmar	18 648	34 319	131 028	43 971	15 570	243 536
Kronoberg	16 607	30 196	109 023	30 095	11 598	197 519
Norrbotten	17 981	34 345	139 708	43 907	15 354	251 295
Skåne	116 017	199 167	767 278	194 286	67 941	1 344 689
Stockholm	206 532	347 131	1 388 890	277 485	88 105	2 308 143
Södermanland	24 346	44 936	156 774	49 324	15 961	291 341
Uppsala	31 099	54 425	215 131	52 006	16 310	368 971
Värmland	21 369	38 834	154 124	48 067	18 005	280 399
Västerbotten	21 302	38 061	152 945	41 524	14 633	268 465
Västernorrland	18 434	36 002	133 086	43 426	15 020	245 968
Västmanland	22 148	40 177	149 796	43 648	15 326	271 095
Västra Götaland	140 988	247 435	975 798	241 534	85 027	1 690 782
Örebro	24 565	44 352	166 752	47 648	15 590	298 907
Östergötland	37 611	67 057	259 796	68 663	24 369	457 496
Sweden	845 135	1 494 380	5 774 581	1 493 476	512 670	10 120 242

TABLE 6.2. Population in Sweden, per year 2000-2018.

	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

TABLE 6.3. Number of admissions and patient-days in somatic medical care in Sweden, 2014-2017. Data represents production by acute care hospitals in all regions except Dalarna.

Year	Admissions	Patient-days
2014	1 411 121	6 293 096
2015	1 378 806	6 087 579
2016	1 298 939	5 710 715
2017	1 296 648	5 773 495

TABLE 6.4. Number of admissions and patient-days in somatic medical care in the regions, 2017. Data represents production by acute care hospitals in all regions except Dalarna.

Region	Admissions	Patient-days
Blekinge	22 811	106 815
Gotland	9 024	39 315
Gävleborg	37 618	164 897
Halland	40 346	158 724
Jämtland	18 019	83 139
Jönköping	48 231	194 218
Kalmar	39 414	144 020
Kronoberg	24 061	107 214
Norrbotten	34 260	166 215
Skåne	171 448	821 276
Stockholm	306 994	1 322 788
Södermanland	35 696	173 321
Uppsala	51 034	257 840
Värmland	39 597	184 412
Västerbotten	44 436	202 917
Västernorrland	34 150	144 269
Västmanland	37 832	169 814
Västra Götaland	219 083	1 002 685
Örebro	42 838	186 635
Östergötland	62 567	249 796
Sweden	**1 319 459**	**5 880 310**

TABLE 6.5. Denominator data from the microbiological laboratories 2018.

Laboratory	Number of analyses 2018									Number of positive samples 2018	Number of positive cultures 2018				
	Blood (pair of bottles)	Cerebro-spinal fluid (CFS)	Nasopharynx	Throat	General culture	Screen MRB	Urine	Faeces SSYC	Faeces *Clostridium difficile* (toxin)	Blood (pair of bottles)	*Staphylococcus aureus*	*Streptococcus pneumoniae*	*Streptococcus pyogenes*	*Escherichia coli*	*Clostridium difficile* (toxinpositive)
Aleris Medilab	1 229	0	7 465	2 242	9 280	11 764	39 103	5 349	1 024	188	4 300	298	814	9 038	140
Borås[a]	21 622	246	4 443	1 330	10 780	3 078	22 399	1 145	1 744	2 836	4 064	292	589	6 546	229
Eskilstuna (Unilabs)[a]	17 110	70	7 557	2 177	8 278	14 448	31 232	4 291	1 918	2 253	5 906	629	726	9 156	281
Falun	21 179	180	5 874	1 273	8 352	2 015	35 066	3 897	1 956	2 530	5 553	349	687	9 545	261
Gävle	17 291	224	4 027	1 011	11 135	8 408	29 486	3 197	2 168	2 703	4 766	229	407	9 735	371
Göteborg	48 631	1 490	2 413	2 694	15 412	26 060	56 646	8 232	4 367	6 006	10 529	712	1 308	13 612	624
Halmstad	17 159	173	4 159	2 106	8 491	12 914	31 129	3 638	1 871	3 606[b]	5 368	717	895	9 544	326
Jönköping	22 662[c]	317	9 135	2 934	18 341	18 174	43 077	7 108	2 559	2 607[c]	9 334	464	1 315	13 522	331
Kalmar[a]	16 427	141	4 085	1 886	7 715	4 055	30 576	4 073	1 230	3 383	5 053	546	607	9 639	107
Karlskrona/ Växjö[a]	26 904	182	8 298	2 762	13 369	4 179	41 539	4 928	2 458	3 302	5 394	748	968	10 717	417
Karlstad	24 770	508	7 358	2 674	16 337	11 652	41 134	4 383	2 515	2 190	7 431	651	1 021	10 970	71
Karolinska Stockholm[a]	101 762	2 486	33 328	7 931	66 928	159 055	157 166	19 669	11 112	14 875	33 805	2 330	3 145	40 741	1 286
Linköping[d]	29 575	862	8 788	2 769	22 522	14 671	53 087	6 559	3 075	4 509	9 565	881	1 075	15 366	519
Lund/Malmö[a]	81 980	1 221	24 353	11 272	37 526	47 251	170 075	23 155	9 491	10 466	23 508	2 010	3 660	42 863	1 190
Skövde (Unilabs)	17 294	184	4 393	2 723	14 650	9 488	64 972	9 698	4565[e]	1 767	7 201	299	1 033	14 740	611[e]
S:t Göran (Unilabs)[d]	17 366	143	6 965	1 494	9 653	30 526	46 363	6 702	2 292	1 672	6 577	535	707	12 162	326
Sunderby Luleå	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Sundsvall	16 945	163	2 054	1 069	6 996	8 979	29 622	3 191	3 659	2 295	4 116	476	398	9 196	324
NÄL Trollhättan	21 104	232	2 481	1 450	7 937	15 415	27 326	3 335	1 417	2 448	4 554	250	485	7 691	195
Umeå	17 274	524	5 234	1 785	8 925	15 280	33 512	3 014	1 810	1 775	5 436	648	877	10 112	292
Uppsala[d]	24 781	788	7 826	1 592	14 960	9 991	35 580	5 354	3 075	2 992	6 709	585	668	9 022	389
Visby[a]	4 966	26	2 098	452	3 134	NP	7 327	857	376	493	1 576	221	228	2 268	25
Västerås	19 584	194	3 292	1 757	10 863	5 238	29 167	3 704	2 015	2 773	5 088	435	516	8 765	190
Örebro[a]	21 204	207	10 435	2 239	13 244	14 908	37 191	5 835	2 885	2 348	6 721	733	757	8 990	310
Östersund[a]	8 783	74	2 826	889	4 939	4 062	18 690	2 044	1 096	1 076	3 287	323	396	6 132	113
Total	**617 602**	**10 635**	**178 887**	**60 511**	**349 767**	**451 611**	**1 111 465**	**143 358**	**70 678**	**81 093**	**185 841**	**15 361**	**23 282**	**300 072**	**8 928**

[a]Svebardata and data from local laboratory [b]Not pair. [c]Data from 20180101-20181105. [d]Data from 2017. [e]Including data from S:t Göran (Unilabs). NA, data not available; NP, not performed.

Animals

Agricultural statistics are provided by Statistics Sweden in collaboration with the Board of Agriculture. The Board of Agriculture maintains a statistical database accessible online (www.jordbruksverket.se). The statistics are also published annually as a Yearbook of Agricultural Statistics and continuously as Statistical Messages (SM). Annual figures on number of animals are given in Table 6.6, on volumes of animals slaughtered in Table 6.7 and 6.8 and average herd size and numbers of holdings in Table 6.9 and 6.10.

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. In the same period, the number of beef cows and sheep has increased, as well as the number of chickens slaughtered.

Data on the number of dogs and cats are also available from the Board of Agriculture. In a study 2012 the numbers of dogs and cats in Sweden were estimated to 784 000 and 1 159 000, respectively. The number of households with dogs was estimated to 572 000 and the number of households with cats to 745 000. This represents an increase by 8% in the number of dogs and a decrease by 8% in the number of cats since the previous study carried out in 2006.

TABLE 6.6. Number of livestock and horses (in thousands) 1980-2018. From the statistical database of the Board of Agriculture.

Animal Species	1980[a]	1985[a]	1990	1995	2000	2005	2010	2015	2016	2017	2018
Cattle											
Dairy cows	656	646	576	482	428	393	348	338	331	322	319
Beef cows	71	59	75	157	167	177	197	184	194	208	214
Other cattle >1 year	614	570	544	596	589	527	513	487	489	500	498
Calves <1 year	595	563	524	542	500	509	479	466	476	472	475
Total, cattle	1 935	1 837	1 718	1 777	1 684	1 605	1 537	1 475	1 490	1 502	1 507
Sheep											
Ewes and rams	161	173	162	195	198	222	273	289	281	301	296
Lambs	231	252	244	266	234	249	292	306	297	304	291
Total, sheep	392	425	406	462	432	471	565	595	578	605	587
Pigs											
Boars & sows	290	260	230	245	206	188	156	142	140	141	132
Fattening pigs >20 kg [a]	1 254	1 127	1 025	1 300	1 146	1 085	937	830	835	836	901
Piglets <20kg [b]	1 170	1 113	1 009	769	566	539	427	384	378	385	361
Total, pigs	2 714	2 500	2 264	2 313	1 918	1 811	1 520	1 356	1 354	1 362	1 393
Laying hens											
Hens	5 937	6 548	6 392	6 100	5 670	5 065	6 061	7 571	8 174	7 294	7 699
Chickens reared for laying	2 636	2 159	2 176	1 812	1 654	1 697	1 647	1 842	1 575	1 994	1 927
Total, hens	8 573	8 708	8 568	7 912	7 324	6 762	7 707	9 413	9 750	9 288	9 626
Horses											
Total, horses						283[c]	363		356		

[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.

TABLE 6.7. Number of animals slaughtered (in thousands) at slaughterhouses, 1980-2018. From the statistical database of the Board of Agriculture.

Animal species	1980	1985	1990	1995	2000	2005	2010	2015	2016	2017	2018
Cattle											
Cattle >1 year	574	584	523	502	490	433	425	406	395	392	410
Calves < 1 year	130	152	70	30	39	33	27	22	16	14	15
Total, cattle	704	736	593	532	529	466	453	428	411	406	426
Sheep	302	328	280	189	202	206	255	256	251	261	280
Pigs	4 153	4 283	3 653	3 743	3 251	3 160	2 936	2 560	2 526	2 576	2 646
Broilers	40 466[a]	36 410[a]	38 577[a]	61 313	68 617	73 458	78 507	95 974	101 322	101 876	100 535
Turkeys							495	475	527	526	526

[a]Data supplied by the National Food Administration.

TABLE 6.8. Quantity of livestock slaughtered (in 1 000 tonnes) at slaughterhouses, 1990-2018. From the statistical database of the Board of Agriculture.

Animal Species	1990	1995	2000	2005	2010	2015	2016	2017	2018
Cattle									
Cattle >1 year	139.5	140.1	145.4	131.4	133.5	129.7	128.6	129,7	134.3
Calves < 1 year	6.8	3.2	4.4	4.5	4.3	3.5	2.7	2,4	2.5
Total, cattle	146.3	143.3	149.8	135.9	137.8	133.1	131.2	132,1	136.9
Sheep	5.0	3.5	3.9	4.1	5.0	4.2	5.0	5,3	5.6
Pigs	293.1	308.8	277.0	275.1	263.5	233.5	232.8	240,7	249.8
Broilers	44.0[a]	73.6[a]	89.9	96.2	112.0	137.7	147.4	148,6	149.3
Turkeys					3.2	3.8	4.2	4,3	4.4

[a]Data supplied by the National Food Administration.

TABLE 6.9. Average number of animals per holding 1995-2018. From the statistical message JO 20 SM 1702.

Animal Species	1995	2000	2005	2010[a]	2015[a, b]	2016[a]	2017[a, b]	2018[a,b]
Cattle								
Dairy cows	27.2	33.7	46	61.9	81.5	85.4	89.1	91.8
Beef cows	9.2	12.0	13.8	16.2	17.7	18.7	19.8	20.6
Sheep	19.5	24.8	29.2	31.7	31.8	32.5	32.7	32.4
Boars and sows	31	63	156	156	186	182	165	158
Fattening pigs	157	294	471	664	845	820	825	852
Laying hens	640	995	471	1 638	2 587	2 822	2 506	2 413

[a]The definition of holdings included changed from 2010; [b]For sheep, pigs and poultry data for 2015, 2017 and 2018 are estimated from a sample and therefore have a larger uncertainty

TABLE 6.10. Number of holdings with animals of different types, 1980-2018. From the statistical database of the Board of Agriculture.

Animal Species	1980	1985	1990	1995	2000	2005	2010	2015	2016	2017	2018
Cattle											
Dairy cows	44 143	35 063	25 921	17 743	12 676	8 548	5 619	4 161	3 872	3 614	3 477
Beef cows	12 436	10 310	10 883	17 069	13 861	12 821	12 190	10 405	10 349	10 471	10 418
Other cattle >1 year	63 179	52 652	42 696	39 160	30 457	24 808	20 295	16 432	16 060	15 722	15 343
Calves <1 year	62 314	52 001	41 986	36 542	27 733	22 888	18 494	15 186	14 839	14 517	14 139
Total holdings with cattle	70 503	58 872	47 292	41 990	32 063	26 179	21 586	17 466	17 046	16 674	16 317
Sheep	10 238	10 595	9 749	10 037	8 089	7 653	8 657	9 110	8 699	9 219	9 120
Pigs	26 122	19 937	14 301	10 753	4 809	2 794	1 695	1 228	1 252	1 272	1 346
Laying hens	23 603	17 531	12 900	9 593	5 678	4 916	3 703	2 927	2 897	2 911	3 197
Chickens reared for laying	5 093	2 714	1 875	1 405	715	634	487	730	389	825	852

Materials and methods, consumption of antibiotics

Legal framework and distribution of medicines

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, antibiotic drugs are usually bought on requisitions from pharmacies, but some regions manage drug supplies to human hospitals by themselves. Veterinarians may deliver products to the animal care-taker in relation to 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. 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.

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 system recommended by the WHO is 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 concept of 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 yearly 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 and day, which give an estimate of the proportion of the population daily exposed to a particular drug. This figure is a rough estimate and should be interpreted with caution.

All data on the number of DDDs in this report are displayed in the 2018 version of the ATC/DDD index, available at https://www.whocc.no/atc_ddd_index/.

Antibiotic consumption in humans

Swedish national statistics on drug utilization

Sales statistics on medicines 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. Out-patient care data includes information on the sales of drugs dispensed on prescription by all Swedish pharmacies by the prescription survey, running since 1974. The statistical material was until 1995 built of 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/1000 inhabitants per day or number of prescriptions/1000 inhabitants.

Hospital care data includes 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 medicines 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 (eHälsomyndigheten).

The Swedish eHealth Agency aims to contribute to improved health care and public health and better caring by pursuing development of a national e-health infrastructure. They are 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

Definitions of DDD 2018

TABLE 6.11. DDD for all antibiotic substances (J01) sold in Sweden in 2018

	DDD (g)		DDD (g)
J01AA02 – doxycycline	0.1	J01FA01 - erythromycin	1
J01AA04 – lymecycline	0.6	J01FA01- erythromycin erythylsuccinat tablets	2
J01AA06 - oxitetracycline	1	J01FA06 - roxithromycin	0.3
J01AA07 - tetracycline	1	J01FA09 - clarithromycin - oral	0.5
J01AA12 - tigecycline	0.1	J01FA10 - azithromycin - parenteral	0.5
J01BA01 - chloramphenicol	3	J01FA10 - azithromycin - oral	0.3
J01CA01 - ampicillin	2	J01FA15 - telithromycin	0.8
J01CA04 - amoxicillin	1	J01FF01 - clindamycin - parenteral	1.8
J01CA08 - pivmecillinam	0.6	J01FF01 - clindamycin - oral	1.2
J01CE01 - benzylpenicillin	3.6	J01GB01 - tobramycin - parenteral	0.24
J01CE02 - fenoximethylpenicillin	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-oral	1	J01GB06 - amikacin	1
J01CR05 - piperacillin and enzyme inhibitor	14	J01GB07 - netilmicin	0.35
J01DB01 - cefalexin	2	J01MA01 - ofloxacin	0.4
J01DB03 - cefalotin	4	J01MA02 - ciprofloxacin - parenteral	0.5
J01DB05 - cefadroxil	2	J01MA02 - ciprofloxacin - oral	1
J01DC02 - cefuroxime- parenteral	3	J01MA06 - norfloxacin	0.8
J01DC02 - cefuroxime - oral	0.5	J01MA12 - levofloxacin	0.5
J01DC08 - loracarbef	0.6	J01MA14 - moxifloxacin	0.4
J01DD01 - cefotaxime	4	J01XA01 - vancomycin	2
J01DD02 - ceftazidime	4	J01XA02 - teicoplanin	0.4
J01DD04 - ceftriaxon	2	J01XB01 - colistin	3 MU
J01DD08 - cefixime	0.4	J01XB02 - polymyxin B	0.15
J01DD14 - ceftibuten	0.4	J01XC01 - fusidic acid	1.5
J01DE01 - cefepime	2	J01XD01 - metronidazole	1.5
J01DF01 - aztreonam - parenteral	4	J01XE01 - nitrofurantoin	0.2
J01DF01 - aztreonam - inhalation	0.225	J01XX01 - fosfomycin - parenteral	8
J01DH02 - meropenem	2	J01XX01 - fosfomycin - oral	3
J01DH03 - ertapenem	1	J01XX04 - spectinomycin	3
J01DH51 - imipenem and enzyme inhibitor	2	J01XX05 - methenamine - hippurate	2
J01EA01 - trimethoprim	0.4	J01XX05 - methenamine - mandelate	3
J01EC02 - sulfadiazin	0.6	J01XX08 - linezolide	1.2
J01EE01 - sulfamethoxazol and trimethoprim	1.92		

re-regulation, regions can choose to manage drug supplies to hospitals by themselves. If so, the regions are not required to report data to the national database. Since October 2013, three regions have chosen to organize their own drug supplies organization for hospitals.

Therefore, no national database with complete sales statistic for hospitals is available at this time. Efforts have been made to complement the data from the Swedish eHealth Agency with data from regions. During 2018 only two regions did not report data to the Swedish eHealth Agency.

Data sources and inclusion criteria

Data on sales of antibiotics in outpatient and hospital care as well as population data for the calculations regarding antibiotic consumption is obtained from the Swedish eHealth Agency through their database Consice. For the overall statistics, the data include all antimicrobial products marketed in Sweden in the ATC class J01. The data includes all sales of these products, even if the antimicrobial (J01) is prescribed by a veterinarian. Throughout this report, methenamine is excluded in all diplays of J01 as a group. Measures used are

defined daily doses per 1000 inhabitants per day (DDD/1000 inhabitants per day) and prescriptions per 1000 inhabitants per year. Every purchase of a medicine prescribed in outpatient care is also recorded in the Prescribed Drug Register, held 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 investigate the actual number of individuals or the fraction of the population treated with a specific medicine. Thus, some of the data is presented as users per 1 000 inhabitants per year. Data on the age-adjusted average body weight of the population in Sweden was obtained from Statistics Sweden, a Swedish authority responsible for official Swedish statistics.

Antibiotic consumption in hospital care is measured as DDD/1000 inhabitants per day and DDD/100 patient-days or admissions. The number of DDDs is obtained from the Swedish eHealth Agency and from local medicines statistics systems in the regions. The National Board of Health and Welfare has provided data on patient-days and admissions 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). Patient-days is defined as each additional day during one hospital stay. The number of patient-days and admissions includes data on somatic medical care by each region (to be distinguished from consumption of the region's inhabitants).

Trend analysis

In this year's report, several general regression models were executed in the section "Consumption of antibiotics". Time was used as explanatory variable and the outcome was the sales of antibiotics, adjusted for population size in Sweden and number of patient-days at the given time. The analyses were exectued on a basis of a negative binomial distribution. In outpatient care the analyses were executed on the sales of antibiotics between 2000 and 2018 for different age groups, on sales of antibiotics commonly used to treat respiratory tract infections between 2000 and 2018 and on sales of antibiotics commonly used to treat UTI in men 65 years and older between 2000 and 2018.

The Swedish Prescribed Drug Register

Since July 2005, the Swedish National Board of Health and Welfare supplies an individually based register on all drugs prescribed and dispensed in outpatient care. Among other, this data gives 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 1000 inhabitants per year (Users/1000/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. Data for 2018 is not available until the end of 2019, and therefore denominator data from 2017 are used in some figures in this report. The number of admissions and patient-days in Swedish somatic medical care (produced by acute care hospitals) 2014-2018 is shown in Table 6.3.

Sales of antibiotics for animals

Data sources, inclusion criteria and analysis

As the result of a new interpretation of existing legislation on confidentiality, it has not been possible for SVA to obtain raw data per product for calculation to kg active substance and subsequent analyses from the Swedish eHealth Agency. Therefore, the Swedish Board of Agriculture has performed the calculations with some methodological support from SVA.

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 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 sold on special license from other sources, e.g. pharmacies.

SVA received data aggregated by class and further in-depth analyses have not been possible. The data source is the same as before, i.e. information in the database of the Swedish eHealth Agency on sales from pharmacies to animal owners (prescriptions dispensed) or to veterinarians (requisition).

Products sold with special licence

Antibiotic products sold with special licence (products prescribed and sold on exemption from general Swedish market authorization) are included in the dataset. 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 identify companies who might have statistics on sales of products sold with special licence to the Swedish market. Whenever the information on number of packages sold per product-packtype from the Swedish eHealth Agency was lower than that obtained from pharmaceutical companies, the figure was adjusted. This means that for some products, the figures may represent a slight overestimate of sales from pharmacies as they may include products kept in stock. The reporting system has been adjusted and it is assumed that from 2015, data from the Swedish 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 broiler 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 2018 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 from turkeys were collected at slaughter throughout the year. Each sample was from a unique flock but not always from a unique production site. Samples cultured were collected at two abattoirs that in 2018 accounted for approximately 98% of the total volume of broilers slaughtered.

Samples from broiler meat were collected throughout the year by municipal environmental departments in twelve different cities in Sweden. In each city, a proportional number of samples in relation to the human population was collected. 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 cats, dogs, rabbit, horses, goats, sheep and cow 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.

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 2018, 401 flocks were positive for *C. jejuni*. From these, 170 isolates of *C. jejuni*, each representing one flock was randomly selected for susceptibility testing. 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 *Actinobacillus pleuropneumoniae* from pigs and 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. from faecal samples. Isolates of *Pasteurella* spp. from pigs are isolated from nasal swabs collected within a control programme for atrophic rhinitis in nucleus and multiplying herds or from tissue samples from lungs taken post mortem. 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 or from milk samples. Isolates of *Klebsiella pneumoniae* are from milk samples. Isolates of *Pasteurella* spp. are from the respiratory tract.

In laying hens, isolates of *E. coli* are from post mortem examinations of birds in production (23 – 81 weeks of age).

In farmed fish, isolates of *Flavobacterium psychrophilum* 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* mainly from the respiratory tract, *S. aureus* from skin samples and *Fusobacterium* spp. from various locations.

In dogs, isolates of *E. coli* are from urine, *Staphylococcus pseudintermedius* is isolated from three sampling collections; skin, wounds and external ear canal, *Staphylococcus schleiferi* from various location (mainly external ear canal, skin and wounds), *Pseudomonas aeruginosa* from the external ear canal and *Pasteurella* spp. 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* from various locations (mainly external ear canal, abscesses, wounds and urine) and *Pasteurella* spp. from various locations (mainly wounds, 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 179 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. *Escherichia coli* like colonies 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 Enterobacteriaceae species the isolate would be further tested for ESBL production.

Meat samples: Briefly, 25 g of surface meat was homogenized in 225 ml BPW and incubated at 37°C overnight. From the BPW homogenizate 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.

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

MRSA and MRSP

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

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

Zoonotic pathogens

Salmonella

Salmonella was isolated and identified at the Dept. of Microbiology, SVA or at regional laboratories in accordance with standard procedures. All samples within official control programmes are cultured according to the procedures detailed by the MSRV (ISO 6579-1:2017) Confirmatory identification and serotyping was performed according to the procedures of Kaufmann and White.

Campylobacter

Campylobacter jejuni from broilers were isolated and identified 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

Most clinical isolates were isolated and identified with accredited methodology, following standard procedures at SVA. Part of the isolates of *Pasteurella* spp. from pigs and cattle and part of the isolates of *E. coli* from cattle were isolated and identified following standard procedures at a regional laboratory.

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, 2018a). The microdilution panels used are produced at Section of Substrate, SVA (VetMIC) and Trek diagnostics LTD (Sensititre). 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. three different protocols are used at SVA. Either the tests are made by dilution in CAMHB supplemented with 5-10% horse serum followed by incubation in aerobic atmosphere, 35°C for 16-18 hours, or by dilution in Haemophilus test medium (HTM) followed by incubation in CO2, 37°C for 16-18 hours. Also dilution in CAMHB supplemented with 5-10% horse serum and incubation in CO_2, 37°C for 16-18 hours was used. For testing of *A. pleuropneumoniae* dilution in HTM broth was used followed by incubation in CO_2 at 37°C for 18-24 hours. Also, *S. equi* subsp. *zooepidemicus* was tested using CAMHB supplemented with 5-10% horse serum followed by incubation at 35°C for 16-18 hours. *Fusobacterium necrophorum* was tested in CAMHB. The inoculum was prepared by colony suspension to a concentration of approximately 10^6 CFU/ml and the inoculation volume was 100 µl per well. Incubation was performed in anaerobic jars at 37°C for 48 hours.

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

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 in brain heart infusion broth (BHI) with 10% foetal calf serum ($1x10^6$-$5x10^6$ CFU/ml) 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 (2014a).

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

Genotyping

Suspected isolates of MRSA 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).

Isolates of Enterobacteriaceae confirmed as $ESBL_A$ phenotypically or suspected being $ESBL_{CARBA}$ were directly 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 transferable genes these isolate were then subjected to genome sequencing.

DNA from confirmed ESBL-producing Enterobacteriaceae, 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. DNA-concentrations were determined using Qubit HS DNA-kit (Life technologies). DNA was then sent to Sci-life clinical genomics (Solna, Sweden) for library preparation and paired-end sequencing using Illumina technologies. The specific ESBL-gene was then determined, for the included Enterobacteriaceae, using "Antimicrobial Resistance Identification By Assembly (ARIBA)" (Hunt et al., 2017) against the Resfinder (https://cge.cbs.dtu.dk/services/ResFinder/) and CARD (https://card.mcmaster.ca/) databases. Reads were then trimmed with Trimmomatic 0.36 and genome assembly was performed with SPAdes v.3.9.1 with the careful parameter, followed by Pilon v1.21 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).

The specific gene variants for a collection of isolates for which genome sequence analysis gave poor results were determined by sequencing using in-house primers and the EZseq™ service by Macrogen Inc. (South Korea) for sequencing.

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 and *Campylobacter jejuni* CCUG 11284 (analogue to *Campylobacter jejuni* 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 participates in two proficiency tests for antibiotic susceptibility testing and one comparative test for isolation and 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 on *Salmonella* and animal pathogens such as source of cultured sample, identification results, antibiotic susceptibility etc. were registered in a database at SVA. Data for indicator bacteria were recorded in an Access database.

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 (ECOFF) issued by EUCAST (www.eucast.org) or values suggested by the European Food Safety Authority are used. For some antibiotics, values based on MIC distributions obtained in Svarm are used. 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, 2015a) or epidemiological cut-offs (ECVs) issued by CLSI (CLSI, 2014b) are also taken into consideration.

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.

TABLE 6.12. Cut-off values (mg/L) for resistance. Values in red are current (March 2019) EUCAST epidemiological cut-off values (ECOFFs), blue underlined values deviate from ECOFFs and for values in black, ECOFFs are not defined.

Antibiotic	*Actinobacillus pleuropneumoniae*	*Brachyspira hyodysenteriae*	*Campylobacter jejuni*	*Campylobacter coli*	*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	>1				>8	>8			>1		>8			
Azithromycin					>16									
Cefepime					0.12									
Cefotaxime					>0.25	>0.25		>0.25			>0.5			
Cefoxitin													>4	
Ceftazidime					>0.5									
Ceftiofur						>1								
Cephalothin												>1	>1	>2
Chloramphenicol	>2				>16	>16			>2		>16			
Ciprofloxacin	>0.06		>0.5	>0.5	>0.06				>0.06		>0.06			
Clindamycin												>0.5	>0.5[a]	>0.5
Colistin					>2	>2		>2		>4	>2			
Doxycycline		>0.5												
Enrofloxacin					>0.12	>0.12		>0.12	>0.25	>2		>0.5	>0.5	
Ertapenem					>0.06									
Erythromycin			>4	>8								>0.5	>1	>0.5
Florfenicol	>4					>16	>2		>4		>16			
Fusidic acid												>1	>0.5	
Gentamicin	>8		>2	>2	>2	>2		>2	>8	>8	>2	>2	>2	
Imipenem					0.5									
Meropenem					>0.12									
Nalidixic acid	>16		>16	>16	>16				>16		>16			
Neomycin						>8		>8			>4			
Nitrofurantoin						>64						>32 (UTI)	>32 (UTI)	
Oxacillin												>0.5	>1	
Oxolinic acid							>0.25							
Penicillin	>0.5								>0.5			[b]	[b]	>0.06
Streptomycin			>4	>4		>16		>16			>16			
Sulphamethoxazole					>64						>256			
Temocillin					>32									
Tetracycline	>1		>1	>2	>8	>8	>0.12	>8	>2		>8	>1	>1	
Tiamulin		>0.25												
Tigecycline					>0.5									
Trimethoprim	>4				>2						>2			
Trim & sulphaa						>1		>1	>4			>0.5	>0.5	>0.5
Tylosin		>16												
Tylvalosin		>1												
Valnemulin		>0.12												
Tylosin		>16												
Tylvalosin		>1												
Valnemulin		>0.12												

[a]Concentration of trimethoprim given, tested with sulphamethoxazole in concentration ratio 1/20; [b]beta-lactamase production; [c]EUCAST ECOFFs are used for MRSA (clindamycin >0.25).

Svarm 2000–2018

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

TABLE 6.13. *Salmonella enterica,* number of isolates 2000-2018.

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

TABLE 6.14. *Campylobacter* spp., number of isolates 2000-2018.

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

TABLE 6.15. Indicator *Escherichia coli,* number of isolates 2000-2018.

Source	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Cattle	293						314			223				197		101		85	
Pigs	260	308		303		390			349			167				200		140	
Pig meat									19			20							
Broilers	274	296	306		300			296			181		194		197		175		178
Broiler meat											77		92						
Laying hens													61						
Turkeys														55	59		85		66
Horses											274								
Dogs							257						74						
Willow grouse						19													
Wild boars		87																	
Sheep									115										

TABLE 6.16. Indicator *Enterococcus faecalis* and *E. faecium*, number of isolates 2000-2018 *(E. faecalis/E. faecium).*

Source	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
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 6.17. Clinical isolates from farmed animals, number of isolates 2000-2018.

Animal species & bacterial species	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Cattle																			
Escherichia coli (enteric)			220		87	39	24			40	15	15	58	30	29	36	29	31	14
Escherichia coli (uterine)														60					
Escherichia coli (milk)				169										142	95	113	74	79	100
Klebsiella spp. (milk)				44			24							41	39	41	36	34	52
Pasteurella spp.	254			100				27	32	14	27	80	37	39	39	46	104	86	79
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
Brachyspira hyodysenteriae	50	75	109	100		31	26	23	15	24	9	7	7	8	7	7	11	15	5
Brachyspira pilosicoli				93		57	72	44	31	24	13	16	17	12	13	7	17	21	22
Escherichia coli (enteric)	399	82	340	340	386	325	298	93	83	102	94	91	74	142	118	84	67	222	52
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	
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		
Flavobacterium columnare								30	16	10	5	8	3	5	9	4	3		
Flavobacterium psychrophilum								42	27	24	21	27	31	23	61	31	16	26	21

TABLE 6.18. Clinical isolates from companion animals and horses, number of isolates 2000-2018.

Animal species & bacterial species	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
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
Rhodococcus equi	73	20			187														
Streptococcus zooepidemicus	301	174	163	150	185	175	174	180	159	152	43	131	140	123	129	82	114	81	97
Staphylococcus aureus										308	131	135	145	139	132	116	75	127	118
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
Pasteurella canis															207	194	253	152	232
Pasteurella multocida					231										29	46	23		
Pseudomonas aeruginosa				234						261	313	353	178	309	389	355	349	306	366
Staphylococcus pseudintermedius (skin)	145	156	133	102	159	126	89	220	258	381	444	388	229	566	513	393	376	417	515
Staphylococcus pseudintermedius (external ear)																		648	784
Staphylococcus pseudintermedius (wound)																		844	1005
Staphylococcus schleiferi															297	201	163	175	240
Cats																			
Escherichia coli (urinary)			46	52	55	74	95	131	170	245	236	274	310	404	461	455	537	539	545
Beta-hemolytic streptococci												184							
Pasteurella dagmatis															20	22	19		
Pasteurella multocida															244	340	349	301	392
Staphylococcus felis															244	227	277	287	310

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SWEDRES|SVARM 2018

This annual report describes the monitoring of antibiotic resistance and antibiotic usage in human and veterinary medicine in Sweden in 2018.

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 to both humans and animals have continued to decrease, and favourable trends regarding prescribers' choices of antibiotics are broadly in line with policy and recommendations.

While the sales of antibiotics indicate positive progress, the trends concerning antibiotic resistance are more worrisome. Especially alarming is the number of cases of $ESBL_{CARBA}$ in humans, which has increased more than fivefold since the start of surveillance in 2012. This increases the risk of introducing $ESBL_{CARBA}$ among vulnerable patients, which can have serious consequences. So far, $ESBL_{CARBA}$ has never been isolated from Swedish animals.

This highlights once again that efforts to optimise antibiotic use, prevent infections, and minimise dissemination of antibiotic resistance must be ongoing and continually improved based on effective monitoring and best available knowledge. Furthermore, it confirms that Swedens' strategies to promote prudent use of antibiotics and for infection prevention and control are effective.

Focus areas:
- IMPACT – A Chinese-Swedish One Health collaboration on antibiotic resistance for sustainable change
- Changes to DDDs of antibiotics
- Reoccuring outbreaks of VRE – a problem in Swedish hospitals
- Organisation of national reference laboratory functions of importance for antibiotic resistance surveillance in Sweden
- ESBL-producing *E. coli* in lamb meat on the Swedish market

New features:
- Combined resistance
- New format antibiotic resistance in humans

The Public Health Agency of Sweden has a national responsibility for public health issues. The Agency promotes good public health by generating knowledge and disseminating it 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.