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SWEDRES | SVARM

Sales of antibiotics and occurrence of antibiotic resistance in Sweden

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

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Preface

Since 2002, the Swedish public health and veterinary sector has collaborated to produce the Swedres-Svarm report on the monitoring of antibiotic resistance and sales in human and veterinary medicine, integrating data from humans, animals and food in a joint analysis. This reflects decades of proactive and interdisciplinary work to mitigate the effects of antibiotic resistance where Sweden has been in the lead, long before the term One Health was coined. Additionally, the Svarm report, covering the monitoring of resistance in bacteria from animals was first issued two years earlier, and celebrates its 20th anniversary this year!

At the time when this preface is written, we are in the midst of the raging covid-19 pandemic. This crisis has exposed the vulnerabilities of our modern global society in an unprecedented way. Possibly this is the first time that humanity has jointly shared a similar experience, and while we are still in a very intense stage we can foresee that many things will change as a result. The outbreak has exposed our dependence on global supply chains and just-in-time deliveries, and how inability to maintain them impacts almost everything in our daily lives. Naturally, this also covers the availability of antibiotics. In the aftermath of the outbreak we can expect that the way society has functioned during the last three decades will be put under scrutiny, and that awareness will have increased of how quickly disruptive events like a pandemic, could impact our ability to care for the sick, the elderly and also for the general public.

On the positive side, there is a rising ambition with respect to antibiotic resistance monitoring in animals and food in the European Union. In December 2018, the new regulation on veterinary medicinal products was adopted by the European Parliament, now embracing prudent approaches such as a prohibition against routine usage of antibiotics to compensate for suboptimal management, and exclusion of antibiotics regarded as last resort in humans from veterinary usage – a requirement which also applies to third countries exporting to the EU. Other improvements relate to the reporting of antibiotic sales and usage data to the European Medical Products Agency, which has now been made compulsory, with an ambition to subsequently move towards reporting of species-specific data for animals. Furthermore, screening for carbapenemase-producing *Escherichia coli* in the EU-harmonised resistance monitoring programme, and a similar strengthening of monitoring activities for resistance in bacteria that are pathogenic to animals is discussed.

At the international level, within the framework of Codex Alimentarius, guidelines for monitoring of both usage of antibiotics and antibiotic resistance levels are being developed by FAO and OIE. This is an important contribution to the global combat against antibiotic resistance, and an incentive for the international community to participate.

Four years have passed since the Public Health Agency of Sweden became WHO Collaborating Centre for Antibiotic Resistance Containment, facilitating participation in, and implementation of, the Global AMR Surveillance System (GLASS). From 2021, Swedish resistance data from *Salmonella* and *Shigella* will be reported to GLASS together with data from invasive- and urinary tract infections. During the last years, monitoring of antibiotic resistance in humans has more and more come to rely on automated collection of all data from the clinical microbiology laboratories. This has saved work and enabled reporting of combined resistance as well as resistance in different age- and gender groups.

The covid-19 outbreak has also had direct impact on this report. Due to the workload on the Public Health Agency during the final stages there has been a need for compromises and prioritisation. For example, denominator data for humans will not be presented for 2019. We are all aware that 2020 will be a very different year, in many ways. By this time next year, we will have a clearer picture of how the covid-19 crisis has impacted the use of antibiotics for treatment of animals and humans. Whether the recently imposed changes in behaviour and mobility, which influences our exposure to resistant microbes, will have had an influence on antibiotic resistance patterns is also yet to be seen.

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Sammanfattning/Summary

Sammanfattning

När det gäller antibiotikaresistens hos bakterier från människor och djur har Sverige fortfarande en gynnsam situation vid en internationell jämförelse. En av anledningarna till detta är 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, vilket motiverar fortsatta ansträngningar inom förebyggande arbete. Ett viktigt exempel är de återkommande utbrotten av vankomycinresistenta enterokocker på sjukhus.

Antibiotikaförsäljningen 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 2019

- Det nationella genomsnittet för antibiotikaförsäljning till människor har fortsatt att minska.
- Antibiotikaförsäljningen inom tandvården fortsätter att visa en tydligt nedåtgående trend, som ytterligare minskat under 2019.
- Ökande antal fall av Enterobacteriaceae med ESBL-CARBA hos människor. Dessa är extremt resistenta och det finns få behandlingsalternativ vid en eventuell infektion. Tidigt upptäckt och förhindrande av smittspridning inom humansjukvården är därför viktigt.
- Flera mindre VRE-utbrott på sjukhus. VRE drabbar oftast känsliga patientgrupper där användningen av antibiotika är hög. Under året drabbades 10 patienter av blodförgiftning med VRE, sju av dessa orsakades av utbrottsstammar.
- Ökande mecillinamresistens hos Escherichia coli och Klebsiella pneumoniae från urin hos människor. Nivån är fortfarande låg men det är viktigt att följa utvecklingen då pivmecillinam är ett av förstahandsalternativen i behandlingsrekommendationen vid urinvägsinfektion.
- Försäljningen av antibiotika för användning till djur är stabilt låg och domineras av penicillin med smalt spektrum.
- MRSA är ovanliga hos både lantbrukets djur och sällskapsdjur.
- Den minskade förekomsten av ESBL-bildande E. coli i prov från slaktkyckling som setts de senaste åren fortsatte under 2019.
- Bakterier som bildar ESBL-CARBA har inte påvisats hos djur i Sverige.

Försäljning av antibiotika

Antibiotikaförsäljning inom humanmedicin

Den totala mängden antibiotika som såldes i Sverige minskade med 2,3 procent under 2019 och ligger nu på 11,1 DDD/1000 invånare och dag. I detta innefattas all antibiotika som sålts på recept till individer och på rekvisition till olika vårdinrättningar och särskilda boenden. Efter en period av restnoteringar har försäljningen av piperacillin-tazobactam (J01CR05) återigen ökat.

Öppenvård

Även antalet antibiotikarecept som hämtades ut på apotek minskade under 2019. Fördelningen av olika sorters antibiotika visar också på en ökad användning av de preparat som rekommenderas i första hand vid urinvägs- och luftvägsinfektioner. Försäljningen minskade mest bland de yngre åldersgrupperna jämfört med år 2018. Antalet recept per 1000 invånare i Sverige under 2019 var 285 och fortsätter att närma sig det nationella målet på 250 recept per 1000 invånare och år. Av de 21 regionerna låg en region under 250-målet 2019.

Den totala försäljningen av antibiotika på recept inom tandvården minskade med 4,4 procent jämfört med 2018, en minskning som pågått i flera år. Sedan år 2007 har den totala tandvårdsförsäljningen minskat med hälften.

De digitala vårdgivarna stod för ungefär 3 procent av förskrivningen av antibiotika inom öppenvården under 2019.

Sjukhus och andra vårdformer

Försäljningen av antibiotika på rekvisition till vårdinrättningar sjönk till 1,42 DDD per 1000 invånare och dag under 2019 och minskade därmed med 0,8 procent från 2018. Denna siffra omfattar framför allt försäljning av antibiotika som används till patienter på sjukhus och till en mindre del antibiotika som beställs till läkemedelsförråd på särskilda boenden och liknande inrättningar.

Antibiotikaförsäljningen till akutsjukhusen ligger på en jämn nivå, mätt som både DDD per 100 vårddagar och DDD per 100 vårdtillfällen. Försäljningen av de flesta antibiotikaklasser minskade mellan 2018 och 2019. En mindre ökning syns för kombinationer av penicilliner och för trimetoprim med sulfonaminder. Betalaktamasresistenta penicilliner (J01CF) är fortsatt den största antibiotikaklassen. Användningen av bredspektrumpreparat – cefalosporiner (J01DB-DE), karbapenemer (J01DH), fluorokinoloner (J01MA) och piperacillin-tazobactam (J01CR05) – visar stora regionala variationer. Även andelen smalspektrumpenicilliner mätt i DDD varierar stort mellan regionerna.

Antibiotikaförsäljning inom veterinärmedicin

Den rapporterade försäljningen av antibiotika för djur uppgick 2019 till 9 601 kilogram varav 58 procent var penicillin med smalt spektrum. Motsvarande värden för 2010 var 14 117 kilogram och 53 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 förändrats över tid. Under 90-talet minskade användningen av antibiotika som läkemedel till hela djurgrupper, och under det senaste decenniet ses också en minskad användning av antibiotika för behandling av enstaka djur.

Jämförelse av försäljning inom human- och veterinärmedicin

Under 2019 såldes 61,0 ton antibiotika för behandling av människor och 9,5 ton för behandling av djur (inkluderar inte produkter för intramammärt eller intrauterint bruk). Uttryckt i relation till kroppsvikt (milligram aktiv substans per skattad kilogram biomassa) var försäljningen 90,8 milligram per kilogram för människor och 12,0 milligram per kilogram för djur. Försäljning inom humanmedicin dominerade för alla inkluderade antibiotikaklasser utom för aminoglykosider.

Anmälningspliktig resistens

ESBL-producerande Enterobacteriaceae

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

Resultat 2019, Enterobacteriaceae med ESBL

- Antal rapporterade fall: 10 717 (föregående år 10 341), relativ förändring +3,6 procent.
- Antal fall med blodförgiftning: 835 (föregående år 703), relativ förändring +19 procent.
- Som tidigare år var Escherichia coli den vanligaste arten, 86 procent, följt av Klebsiella pneumoniae, 10 procent.

Resultat 2019, Enterobacteriaceae med ESBL-CARBA

- Antal rapporterade fall: 201 (föregående år 144), relativ förändring +40 procent.
- Antal fall med blodförgiftning: 6 (föregående år 7).
- Även bland Enterobacteriaceae med ESBL-CARBA var E. coli den vanligaste arten, 64 procent, följt av K. pneumoniae, 28 procent.

Bakterier som bildar ESBL är inte anmälningspliktigt vid fynd hos djur. Sådana bakterier är ovanliga hos djur i Sverige. Tidigare var förekomsten hos slaktkyckling hög men den har minskat under senare år. Under 2019 undersöktes förekomsten av ESBL-bildande E. coli i tarm- och köttprov från gris, i tarmprov från slaktkyckling samt i köttprov från nöt med selektiva metoder. Sådana bakterier hittades i 3 procent av tarmproven från såväl gris som slaktkyckling och i <1 respektive 0 procent av gris- och nötköttsproven med svenskt ursprung. 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 smittade med MRSA i Sverige, med två tredjedelar av fallen. Från 2015 rapporteras familje-/hushållssmitta och samhällsförvärvad smitta separat. Familje-/hushållssmitta utgjorde 33 procent av fallen.

Resultat 2019

- Antal rapporterade fall: 3 858 (föregående år 3 864), relativ förändring -0,2 procent.
- Antal fall med blodförgiftning: 72 (föregående år 64), relativ förändring +13 procent.

Förekomsten av MRSA hos djur i Sverige är fortfarande låg, vilket begränsar risken för spridning till människor. Under året isolerades MRSA sporadiskt från djurslagen hund, häst, katt, kanin och get. 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 2019 var antalet anmälda fall av meticillinresistenta Staphylococcus pseudintermedius (MRSP) hos djur på samma nivå som de senaste åren. Totalt anmäldes 48 fall av MRSP till Jordbruksverket, varav isolat från 42 (38 från hund, 3 från katt och 1 från häst) fanns tillgängliga för vidare undersökning. De första åren efter att MRSP hade hittats hos djur i Sverige var i princip alla fall av en viss sekvenstyp (ST71). Numera förekommer dock ett flertal olika sekvenstyper och ST71 har blivit mer ovanligt.

MRSP är inte anmälningspliktig vid förekomst hos människa.

Streptococcus pneumoniae med nedsatt känslighet för penicillin (PNSP)

Resultat 2019

- Antal rapporterade fall: 118 (föregående år 91), relativ förändring +30 procent.
- Antal fall med blodförgiftning: 9 (föregående år 3).
- Förändringar i metodologin för detektion av PNSP gör att fler fall rapporterats.
- En mindre smittspridning kopplat till en förskola rapporterades.

Enterococcus faecium och faecalis resistenta mot vankomycin (VRE)

Resultat 2019

- Totalt antal rapporterade fall: 232 (föregående år 444), relativ förändring -48 procent.
- Antal rapporterade fall av E. faecium med vankomycinresistens: 221 (föregående år 438), relativ förändring -50 procent.
- Antal rapporterade fall av E. faecalis med vankomycinresistens: 11 (föregående år 6).
- Antal fall med blodförgiftning: 10 (föregående år 9).
- Tjugotvå sjukhusrelaterade utbrott rapporterades under året. Fem utbrott med 5-15 fall vardera och de övriga var små smittspridningar med 2-4 fall vardera.

Resistens hos zoonotiska smittämnen

Salmonella är ovanligt hos djur i Sverige och isolerade stammar är oftast känsliga för antibiotika. Resistens mot antibiotikagruppen fluorokinoloner är mycket ovanlig och under 2019 påvisades för första gången överförbar resistens mot tredje generationens cefalosporiner, då i ett miljöprov från en gård. För Salmonella-arter var resistensen bland faecesisolat från människor högst mot kinoloner, 20 procent. Ingen resistens mot meropenem rapporterades. Salmonella från svenska djur är en osannolik källa till invasiva infektioner hos människor, bland annat på grund av skillnader i resistens där exempelvis kinolonresistens är 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 61 procent och mot tetracyklin 33 procent 2019. En procent var resistenta mot erytromycin.

Vanligtvis behandlas inte infektioner som orsakas av Salmonella eller Campylobacter med antibiotika, varken hos människor eller hos djur. Hos 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 mikrobiologiska laboratorierna och Folkhälsomyndigheten.

- Escherichia coli: Resistens hos blodisolat mot cefotaxim och ceftazidim var 7-8 procent, att jämföra med antalet anmälningar av E. coli ESBL från blod 2019: 700. Resistens mot ciprofloxacin är nu 14 respektive 11 procent hos isolat från blod respektive urin, ett observandum vid val av empirisk behandling av febril urinvägsinfektion.
- När E. coli från urin ålders- och könsfördelas ses vissa skillnader i resistens. Speciellt tydligt är den höga ciprofloxacinresistensen hos män, 20 år och äldre.
- Klebsiella pneumoniae: Resistens hos blodisolat mot cefotaxim och ceftazidim var 7 procent, att jämföra med antalet anmälningar av K. pneumoniae ESBL från blod 2019: 125. Liksom för E. coli är resistens mot ciprofloxacin nu relativt hög, 11 respektive 8 procent hos isolat från blod och urin, ett observandum vid val av empirisk behandling av febril urinvägsinfektion.
- En ökande mecillinamresistens ses hos både E. coli och K. pneumoniae från urin och är nu 5 respektive 10 procent.
- Staphylococcus aureus: Resistens mot cefoxitin (som indikerar MRSA) hos isolat från blod och prover från hud- och mjukdelar var under 2 procent, att jämföra med antalet anmälningar av MRSA från blod 2019: 72.
- Enterococcus faecalis och Enterococcus faecium: Vankomycinresistensen hos isolat från blod är fortsatt låg (0,1 respektive 1 procent) och den höggradiga aminoglykosidresistensen minskar.
- 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 och grisar. Resistensundersökning är motiverat för val av lämpligt antibiotikum vid behandling, särskilt för stafylokocker, E. coli och Brachyspira spp.

Indikatorbakterier från friska djur

Resistens hos E. coli i tarmfloran hos friska djur kan användas som indikator för utbredningen av antibiotikaresistens hos bakteriefloran i en djurpopulation och indirekt som indikator på omfattningen av antibiotikaanvändning till djuren. I Sverige är förekomsten av resistens hos dessa indikatorbakterier låg hos de flesta undersökta djurslag och situationen är gynnsam ur ett internationellt perspektiv.

Summary

The situation in Sweden regarding antibiotic resistance in bacteria from 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 in hospitals.

In the last decades the sales of antibiotics in Sweden have decreased for both humans and for animals. In addition, the sales of broad-spectrum antibiotics have decreased while the use of narrow-spectrum antibiotics have 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 2019

- The national average for antibiotic prescriptions to humans continued to decrease in 2019.
- The sales of antibiotics in dentistry show a trend downwards, which has continued to decrease.
- Increasing numbers of Enterobacteriaceae with $ESBL_{CARBA}$ in humans. These are extremely resistant and there are few treatment options in case of infection. Early detection and prevention of the spread within human health care is therefore important.
- Several small VRE outbreaks in hospitals. VRE usually affects sensitive patient groups where the use of antibiotics is high. During the year, VRE caused septicemia in ten patients, seven of which were caused by outbreak strains.
- Increasing mecillinam resistance in *Escherichia coli* and *Klebsiella pneumoniae* from urine from humans. The levels are still quite low but it is of importance to continue to follow this trend as pivmecillinam is one of the recomended first-line treatments for urinary tract infections.
- Sales of antibiotics for animals are stable at a low level and dominated by narrow-spectrum penicillin.
- MRSA is unusual among both farm and companion animals.
- The decreased occurence of ESBL-producing *E. coli* in samples from broilers that has been seen in the latest years continued in 2019.
- $ESBL_{CARBA}$-producing bacteria have not been detected in animals in Sweden.

Sales of antibiotics

Sales of antibiotics for humans

The total sales of antibiotics for humans in Sweden were 2.3% lower in 2019 and are now 11.1 DDD per 1 000 inhabitants per day. This figure encompasses all antibiotics sold on prescriptions to individuals, as well as antibiotics sold to hospitals and other health care facilities for dispensing to patients and clients. After a shortage of combinations of penicillins (J01CR), the sales of this antibiotic subclass has now increased.

Outpatient care

A decrease was seen among the sales of antibiotics in outpatient care in 2019. The distribution of use of the different antibiotic classes shows a trend towards an increased use of first-line antibiotics. Compared to 2018, the biggest decrease of sales in the different age groups is found among children. The national average sales in prescriptions per 1 000 inhabitants per year were 285 in 2019 and continue to decrease. One region was below the long-term target of 250 prescriptions per 1000 inhabitants per year.

The sales of antibiotics in dentistry have decreased for several years and continued to do so in 2019 by an additional 4.4%, compared with 2018. Since 2007 the sales in dentistry have been reduced by half.

Around 3% of prescriptions in outpatient care were issued in telemedicine in 2019.

Hospitals and other health and social care facilities

In 2019, the sales of antibiotics on requisition decreased to 1.42 DDD per 1 000 inhabitants per day, a decrease of 0.8% compared with 2018. This reflects all antibiotics sold for dispensing in hospitals, nursing homes and other healthcare facilities.

The sales of antibiotics to acute care hospitals show an even level, expressed both as DDD per 100 patient-days and as DDD per 100 admissions. An increase is seen among combinations of penicillins and trimethoprim with sulphonamides. Beta-lactamase resistant penicillins (J01CF) still represent the highest number of DDDs. There are large differences in sales of antibiotics between Swedish acute care hospitals, for example in the relative use of narrow-spectrum penicillins. The use of broad-spectrum antibiotics – cephalosporins, carbapenems, fluoroquinolones and piperacillin-tazobactam – also shows regional variation in terms of which substances are used.

Sales of antibiotics for animals

In 2019, reported sales of antibiotics for animals were 9 601 kg, of which 58% were penicillins with narrow-spectrum. The corresponding figures for 2010 were 14 117 kg and 53%, respectively.

Since the withdrawal of growth-promoting antibiotics from the Swedish 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 sales of antibiotics in human and veterinary medicine

In 2019, a total of 61.0 tonnes of antibiotics were sold for human use and 9.5 tonnes were sold for animal use (excluding products for intramammary or intrauterine use). Measured as milligrams of active substance per kilogram biomass, the sales were 90.8 and 12.0 milligrams per kilogram, respectively. Antibiotic sales for humans still dominate for all included classes of antibiotics except for aminoglycosides.

Notifiable resistance

ESBL-producing Enterobacteriaceae

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

Results 2019, Enterobacteriaceae with ESBL

- Number of reported cases: 10 717 (previous year 10 341), relative change +3.6%.
- Number of bloodstream infections: 835 (previous year 703), relative change +19%.
- As in previous years, *Escherichia coli* was the most common species, 86%, followed by *Klebsiella pneumoniae*, 10%.

Results 2019, Enterobacteriaceae with $ESBL_{CARBA}$

- Number of reported cases: 201 (previous year 144), relative change +40%.
- Number of bloodstream infections: 6 (previous year 7).
- Among Enterobacteriaceae with $ESBL_{CARBA}$, *E. coli* was the most common species, 64%, followed by *K. pneumoniae*, 28%.

ESBL-producing Enterobacteriaceae are rare among animals in Sweden. Previously, the occurrence in intestinal samples from broilers was high but it has decreased in recent years. In 2019, the occurrence of ESBL-producing *E. coli* in intestinal samples from pigs and broilers, as well as samples of pork and beef was investigated with screening methods. Such bacteria were isolated from 3% of the intestinal samples from pigs and broilers respectively, and <1% and 0 % of the pork and beef samples of Swedish origin.

MRSA

Community-acquired infection has long been the most common type in humans, with two-thirds of the cases. In 2015, community-acquired infection was divided into family-/household-related infection and community-acquired infection. Family-/household-related infections accounted for 33% of the cases.

Results 2019

- Number of reported cases: 3 858 (previous year 3 864), relative change -0.2%.
- Number of bloodstream infections: 72 (previous year 64), relative change +13%.

The occurrence of MRSA in animals in Sweden is still low, which limits the spread from animals to humans. MRSA was found sporadically in dog, cat, horse, rabbit and goat in 2019, 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 2019, the number of reported cases of methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) in animals was around the same level as in previous years. In total 48 cases of MRSP were notified to the Swedish Board of Agriculture, and isolates from 42 cases (38 dogs, 3 cats and 1 horse) were available for further investigations. 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 2019

- Number of reported cases: 118 (previous year 91), relative change +30%.
- Number of bloodstream infections: 9 (previous year 3).
- Changes in the methodology for detection of PNSP resulted in more cases reported.
- One small outbreak in a preschool was reported.

VRE

Results 2019

- Total number of reported cases: 232 (previous year 444), relative change -48%.
- Number of reported cases of *E. faecium* with vancomycin resistance: 221 (previous year 438), relative change -50 %.
- Number of reported cases of *E. faecalis* with vancomycin resistance: 11 (previous year 6).
- Number of bloodstream infections: 10 (previous year 9).
- Twenty-two hospital-related outbreaks were reported during the year. Five outbreaks with 5-15 cases each and the remaining were small clusters with 2-4 cases each.

Zoonotic pathogens

Salmonella is rare in animals in Sweden, and only a few of the incidents involve antibiotic-resistant strains. Resistance to fluoroquinolones is rare and in 2019 a strain with ESBL resistance was for the first time detected, this in an environmental sample from a farm. For *Salmonella* species isolated from human faeces the highest occurrence of resistence was against quinolones, 20%. No resistance to meropenem was reported. 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. In *Campylobacter jejuni* from humans, resistance to ciprofloxacin was 61% and to tetracycline 33% in 2019. One percent was resistant to erythromycin.

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

Human clinical isolates

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

- *Escherichia coli*: resistance in blood isolates to cefotaxime and ceftazidime was 7-8 percent, to compare with the number of reported *E. coli* ESBL from blood 2019: 700. Resistance to ciprofloxacin is now 14% and 11%, respectively, in isolates from blood and urine. This needs to be noted when choosing empirical treatment for febrile urinary tract infection.
- When *E. coli* from urine are age and gender distributed, some differences in resistance are seen. Most prominent is the high ciprofloxacin resistance seen among men, 20 years and older.
- *Klebsiella pneumoniae*: resistance in blood isolates to cefotaxime and ceftazidime was 7%, to compare with the number of reported *K. pneumoniae* ESBL from blood 2019: 125. As for *E. coli*, resistance to ciprofloxacin is now relatively high, 8-10% in isolates from blood and urine.
- *Staphylococcus aureus*: Resistance to cefoxitin (which is indicative of MRSA) in isolates from blood and samples from skin and soft tissue was below 2%, to compare with the number of reported MRSA from blood 2019: 72.
- *Enterococcus faecalis* and *Enterococcus faecium*: Vancomycin resistance in isolates from blood remains low (0.1 and 1%, respectively) and the high-lewel aminoglycoside resistance decreases.
- *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 and pigs. Susceptibility testing for guidance in antibiotic therapy is warranted, especially for staphylococci, *E. coli* and *Brachyspira* spp.

Indicator bacteria from healthy animals

Antibiotic resistance in *E. coli* from the intestinal flora of healthy animals serves as an indicator for the presence of resistance in an animal population. The prevalence of acquired resistance in such commensal bacteria also indirectly indicates the magnitude of the selective pressure from the use of antibiotics in an animal population. The prevalence of resistance in indicator bacteria from animals in Sweden is low, and the situation is favourable in an international perspective.

Guidance for readers

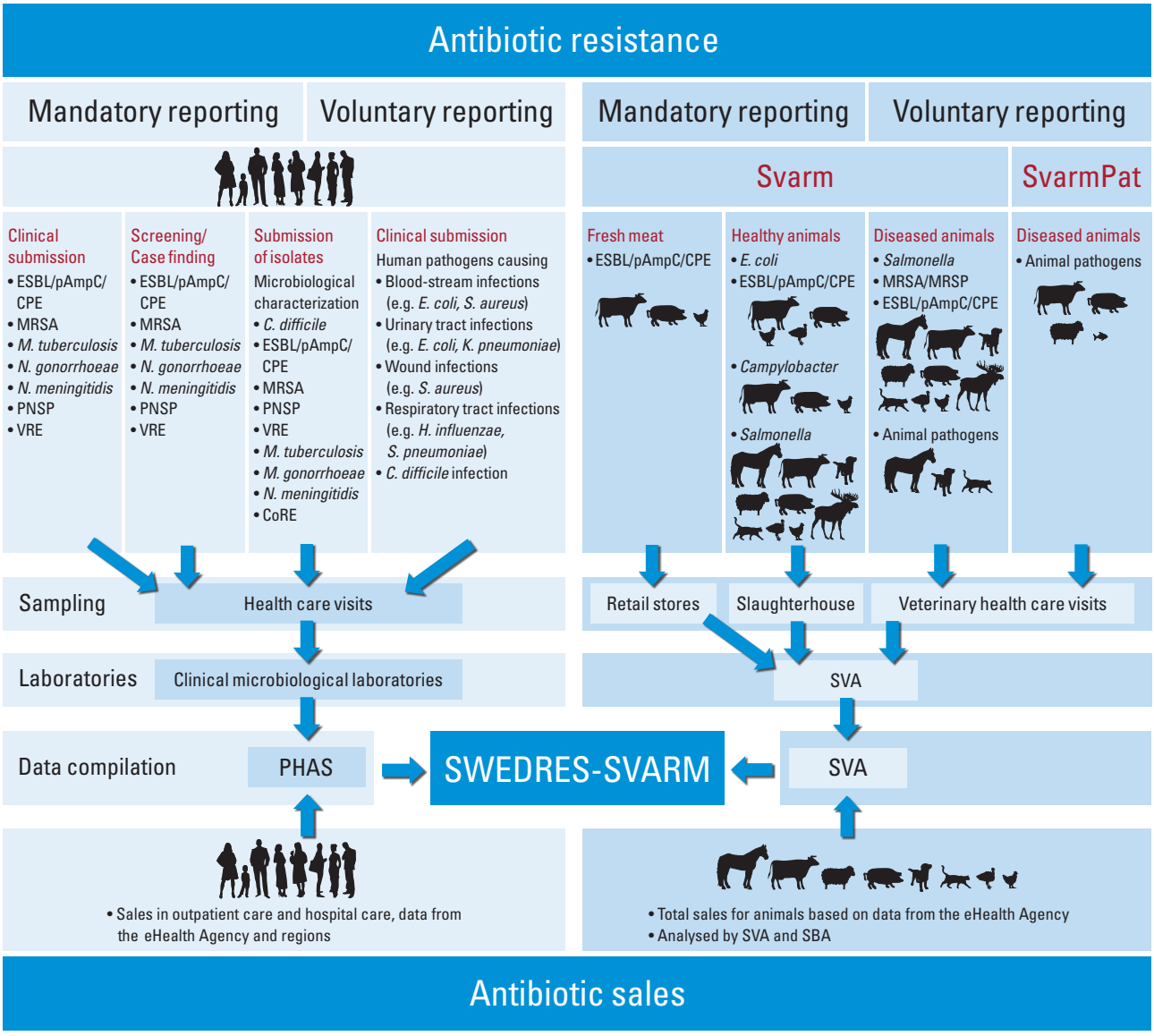
The Swedres-Svarm report is the result of a cooperation between the Public Health Agency of Sweden and the National Veterinary Institute with the aim to present data relating to both humans and animals on the sales of antibiotics and on antibiotic resistance in a joint report.

Data on occurrence of notifiable 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.

Schematic view of antimicrobial sales and resistance monitored in Sweden 2019.

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



Embedded files in the PDF-file version of the report

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

Antibiotic sales

Antibacterials for systemic use in humans are indexed as J01 in the Anatomical Therapeutic Chemical classification system. The J01 group also includes the antiseptic substance methenamine, which is not an antibiotic and 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 sales 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. These sales are 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 are displayed (children 0-6 years, women 15-79 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 sales to hospitals in Sweden are combined with sales to some nursing homes and other facilities, the figures are not suitable for evaluation of antibiotic use in hospital care. Therefore, data on sales exclusively to acute care hospitals have been provided by pharmacists in local Strama groups in all regions.

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

Antibiotic resistance

Swedres - Humans

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

Svarm - Animals and food

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

Abbreviations

AST	Antimicrobial susceptibility testing
ATC	Anatomical therapeutic chemical classification system
BSI	Blood stream infection
CDI	*Clostridioides difficile* infection
CPE	Carbapenemase producing Enterobacteriaceae
CSF	Cerebrospinal fluid
DDD	Defined daily dose
ECDC	European Centre for Disease Prevention and Control
ECOFF	Epidemiological cut-off value for non-susceptibility
EARS-Net	European antimicrobial resistance surveillance network
EMA	The European Medicines Agency
EPIS AMR-HAI	Epidemic Intelligence Information System for Antimicrobial Resistance and Healthcare-associated Infections
ESC	Extended spectrum cephalosporin
ESBL	Extended spectrum beta-lactamase
$ESBL_A$	Extended spectrum beta-lactamase, plasmid-mediated, inhibited by clavulanic acid (A = classical)
$ESBL_M$	Extended spectrum beta-lactamase inhibited by cloxacillin, also called plasmid-mediated AmpC (M = miscellaneous)
$ESBL_{CARBA}$	Extended spectrum beta-lactamase with activity against carbapenems
EUCAST	European Committee on Antimicrobial Susceptibility Testing
GAS	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
PHAS	The Public Health Agency of Sweden
PNSP	Penicillin non-susceptible *Streptococcus pneumoniae*
PVL	Panton-Valentine leukocidin
ResNet	Webb application for Resistance surveillance and quality control programme
RTI	Respiratory tract infection
spa	*Staphylococcus aureus* protein A gene
SSTI	Skin and soft tissue infection
ST	Sequence type
Strama	Swedish strategic programme against antibiotic resistance
SVA	Statens veterinärmedicinska anstalt (National veterinary institute)
Svarm	Swedish veterinary antibiotic resistance monitoring programme
Swedres	Swedish utilisation and resistance in human medicine
TB	Tuberculosis
UTI	Urinary tract infection
VRE	Vancomycin resistant enterococci
XDR	Extreme drug resistance (used for *Mycobacterium tuberculosis*)

Sales of antibiotics for humans

Total sales of antibiotics for humans

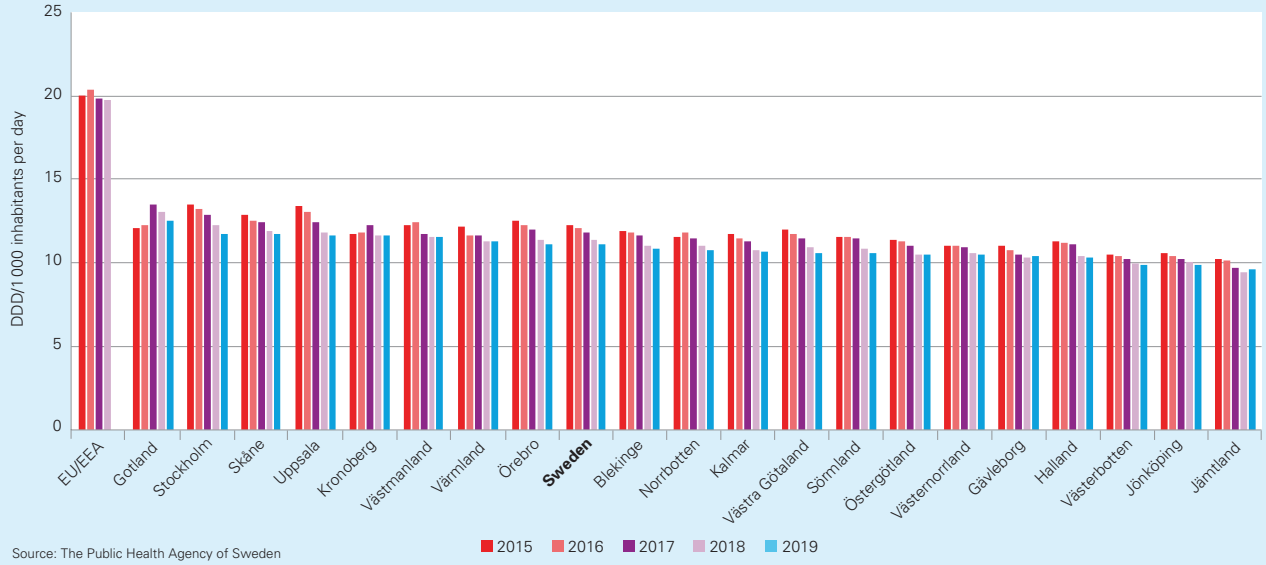
Results

- The total sales of antibiotics (J01 excl. methenamine) decreased with 2.3% compared with 2018 (from 11.3 DDD to 11.1 DDD per inhabitants per year), Figure 1.1.
- The sales of fluoroquinolones and cephalosporins continues to decrease and sales of combinations of penicillins are increasing, Figure 1.2.
- Beta-lactamase sensitive penicillins and tetracyclines were the two most sold antibiotic classes in Sweden during 2019, despite decreased sales, Figure 1.2.

Comments

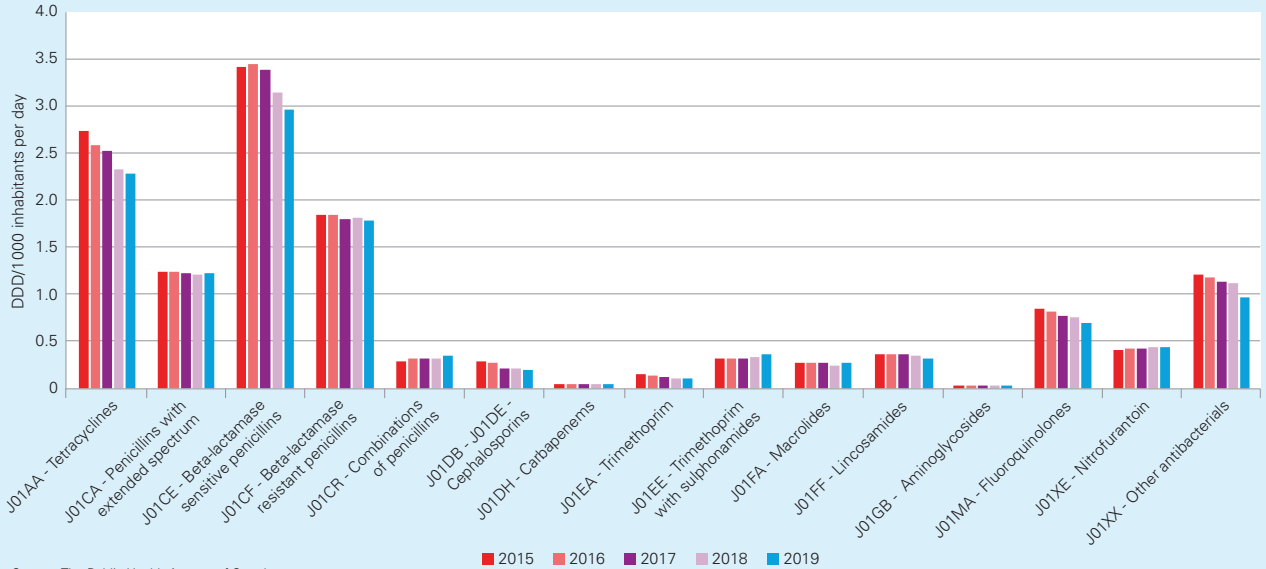
The 2019 data on antibiotic sales add to an overall downward trend in Sweden. A comparison with the annual number, population-weighted mean, in the EU/EEA countries 2015-2018 (ECDC, 2019), gives an indication of Sweden's restrictive position regarding antibiotic prescribing. However, there are considerable differences between the regions in Sweden with total sales ranging from 12.5 to 9.6 DDD per 1 000 inhabitants per day, Figure 1.1.

FIGURE 1.1. Sales of antibiotics (J01 excl. methenamine) for humans, all genders, per region, 2015-2019, DDD/1 000 inhabitants per day. Data include prescriptions to individuals as well as antibiotics dispensed in hospitals, nursing homes etc. Region Dalarna is not included in the statistics showing total sales.



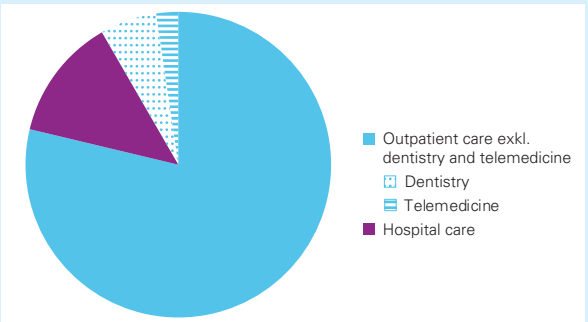
Source: The Public Health Agency of Sweden

FIGURE 1.2. Sales of antibiotics for humans, all genders, ATC-5, 2015-2019, DDD/1 000 inhabitants per day. Data include prescriptions to individuals as well as antibiotics dispensed in hospitals, nursing homes etc. Region Dalarna is not included in the statistics showing total sales.



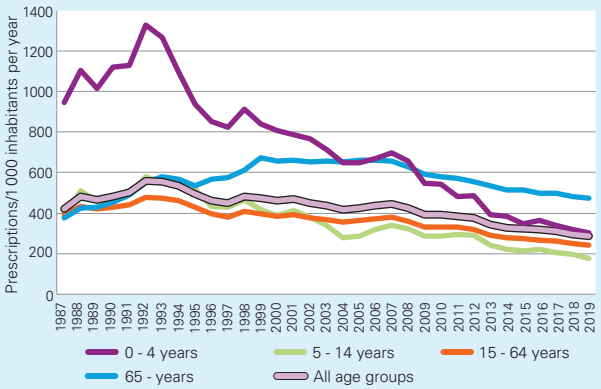
Source: The Public Health Agency of Sweden

FIGURE 1.3. Proportion of sales of antibiotics (J01 excl. methenamine) for humans, all genders, hospital care and outpatient care, dentistry and telemedicine extracted from outpatient care, DDD/1 000 inhabitants per day, 2019. Region Dalarna is not included in the statistics showing total sales.



Source: The Public Health Agency of Sweden

FIGURE 1.4. Sales of antibiotics (J01 excl. methenamine) for humans, all genders, per age, 1987-2019, prescriptions/1 000 inhabitants per year.



Source: The Public Health Agency of Sweden

Antibiotics in outpatient care

Total sales

Results

- The sales of antibiotics in outpatient care were 3.5% lower in 2019 than in 2018.
- A decrease can be seen in several antibiotic classes, with the biggest decrease in antibiotics commonly prescribed to treat respiratory tract infections.
- The trend towards increased use of first-line antibiotics against urinary tract infections continues.

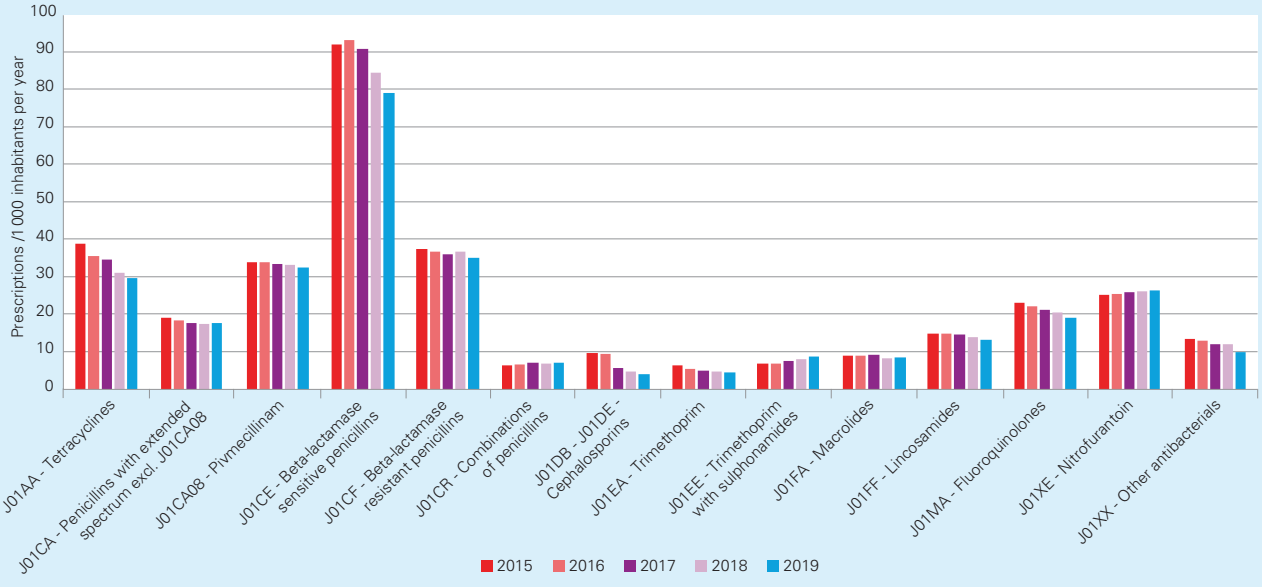
Comments

The statistics for outpatient care includes all sales of antibiotics on prescriptions issued to individuals; both from healthcare centres in the community and from hospitals. Since 1992, when the total sales of antibiotics on prescriptions peaked, the sales have decreased by 49%, Figure 1.4. The greatest change during these years is seen among young children (the age group 0-4 years), where sales decreased from 1 328 prescriptions per 1 000 inhabitants per year in 1992 to 301 in 2019. In the last year, the biggest change can be seen in the age group 5-14 years, with a decrease of 10.5%. The total number of prescriptions per 1 000 inhabitants per year for all age groups was 285 in 2019.

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).

Persistent availability problems affecting cefadroxil, as well as the withdrawal of ceftibuten in 2017, may partly explain the lower sales of cephalosporins (J01DB-DE) in outpatient care. Measured in prescriptions, beta-lactamase sensitive penicillins (J01CE) and beta-lactamase resistant penicillins (J01CF) were the most commonly sold antibiotics. If measured in

FIGURE 1.5. Sales of antibiotics for humans, all genders, ATC-5, 2015-2019, prescriptions/1 000 inhabitants per year.



Source: The Public Health Agency of Sweden

DDD per 1000 inhabitants per day, beta-lactamase sensitive penicillins (J01CE) and tetracyclines (J01AA) were the most commonly sold antibiotics in 2019. Doxycycline (J01AA02) represents the major part of the tetracycline DDDs, Figure 1.5 and Table 1.1.

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

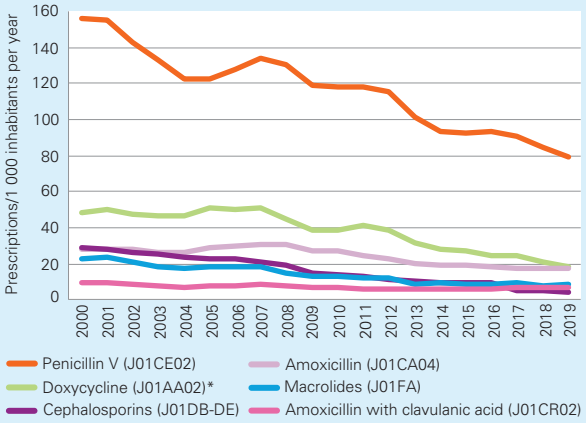
Results

- Narrow-spectrum penicillin (J01CE) decreased by 6.3% and the overall sales of RTI antibiotics decreased by 5.6% compared with 2018.
- Antibiotics commonly prescribed against UTIs in women have decreased by 2.6% in the last year.

Comments

Antibiotics commonly used to treat respiratory tract infections (RTIs) are overall the most frequently prescribed antibiotics in Sweden. The antibiotics included in this measure are doxycycline (J01AA02; excluding packages larger than 50 tablets), penicillin V (J01CE02), amoxicillin (J01CA04), amoxicillin with enzyme inhibitor (J01CR02), cephalosporins (J01DB-DE), and macrolides (J01FA), Figure 1.6. The sales of these antibiotic classes have decreased significantly ($p < 0.001$) in the latest years, except for amoxicillin with enzyme inhibitor, which shows a slight increase, Figure 1.6.

Figure 1.6. Sales of antibiotics commonly used to treat respiratory tract infections, humans, all genders, 2000-2019, per year, prescriptions/ 1 000 inhabitants per year.

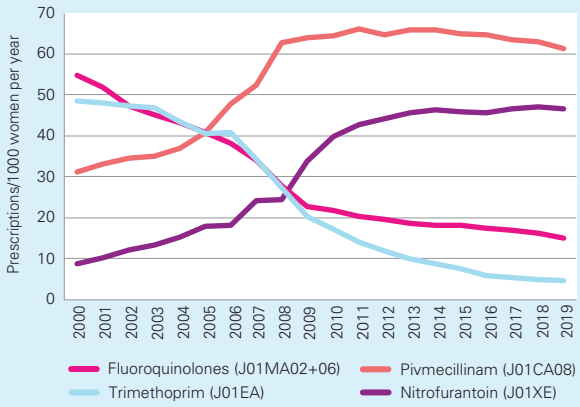


*Doxycycline (J01AA02) excl.packages with more than 50 tablets.
Source: The Public Health Agency of Sweden

Narrow-spectrum penicillin, (J01CE), is the recommended first-line antibiotic for treatment of lower RTIs in Sweden (Swedish Medical Products Agency, 2008) and the most frequently prescribed antibiotic in outpatient care, measured both in DDD per 1 000 inhabitants per day and in prescriptions per 1 000 inhabitants per year, Figure 1.6 and Table 1.1. Beta-lactamase resistant penicillins (J01CF) was the second most frequently prescribed antibiotic in outpatient care measured in prescriptions per 1 000 inhabitants. The sales of this class decreased by 4.2% in 2019 compared with 2018.

National treatment recommendations for urinary tract infections (Swedish Medical Products Agency, 2017), recommends pivmecillinam (J01CA08) and nitrofurantoin (J01XE01) over trimethoprim (J01EE01) against UTIs in women aged 15 years or older and the trend towards increased use of first-line antibiotics continues, Figure 1.7.

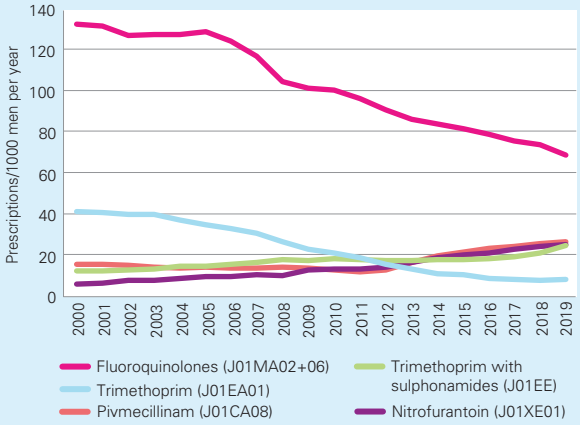
Figure 1.7. Sales of antibiotics commonly used to treat urinary tract infections in women, humans, 15-79 years, 2000-2019, per year, prescriptions/1 000 women per year.



Source: The Public Health Agency of Sweden

The total sales of antibiotics commonly used to treat UTIs in men aged 65 years and older have decreased since 2000, but in the latest years a slight increase has been seen in all classes except trimethoprim and fluoroquinolones. Fluoroquinolones continue to decrease significantly ($p < 0.001$), by 6.7% from 2018 to 2019. As nitrofurantoin and pivmecillinam are now recommended as first-line antibiotics for treatment of symptomatic UTI without fever in men (Swedish Medical Products Agency, 2017), the increased use is in line with treatment recommendations. The increase of sales of first-line antibiotics is significant ($p < 0.001$) and the rate gets higher over time, Figure 1.8.

Figure 1.8. Sales of antibiotics commonly used to treat urinary tract infections in men, 65 years and older, humans, 2000-2019, per year, prescriptions/1 000 men per year.



Source: The Public Health Agency of Sweden

Table 1.1. Sales of antibiotics in outpatient care, humans, all genders, by antibiotic class or substance, age groups, per year, 2015-2019, 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				
	2015	2016	2017	2018	2019	2015	2016	2017	2018	2019	2015	2016	2017	2018	2019
Tetracyclines (J01AA)															
0-6	0.00	0.00	0.01	0.01	0.01	0.05	0.07	0.28	0.30	0.31	0.04	0.06	0.22	0.23	0.23
7-19	2.59	2.67	2.65	2.59	2.72	23.30	23.18	22.77	21.24	21.96	14.58	14.79	15.04	14.09	14.59
20-64	2.78	2.55	2.47	2.26	2.21	41.40	37.54	35.75	32.00	30.47	31.58	29.09	27.84	25.09	23.98
65-79	3.02	2.78	2.82	2.54	2.44	59.88	54.30	54.90	49.12	45.74	44.86	41.62	42.27	38.10	35.45
80-	2.06	1.90	2.05	1.90	1.80	47.99	43.79	46.88	42.47	40.11	38.40	35.20	37.41	34.25	32.19
All age groups	2.55	2.40	2.35	2.16	2.14	38.73	35.57	34.59	31.06	29.69	28.79	26.75	26.27	23.77	22.72
Penicillins with extended spectrum (J01CA) excl. pivmecillinam (J01CA08)															
0-6	0.67	0.67	0.63	0.65	0.61	40.17	40.12	37.56	38.73	35.82	30.27	30.22	28.35	29.08	27.07
7-19	0.21	0.21	0.21	0.21	0.20	8.22	8.14	7.81	7.89	7.22	6.43	6.39	6.06	6.08	5.63
20-64	0.37	0.35	0.34	0.34	0.36	13.05	12.16	11.75	11.36	11.96	10.22	9.57	9.25	8.90	9.39
65-79	0.97	0.94	0.96	0.95	0.99	32.55	31.10	31.02	30.01	30.71	24.55	23.87	24.11	23.14	23.67
80-	1.20	1.17	1.24	1.23	1.36	38.05	36.18	37.65	37.04	39.09	30.13	28.67	29.99	29.45	30.54
All age groups	0.51	0.49	0.49	0.49	0.51	19.03	18.23	17.69	17.34	17.70	14.48	13.92	13.63	13.31	13.49
Pivmecillinam (J01CA08)															
0-6	0.01	0.02	0.02	0.02	0.02	1.07	1.21	1.42	1.71	1.60	0.99	1.13	1.28	1.56	1.47
7-19	0.19	0.19	0.19	0.19	0.18	12.74	12.69	12.89	12.71	12.36	10.94	11.06	11.24	11.13	10.86
20-64	0.47	0.47	0.47	0.46	0.45	29.40	29.49	29.12	28.80	28.30	24.13	24.33	24.04	23.84	23.57
65-79	1.01	1.02	1.00	1.00	0.98	59.35	59.05	58.28	58.31	56.68	43.12	43.66	43.27	43.37	42.26
80-	1.91	1.94	1.92	1.92	1.90	114.15	114.21	113.02	112.75	111.29	81.37	81.61	81.04	80.78	80.17
All age groups	0.55	0.56	0.55	0.54	0.53	33.73	33.83	33.33	33.07	32.42	26.00	26.23	25.99	25.87	25.48
Beta-lactamase sensitive penicillins (J01CE)															
0-6	2.60	2.89	2.68	2.53	2.33	195.54	209.30	196.07	185.01	171.14	146.37	155.69	147.11	139.97	130.92
7-19	2.61	2.72	2.63	2.43	2.20	92.88	96.85	92.47	86.04	76.35	73.28	77.04	73.43	68.72	61.39
20-64	3.22	3.19	3.17	2.93	2.76	77.19	76.54	75.78	70.27	66.47	65.30	65.21	64.67	59.89	56.69
65-79	3.62	3.51	3.61	3.36	3.26	84.39	81.39	83.98	77.92	75.51	69.49	68.14	70.50	65.60	63.41
80-	3.17	3.05	3.10	3.05	2.97	76.71	73.38	74.34	72.69	70.74	65.08	62.27	63.46	62.12	59.69
All age groups	3.19	3.20	3.15	2.93	2.76	92.07	93.22	90.77	84.43	79.09	73.85	74.78	73.67	68.84	64.71
Beta-lactamase resistant penicillins (J01CF)															
0-6	0.24	0.24	0.27	0.28	0.24	24.84	23.91	27.26	28.35	24.06	19.53	19.01	21.61	22.27	18.94
7-19	0.74	0.74	0.72	0.73	0.72	26.25	25.43	25.20	26.24	24.97	20.91	20.42	20.04	20.95	19.88
20-64	1.26	1.25	1.21	1.22	1.20	30.83	30.31	29.57	29.98	29.14	24.28	24.07	23.43	23.87	23.14
65-79	2.69	2.64	2.54	2.60	2.54	54.87	53.36	51.95	53.19	51.03	35.45	35.38	34.39	35.67	33.92
80-	5.22	5.26	5.23	5.21	5.13	101.59	100.41	99.14	98.77	94.99	61.23	61.19	59.86	60.88	58.73
All age groups	1.54	1.53	1.48	1.49	1.46	37.40	36.73	36.05	36.61	35.06	26.92	26.67	26.25	26.92	25.71
Combinations of penicillins (J01CR)															
0-6	0.12	0.12	0.13	0.10	0.12	11.55	11.52	12.85	9.25	10.98	7.23	6.90	7.68	5.70	6.45
7-19	0.10	0.10	0.11	0.11	0.11	4.11	4.21	4.76	4.07	4.42	2.67	2.73	2.81	2.56	2.56
20-64	0.16	0.17	0.18	0.19	0.19	5.14	5.32	5.59	5.71	5.80	4.07	4.27	4.45	4.54	4.66
65-79	0.27	0.30	0.33	0.35	0.38	8.19	8.81	9.90	9.96	10.57	5.98	6.39	7.15	7.23	7.57
80-	0.26	0.29	0.35	0.39	0.42	7.63	8.79	10.14	10.97	12.19	5.76	6.55	7.46	8.03	9.01
All age groups	0.17	0.18	0.20	0.21	0.22	6.19	6.47	7.02	6.72	7.12	4.50	4.69	5.03	4.92	5.15
Cephalosporins (J01DB-DE)															
0-6	0.25	0.24	0.03	0.01	0.01	25.00	24.25	2.94	1.03	0.74	20.73	19.99	2.55	0.81	0.54
7-19	0.13	0.13	0.05	0.04	0.03	8.99	8.95	3.73	2.62	1.84	7.22	7.10	3.11	2.20	1.53
20-64	0.11	0.11	0.08	0.07	0.06	6.57	6.38	5.09	4.61	3.82	5.31	5.14	4.09	3.71	3.01
65-79	0.18	0.17	0.12	0.10	0.09	9.65	9.37	7.48	6.67	5.83	6.91	6.89	5.57	4.92	4.20
80-	0.29	0.30	0.21	0.19	0.16	17.43	17.64	13.61	12.54	10.54	13.19	13.17	10.39	9.65	8.15
All age groups	0.14	0.14	0.08	0.07	0.06	9.58	9.40	5.55	4.76	3.94	7.52	7.33	4.36	3.72	3.02

Age groups (years)	DDD/1 000 per day					Prescriptions/1 000 per year					User/1 000 per year				
	2015	2016	2017	2018	2019	2015	2016	2017	2018	2019	2015	2016	2017	2018	2019
Trimethoprim (J01EA)															
0-6	0.06	0.06	0.06	0.06	0.05	8.09	7.51	7.80	8.22	7.00	6.10	5.59	5.80	6.15	5.22
7-19	0.04	0.03	0.03	0.03	0.02	2.34	1.94	1.87	1.73	1.50	1.82	1.56	1.39	1.29	1.14
20-64	0.09	0.07	0.06	0.06	0.05	3.34	2.56	2.22	2.02	1.88	2.53	1.91	1.65	1.49	1.37
65-79	0.31	0.25	0.24	0.23	0.22	11.84	9.48	8.95	8.26	8.36	8.05	6.49	5.91	5.57	5.55
80-	0.69	0.62	0.58	0.54	0.55	32.65	30.30	28.37	26.38	27.70	17.09	14.21	12.92	12.36	12.78
All age groups	0.14	0.12	0.11	0.10	0.10	6.37	5.35	4.98	4.67	4.54	4.28	3.47	3.16	3.00	2.86
Trimethoprim with sulphonamides (J01EE)															
0-6	0.08	0.07	0.09	0.09	0.09	8.73	8.06	10.32	10.96	10.12	4.84	4.56	6.60	7.03	6.46
7-19	0.10	0.10	0.11	0.11	0.11	3.85	3.80	4.62	4.77	4.72	1.90	1.81	2.25	2.29	2.22
20-64	0.21	0.20	0.20	0.21	0.22	4.84	4.87	5.11	5.32	5.67	2.61	2.66	2.78	2.89	3.15
65-79	0.60	0.62	0.62	0.67	0.73	13.21	13.66	14.53	15.57	17.82	8.37	8.86	9.23	9.81	11.15
80-	0.53	0.55	0.54	0.62	0.74	13.06	13.98	14.92	16.74	20.87	9.75	10.25	10.68	11.51	13.84
All age groups	0.26	0.26	0.26	0.28	0.30	6.78	6.85	7.44	7.86	8.55	3.90	3.99	4.37	4.61	5.01
Macrolides (J01FA)															
0-6	0.23	0.25	0.26	0.24	0.19	11.13	11.61	12.45	11.55	9.89	8.50	8.97	9.54	8.61	7.23
7-19	0.21	0.22	0.22	0.19	0.18	8.30	8.70	9.35	7.79	7.06	5.74	6.09	6.49	5.13	4.71
20-64	0.23	0.23	0.21	0.19	0.23	8.86	8.39	8.23	7.48	7.86	6.50	6.30	6.30	5.66	6.10
65-79	0.30	0.29	0.32	0.28	0.35	8.98	8.34	9.04	8.33	9.18	5.70	5.40	5.65	4.98	5.80
80-	0.21	0.22	0.22	0.21	0.27	6.47	6.33	6.61	6.40	7.63	4.24	3.97	4.45	3.87	4.91
All age groups	0.24	0.24	0.24	0.22	0.25	8.98	8.91	9.19	8.16	8.35	6.32	6.24	6.41	5.63	5.88
Lincosamides (J01FF)															
0-6	0.02	0.02	0.04	0.03	0.04	4.75	5.03	7.66	7.07	7.76	3.33	3.70	5.70	5.40	6.01
7-19	0.11	0.11	0.12	0.11	0.11	7.11	7.22	7.72	7.37	7.26	5.43	5.70	6.00	5.75	5.61
20-64	0.30	0.30	0.29	0.28	0.26	14.45	14.34	13.64	13.06	12.34	11.33	11.38	10.80	10.28	9.78
65-79	0.57	0.56	0.56	0.53	0.48	22.98	22.52	21.94	21.39	19.54	15.32	15.57	15.10	14.56	13.51
80-	0.72	0.72	0.75	0.72	0.71	30.15	30.05	29.99	29.39	28.37	18.63	18.83	18.48	18.15	17.62
All age groups	0.32	0.32	0.31	0.30	0.28	14.84	14.76	14.48	13.90	13.20	10.77	10.91	10.70	10.24	9.80
Fluoroquinolones (J01MA)															
0-6	0.02	0.02	0.02	0.02	0.02	0.74	0.83	0.98	1.09	0.99	0.47	0.50	0.55	0.64	0.60
7-19	0.11	0.10	0.10	0.09	0.10	3.84	3.25	3.47	3.30	3.27	3.00	2.51	2.69	2.56	2.52
20-64	0.57	0.55	0.52	0.49	0.45	18.42	17.62	16.78	16.07	14.71	13.30	12.83	12.24	11.69	10.71
65-79	1.58	1.53	1.47	1.41	1.31	53.59	51.73	49.97	48.17	44.49	35.62	35.22	33.97	32.59	30.15
80-	1.91	1.90	1.82	1.83	1.70	70.99	70.11	67.28	67.51	62.76	49.78	49.10	47.22	46.72	43.38
All age groups	0.68	0.66	0.63	0.60	0.56	22.92	22.11	21.20	20.49	18.93	15.88	15.45	14.84	14.28	13.19
Nitrofurantoin (J01XE)															
0-6	0.05	0.06	0.06	0.07	0.07	7.12	7.37	8.04	7.49	8.66	5.15	5.46	6.11	6.11	6.80
7-19	0.12	0.12	0.12	0.11	0.11	9.23	9.12	9.21	8.71	8.85	7.79	7.72	7.83	7.41	7.50
20-64	0.31	0.31	0.32	0.33	0.32	20.88	20.88	21.51	21.86	21.70	16.72	16.84	17.22	17.45	17.29
65-79	0.76	0.76	0.78	0.80	0.81	45.23	45.21	45.72	46.23	46.58	31.72	32.22	32.42	32.53	32.29
80-	1.35	1.38	1.44	1.46	1.49	87.05	87.65	90.38	91.64	93.85	53.77	53.10	53.66	53.61	54.07
All age groups	0.38	0.39	0.40	0.40	0.41	25.22	25.32	25.86	26.02	26.24	18.56	18.68	19.01	19.08	19.05
All agents (J01 excl. methenamine)															
0-6	4.36	4.66	4.30	4.13	3.80	339.01	350.96	325.85	310.94	289.25	206.37	213.20	200.20	193.33	181.09
7-19	7.28	7.46	7.29	6.97	6.83	211.81	214.06	206.47	194.98	182.28	136.08	138.87	133.58	127.80	118.96
20-64	10.11	9.78	9.54	9.04	8.78	275.15	267.17	260.87	249.19	240.72	171.26	168.36	164.83	158.05	152.70
65-79	15.92	15.44	15.44	14.88	14.62	466.25	449.99	449.06	434.48	423.12	238.93	235.37	236.19	228.14	221.15
80-	19.60	19.37	19.50	19.32	19.25	645.87	634.73	634.08	626.87	621.40	306.75	301.19	301.50	298.15	293.00
All age groups	10.70	10.52	10.28	9.81	9.58	322.74	317.65	308.95	295.86	285.50	185.99	184.49	180.70	173.97	167.30

Age and gender comparisons

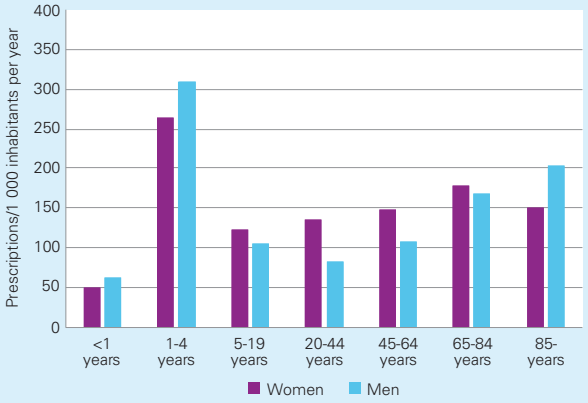
Results

- Antibiotics commonly prescribed against RTIs are the most frequently sold in the age group 1-4 years and represent 82% of the total antibiotic sales in this age group. RTI antibiotics are prescribed more to women than to men except among the younger children and among the oldest inhabitants, Figure 1.9.
- Antibiotics commonly used to treat UTIs are mostly prescribed to women, Figure 1.10. These antibiotics are to a larger extent prescribed to the older age groups.
- The sales of antibiotics that are commonly prescribed against skin and soft tissue infections are similar to men and women and between age groups, with an increase towards the elderly, Figure 1.11.
- Antibiotics commonly used to treat acne are mainly used in the age groups 5-19 years and 20-44 years and predominately by women, Figure 1.12. In the age group 20-44 most of the prescriptions are found among 20-29 year-olds (data not shown).
- 60% of all antibiotic prescriptions in Sweden during 2019 were issued to women.

Comments

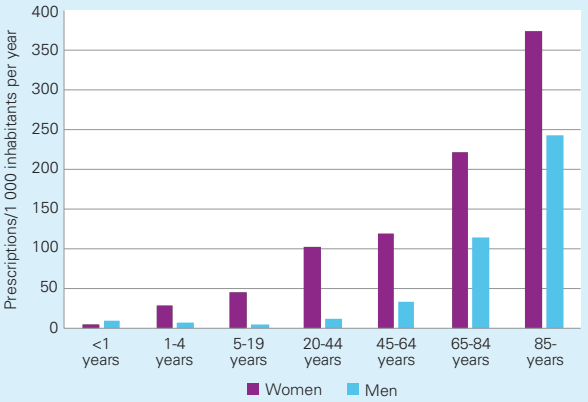
Concerning antibiotics that are commonly prescribed against skin and soft tissue infections and acne, people in the older age groups tend to be prescribed longer treatments, which impacts the amount of antibiotics used. The elderly are treated with the same antibiotics that are used for acne, but prescribed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

Figure 1.9. Sales of antibiotics that are commonly prescribed against respiratory tract infections to humans, prescriptions/1 000 inhabitants per year. This measure includes doxycycline (J01AA02; excluding packages larger than 50 tablets), penicillin V (J01CE02), amoxicillin (J01CA04), amoxicillin with enzyme inhibitor (J01CR02), cephalosporins (J01DB-DE), and macrolides (J01FA).



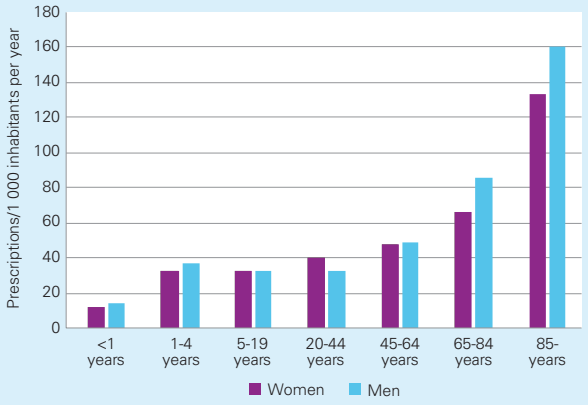
Source: The Public Health Agency of Sweden

Figure 1.10. Sales of antibiotics that are commonly prescribed against urinary tract infections to humans, prescriptions/1 000 inhabitants per year. This measure includes pivmecillinam (J01CA08), trimethoprim (J01EA01), ciprofloxacin (J01MA02) and nitrofurantoin (J01XE01).



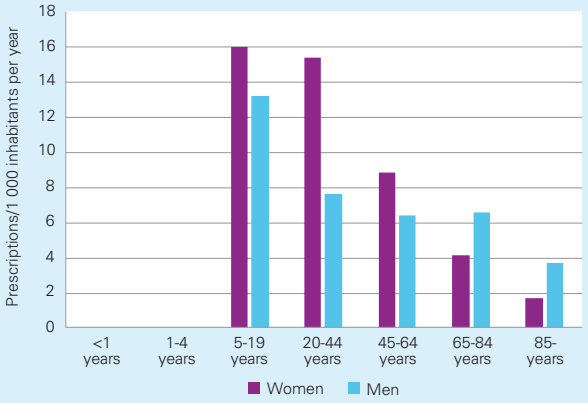
Source: The Public Health Agency of Sweden

Figure 1.11. Sales of antibiotics that are commonly prescribed against skin and soft tissue infections to humans, prescriptions/1 000 inhabitants per year. This measure includes clindamycin (J01FF01) and flucloxacillin (J01CF05).



Source: The Public Health Agency of Sweden

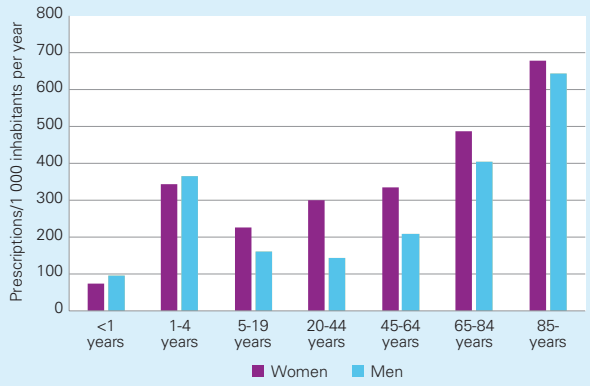
Figure 1.12. Sales of antibiotics that are commonly prescribed against skin and soft tissue infections (acne) to humans, prescriptions/1 000 inhabitants per year. This measure includes doxycycline (J01AA02; packages over 50 tablets), lymecycline (J01AA04), oxytetracycline (J01AA06) and tetracycline (J01AA07).



Source: The Public Health Agency of Sweden

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

Figure 1.13. Sales of antibiotics (J01 excl. methenamine) to humans, 2019, per age and gender, prescriptions/1 000 inhabitants per year.



Source: The Public Health Agency of Sweden

Antibiotic sales for children

Results

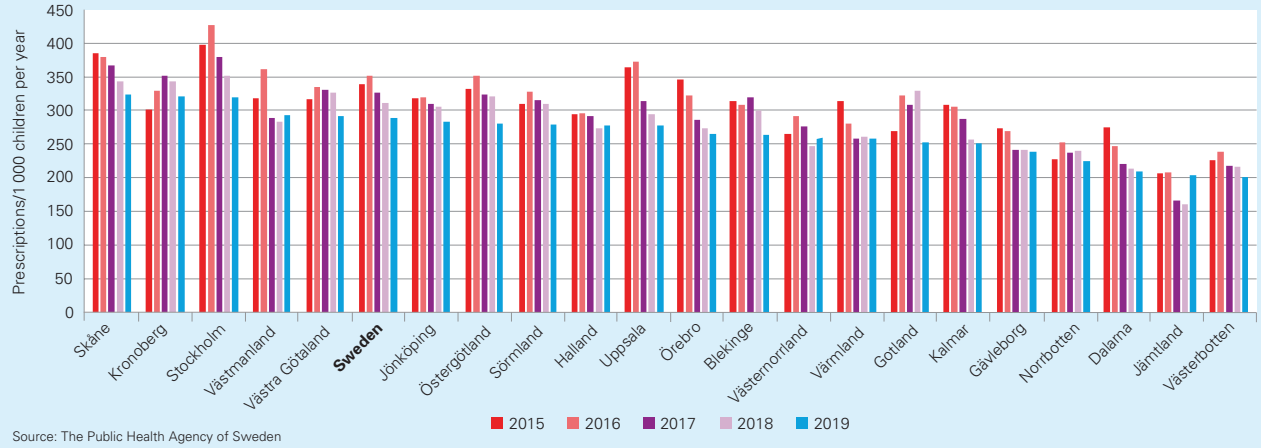
- Sales of antibiotics for children aged 0-6 years were 7.0% lower in 2019 than in 2018, Figure 1.14.
- The antibiotics most sold for children were beta-lactamase sensitive penicillins (J01CE) (59.2%), Table 1.1.
- The proportion of children (0-6 years) treated with at least one course of antibiotics decreased in 2019, Figure 1.15.

Comments

The decrease in sales of antibiotics for children aged 0-6 years encompasses 17 out of 21 regions. There are still large variations within Sweden; from 323 prescriptions per 1 000 children and year in Region Skåne to 201 in Region Västerbotten, Figure 1.14. The last few years have also seen substantial changes in several regions.

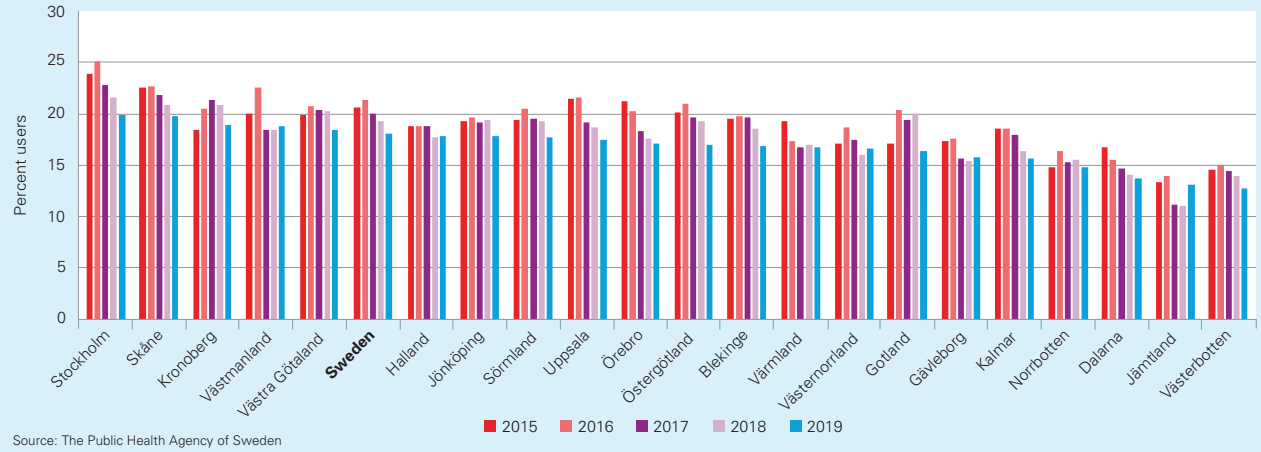
The proportion of children (0-6 years) treated with at least one course of antibiotics in 2019 was 18.1%, Figure 1.15. The proportion decreased in 17 out of 21 regions during 2019, which corresponds well to the decrease in sales of antibiotics, Figure 1.14.

Figure 1.14. Sales of antibiotics (J01 excl. methenamine) for humans, all genders, children 0-6 years, per region, 2015-2019, prescriptions/1 000 children per year.



Source: The Public Health Agency of Sweden

Figure 1.15. Proportion (%) of children aged 0-6 years treated with at least one course of antibiotics (J01 excl. methenamine), humans, all genders, per region, 2015-2019.



Source: The Public Health Agency of Sweden

Regional comparisons

Results

- The annual average sales of antibiotics were 285 prescriptions/1000 inhabitants in 2019.
- 16.7% of the Swedish population was treated with at least one course of antibiotics in 2019, Figure 1.17.

Comments

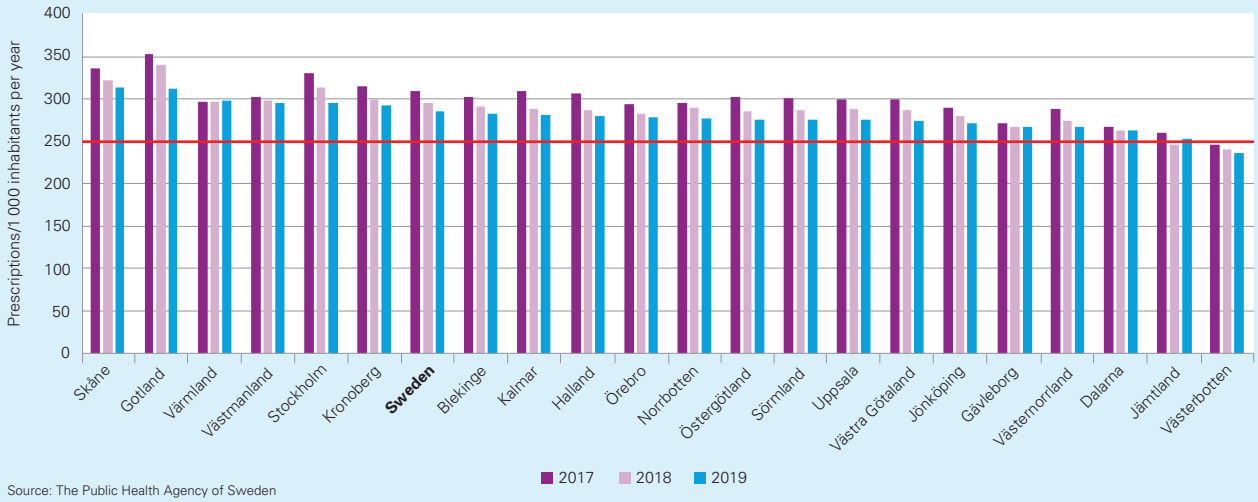
The proportion of people using antibiotics varies between the regions, from 18.1% in Region Skåne to 13.5% in Region Västerbotten, Figure 1.17. Both the proportion of people and of children treated with antibiotics during the last five years have decreased on a national level.

In 2018, the annual average sales of antibiotics were for the first time below 300 prescriptions/1000 inhabitants since national monitoring started. The trend continued downwards in 2019 and now a further reduction of 14.0% is needed to reach the long-term target of 250 prescriptions per 1 000 inhabitants per year. In 2019, only one region reached lower than the target. These data also show a regional variation in Sweden, ranging from 313 in Region Skåne to 236 in Region Västerbotten, Figure 1.16.

Strama has proposed quality targets for antibiotic prescribing in outpatient care; for instance one focusing on the use of narrow-spectrum penicillins in children and the other on fluoroquinolones in the treatment of UTIs in women.

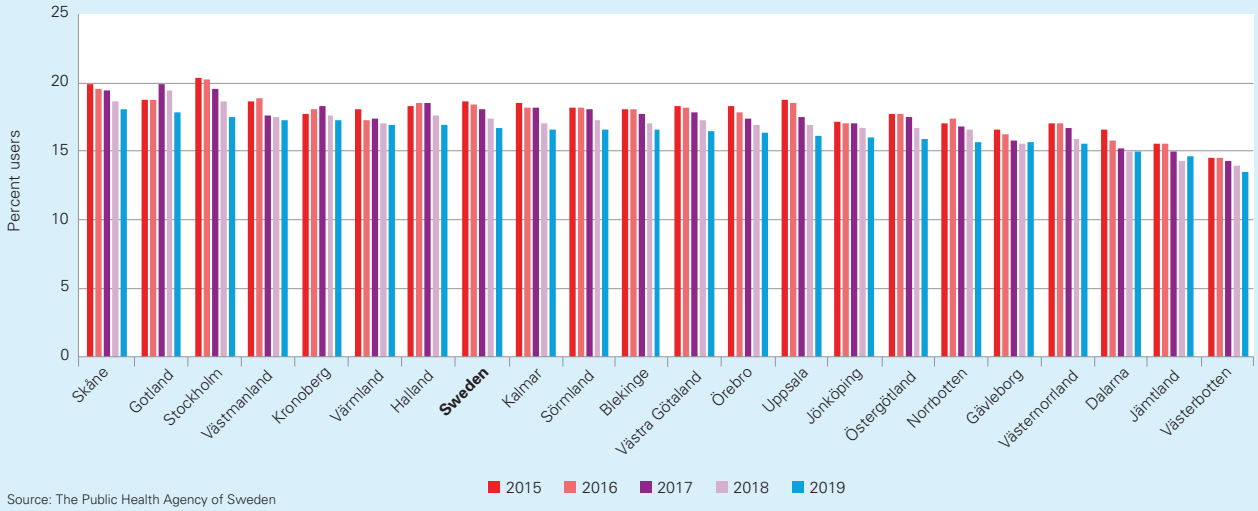
The target for narrow-spectrum penicillins in children between 0 and 6 years of age is set to 80% or more of prescriptions, with penicillin V (J01CE02) as the numerator and amoxicillin (J01CA04), penicillin V (J01CE02), amoxicillin with clavulanic acid (J01CR02), cephalosporins (J01DB-DE) and macrolides (J01FA) as the denominator. In 2019 the proportion of penicillin V was 75% on a national level, Figure 1.18.

Figure 1.16. Sales of antibiotics (J01 excl. methenamine) for humans, all genders, per region, per year, 2017-2019, prescriptions/1 000 inhabitants per year.



Source: The Public Health Agency of Sweden

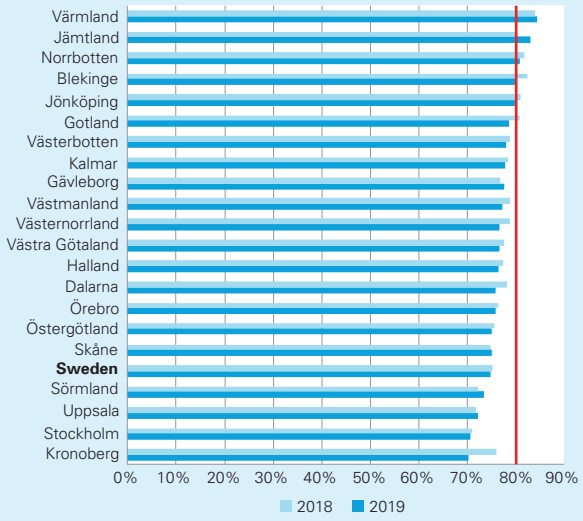
Figure 1.17. Proportion (%) of the population treated with at least one course of antibiotics (J01 excl. methenamine), humans, all genders, per region, 2015-2019.



Source: The Public Health Agency of Sweden

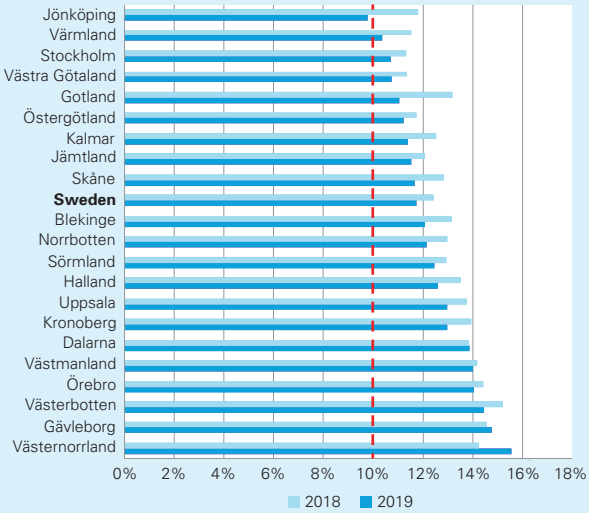
The target for prescribing fluoroquinolones to women is set to the age group 18-79 years of age, despite the treatment recommendations for UTIs concerning women >15 years. In Figure 1.19 the proportion of fluoroquinolones is shown for women 15-79 years, which corresponds well to the group 18-79. Data on both age groups are found in the embedded file. 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 target is set to a maximum of 10% fluoroquinolones, Figure 1.19.

Figure 1.18. Proportion penicillin V of antibiotics that are commonly prescribed to treat respiratory tract infections in children 0-6 years, humans, all genders, per region, 2018 and 2019. The red line indicates Strama's target at a minimum of 80%.



Source: The Public Health Agency of Sweden

Figure 1.19. Proportion fluoroquinolones of antibiotics commonly prescribed to treat urinary tract infections in women 15-79 years, humans, women, per region, 2018 and 2019. The dashed line indicates Strama's target of maximum 10% fluoroquinolones for women 18-79 years.



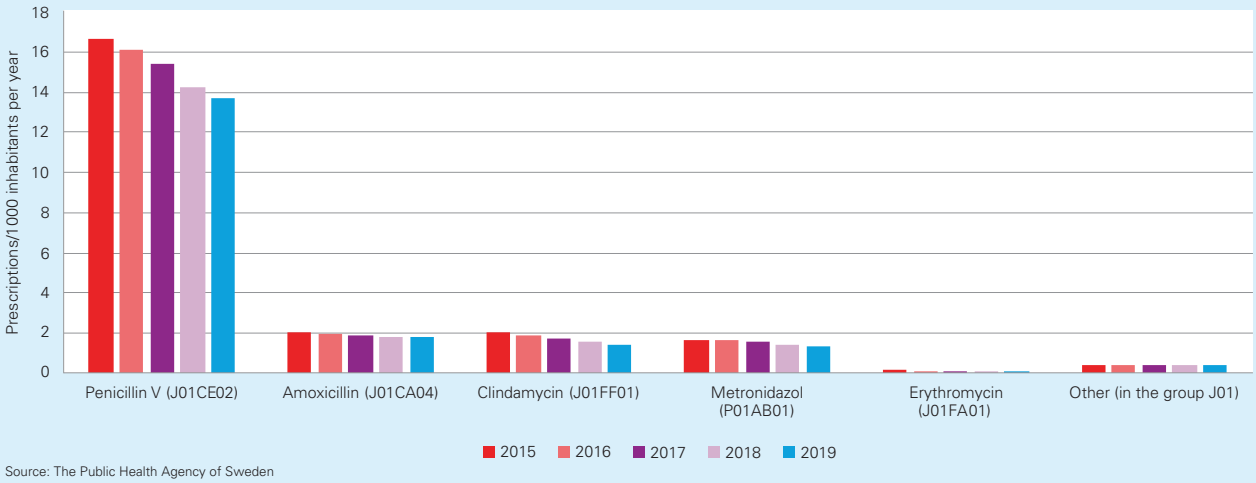
Source: The Public Health Agency of Sweden

Antibiotics in dentistry

Results

- Dentists continue to account for around 6 % of all antibiotics prescribed in outpatient care in Sweden
- The sales of antibiotics (J01 excl. methenamine; metronidazole P01AB01) decreased from 20 to 19 prescriptions per 1 000 inhabitants per year, relative change -4.4 %, compared to 2018. The sales of erythromycin and clindamycin decreased the most, relative change -20.4 % and -8.4 %, respectively, Figure 1.20.
- The most commonly prescribed antibiotic by dentists was penicillin V (73.1 %), which decreased by 4.0% compared with 2018.

Figure 1.20. Antibiotics prescribed by dentists in outpatient care, humans, all genders, 2015-2019, prescriptions/1000 inhabitants per year.



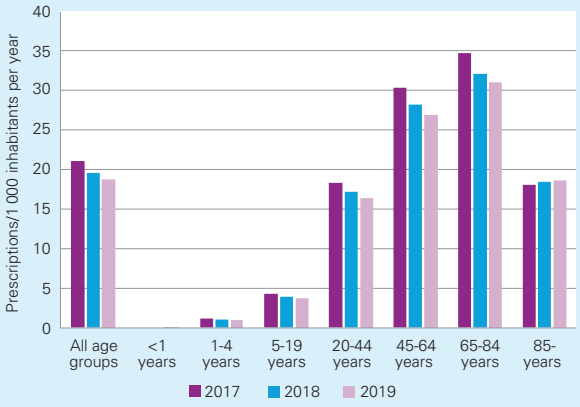
Source: The Public Health Agency of Sweden

Comments

The most prescriptions of antibiotics issued by dentists are found in the age group 65-84 years, followed by the age group 45-64 years, compared to all outpatient care where the group 85 years and older is the group with the most prescriptions, Figure 1.21. Between 2000 and 2007, an increase was seen in all age groups (data not shown), but since 2007 there has been an overall decrease, that has continued in the last three years, Figure 1.21.

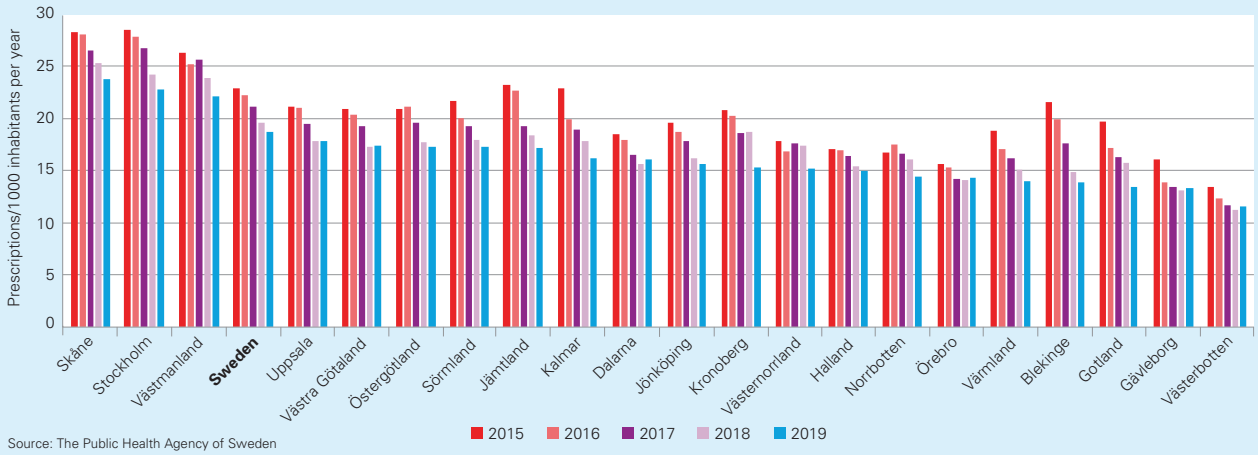
The total sales of antibiotics in dentistry (J01 excl. methenamine; metronidazole P01AB01), measured in prescriptions per 1 000 inhabitants per year, were lower in 17 of 21 regions in 2019 compared with 2018. There are regional differences; dentists in Region Skåne prescribed the most with 24 prescriptions per 1 000 inhabitants. This is more than twice as much as dentists in Region Västerbotten who prescribed the least (12 prescriptions per 1 000 inhabitants) in 2019. These differences correspond to some extent to the differences in the total outpatient care, Figure 1.16 and Figure 1.22.

Figure 1.21. Antibiotics (J01 excl. methenamine; metronidazole P01AB01) prescribed by dentists in outpatient care, humans, all genders, 2017-2019, by age group, prescriptions/1 000 inhabitants per year.



Source: The Public Health Agency of Sweden

Figure 1.22. Antibiotics (J01 excl. methenamine; metronidazole P01AB01) prescribed by dentists in outpatient care, humans, all genders, 2015-2019, prescriptions/1 000 inhabitants per year.



Source: The Public Health Agency of Sweden

Antibiotics in telemedicine

The concept of telemedicine is relatively new in Sweden and has grown in the recent years. In this report, telemedicine refers to digital consultations provided by caregivers registered for services in digital care, through applications for telephones and web based consultations. Data on telemedicine were aggregated by the eHealth Agency, based on registration numbers for telemedicine caregivers. These registration numbers are issued to all caregivers in Sweden and can for example give the opportunity to measure prescriptions in health care centres and among individual prescribers. The registration numbers in this measure include both private companies providing telemedicine and telemedicine organised on a regional level. It should be taken into account that prescriptions issued by health care centres that provide both physical care and telemedicine services are accounted for under the same registration number, in this case the physical care unit. Therefore the measure of telemedicine is not entirely reliable, but gives an indication of the situation in 2019.

Results

- In 2019, telemedicine accounted for 2.9% of all prescriptions in outpatient care.
- In the age group 20-44 years, telemedicine accounts for 6.3% of all prescriptions in outpatient care (data not shown).
- In the class other antibacterials excl. methenamine (J01X excl. J01XX05), telemedicine accounts for 9.2% of all prescriptions in outpatient care, Table 1.2. Among others, nitrofurantoin is found in this class.

Comments

In the class other antibacterials excl. methenamine (J01X excl. J01XX05), telemedicine accounts for 9.2% of all prescriptions in outpatient care. In this class nitrofurantoin is found, a first-line antibiotic for UTIs, which might indicate that many prescriptions for antibiotics against UTIs are made by digital caregivers. The age group to which most prescriptions in all classes are issued, is the group 20-44 years. In telemedicine, data are only available on the level of ATC-4 and therefore further analyses are not possible.

Table 1.2. Sales of antibiotics in telemedicine, ATC-4, to humans, all genders, 2019, prescriptions/1 000 inhabitants per year and proportion of prescriptions in telemedicine of prescriptions in outpatient care.

	Prescriptions/ 1000 inhabitants	Proportion telemedicine of total prescriptions in outpatient care
J01A - Tetracyclines	1.06	3.6%
J01B - Amphenicols		
J01C - Beta-lactamase antibacterials	4.56	2.7%
J01D - Cephalosporins	0.01	0.3%
J01E - Sulphonamides and trimethoprim	0.03	0.2%
J01F - Macrolides	0.20	0.9%
J01G - Aminoglycoside antibacterials		
J01M - Quinolone antibacterials	0.02	0.1%
J01X exkl J01XX05 - Other antibacterials excl. methenamine	2.44	9.2%
Antibiotics excl. methenamine (J01XX05)	8.32	2.9%

Antibiotics in hospital care

Data shown in this section include sales to all Swedish hospitals and other facilities, covering acute care hospitals, 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 a national level, the proportion of antibiotics in hospital care sold to acute care hospitals is about 70%. Region Dalarna is not included in the statistics showing hospital care and admissions and patient-days from Dalarna are excluded. Data from 2014 from Jönköping are incomplete.

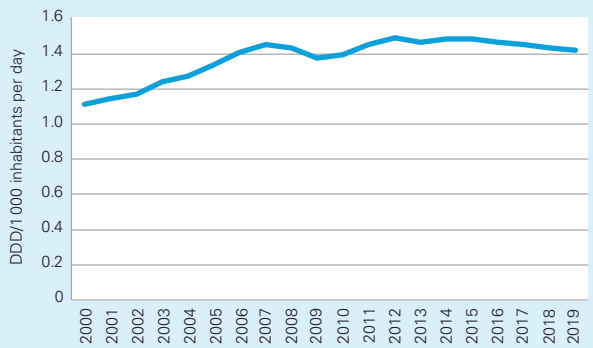
Antibiotic sales in hospitals and other health and social care facilities

Results

- The total sales of antibiotics (J01 excl. methenamine) in hospital care in Sweden were 1.42 DDD/1 000 inhabitants per day in 2019.
- Beta-lactamase resistant penicillins (J01CF) have increased in hospital care.
- Combinations of penicillins (J01CR) increased in 2019, Figure 1.24.

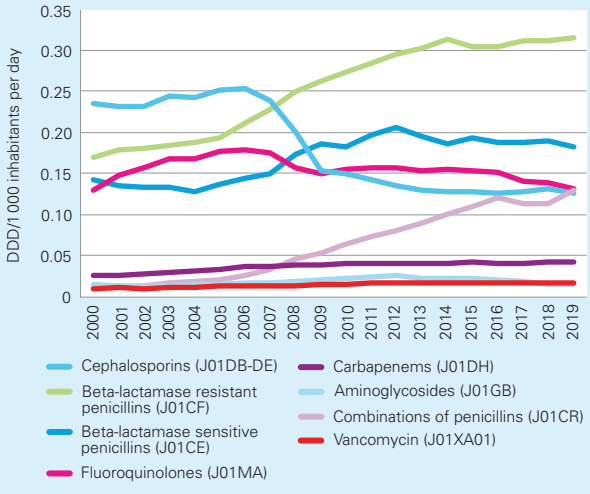
The change in the sales of cephalosporins around 2006-2009 is explained in part by a shift from one substance to another (cefuroxime to cefotaxime) meaning the number of DDDs appear lower. However, some of the decrease in cephalosporins was due to altered prescribing; since then more narrow-spectrum penicillins (J01CE) and combinations of penicillins (J01CR), mainly piperacillin-tazobactam (J01CR05), have gradually replaced the cephalosporins. Overall, a varying availability of certain substances might be the cause of fluctuations in the data. For instance, in 2017-2018 there was a shortage of piperacillin-tazobactam, which is noticeable in the data and the sales have now increased, Figure 1.24.

Figure 1.23. Sales of antibiotics (J01 excl. methenamine) in hospital care, for humans, all genders, 2000-2019, DDD/1 000 inhabitants per day.



Source: The Public Health Agency of Sweden

Figure 1.24. Sales of antibiotics in hospital care, for humans, all genders, ATC-5 and ATC-7, 2000 to 2019, DDD/1 000 inhabitants per day.



Source: The Public Health Agency of Sweden

Antibiotic sales in Swedish acute care hospitals

Results

- Data from acute care hospitals show that the sales of antibiotics decreased slightly in 2019 compared with 2018, Table 1.3.
- Beta-lactamase resistant penicillins (J01CF) are the most common antibiotics, making up 22% of the sales.
- Cephalosporins (J01DB-DE) decreased slightly in 2019.
- The proportion of narrow-spectrum antibiotics increased in 10 of 20 regions in 2019 compared with 2018.
- The proportion of cephalosporins of all antibiotics in acute care hospitals varied between 3.4% and 14.0% during 2019, and the corresponding numbers for fluoroquinolones were 5.7% and 12.5%. Piperacillin-tazobactam varied between 5.7% and 13.2% and carbapenems between 2.1% and 5.5%, Figure 1.26.

Comments

Major classes apart from beta-lactamase resistant penicillins (J01CF) are the beta-lactamase sensitive penicillins (J01CE), cephalosporins (J01DB-DE), fluoroquinolones (J01MA) and combinations of penicillins (J01CR), which mainly consists of piperacillin-tazobactam (J01CR05). Cephalosporins (J01DB-DE) and carbapenems (J01DH) have shown increasing sales over the last few years, but cephalosporins decreased in 2019. They now represent 11% and 4% respectively, Table 1.3.

According to available data, there are large differences in sales of antibiotics between Swedish acute care hospitals. One example is the use of narrow-spectrum penicillins, Figure 1.25. There are great differences in 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 1g three times a day to 3g 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.

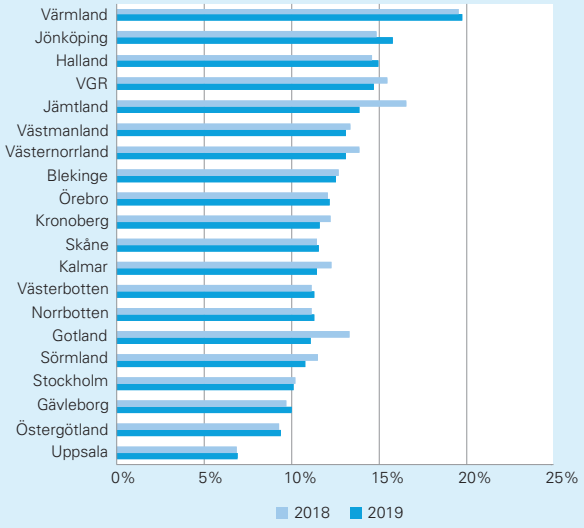
The proportion of all broad-spectrum antibiotics (fluoroquinolones, cephalosporins, piperacillin-tazobactam and carbapenems) in Swedish acute care hospitals varies between the regions and there are major differences regarding the distribution of classes of broad-spectrum antibiotics that are used, Figure 1.26.

Table 1.3. Sales of antibiotics to acute care hospitals, humans, all genders, ATC-5 & ATC-7, 2015 to 2019. DDD/100 admissions and DDD/100 patient-days.

	DDD/100 admissions					DDD/100 patient-days				
	2015	2016	2017	2018	2019[a)]	2015	2016	2017	2018	2019[a)]
Beta-lactamase resistant penicillins (J01CF)	55.7	58.4	61.7	63.9	63.8	12.3	12.9	13.8	14.6	14.5
Beta-lactamase sensitive penicillins (J01CE)	32.6	32.3	35.3	35.7	34.9	7.2	7.2	7.9	8.1	7.9
Combinations of penicillins (J01CR)	25.2	29.1	28.2	28.9	33.4	5.6	6.4	6.3	6.6	7.6
Cephalosporins (J01DB-DE)	28.8	29.9	31.4	32.7	31.3	6.3	6.6	7,0	7.5	7.1
Piperacillin-tazobactam (J01CR05)	21.5	24.7	23.0	23.3	27.2	4.7	5.5	5.1	5.3	6.2
Fluoroquinolones (J01MA)	27.5	27.6	27.3	27.1	25.5	6.1	6.1	6.1	6.2	5.8
Penicillins with extended spectrum (J01CA)	23.1	22.9	23.9	23.6	23.3	5.1	5.1	5.4	5.4	5.3
Tetracyclines (J01AA)	23.1	21.7	21.6	20.4	19.5	5.1	4.8	4.8	4.6	4.5
Trimethoprim with sulphonamides (J01EE)	10.3	11.2	11.4	12.0	12.8	2.3	2.5	2.5	2.7	2.9
Carbapenems (J01DH)	9.6	9.7	10.2	10.9	10.9	2.1	2.1	2.3	2.5	2.5
Lincosamides (J01FF)	8.1	8.4	8.6	8.5	7.8	1.8	1.9	1.9	1.9	1.8
Pivmecillinam (J01CA08)	8.9	8.5	8.4	8.4	7.7	2.0	1.9	1.9	1.9	1.8
Macrolides (J01FA)	4.6	5.2	5.6	5.2	5.5	1.0	1.1	1.3	1.2	1.3
Glycopeptides (J01XA)	4.5	4.6	4.7	4.8	4.6	1.0	1.0	1.1	1.1	1.1
Imidazole derivates (J01XD)	4.1	3.9	4.6	4.8	4.2	0.9	0.9	1.0	1.1	1.0
Aminoglycosides (J01GB)	5.2	5.0	4.7	4.0	3.7	1.1	1.1	1.1	0.9	0.8
Nitrofurantoin (J01XE)	2.1	2.2	2.3	2.3	2.1	0.5	0.5	0.5	0.5	0.5
Moxifloxacin (J01MA14)	1.6	1.8	1.9	1.9	1.6	0.3	0.4	0.4	0.4	0.4
Trimethoprim (J01EA)	1.6	1.0	0.7	0.7	0.7	0.4	0.2	0.2	0.2	0.2
Other (from J01 and A07)	4.7	4.3	4.5	4.5	4.1	1.0	1.0	1.0	1.0	0.9
All agents (J01)	269.8	277.1	286.4	289.4	288.6	59.5	61.4	64.1	65.9	65.7

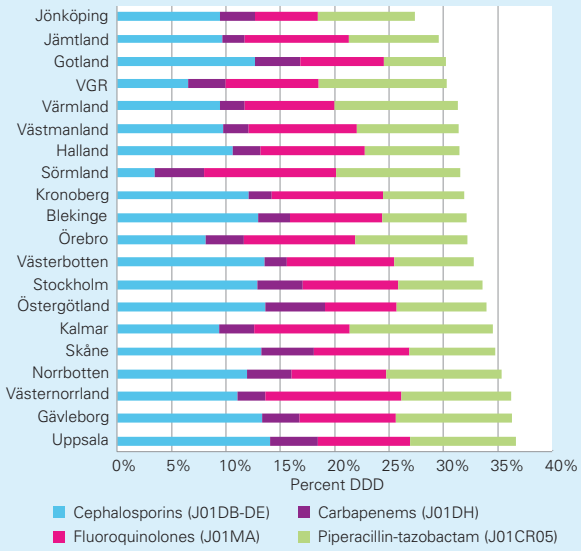
[a)] Denominator data from 2018.

Figure 1.25. Proportion (%) of narrow-spectrum penicillins (penicillin V and G, J01CE) of all antibiotics in Swedish acute care hospitals, per region, 2018 and 2019.



Source: The Public Health Agency of Sweden

Figure 1.26. Proportion (%) of broad-spectrum antibiotics (cephalosporins, carbapenems, fluoroquinolones and piperacillin-tazobactam) of all antibiotics in Swedish acute care hospitals, per region, 2019.



Source: The Public Health Agency of Sweden

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 and the patients. The antibiotic-related adverse reactions reported from health care professionals and patients between 2015 and 2019 were analysed for various groups of agents.

There were 2 976 reports of side effects caused by the use of antibiotics during this period.

The following organ system groups received most reports related to the use of systemic antibiotic drugs: skin- and subcutaneous tissue disorders (n=1425), gastrointestinal disorders (n=654), general disorders (n=392), neurological reactions (n=384), respiratory disorders (n=224), immune system disorders (n=170), musculoskeletal disorders (n=176), investigations (n=123), hepato-biliary disorders (n=129), psychiatric disorders (n=103), renal and urinary disorders (n=106) and blood and lymphatic system disorders (n=60). The majority of the reports (64%) 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 sold substances and regardless of the cause of the report, are presented in Table 1.4.

Table 1.4. Substances most commonly associated with adverse reactions reported to the Swedish Medical Products Agency 2015-2019.

Antibiotic	Total number of adverse drug reaction reports 2015 to 2019	Number of 'serious' reports	Number of fatal cases
Phenoxymethyl-penicillin	424	123	0
Flucloxacillin	311	146	10
Ciprofloxacin	272	175	4
Clindamycin	240	92	3
Nitrofurantoin	240	92	2
Sulfamethoxazole and trimethoprim	182	114	2
Amoxicillin	174	65	0
Doxycycline	145	36	0
Piperacillin and beta-lactamase inhibitor	123	77	3
Cefotaxime	82	43	1

Clinical trial – Duration of treatment for tonsillitis

This clinical trial demonstrated that penicillin V four times daily for five days had comparable (non-inferiority) clinical efficacy to the commonly recommended 10-day treatment for pharyngotonsillitis caused by group A streptococci (GAS).

Introduction

Increasing antibiotic resistance and the shortage of new antimicrobial agents highlights the importance of optimising the use of existing antibiotics. In 2014, the Public Health Agency of Sweden was commissioned by the government to evaluate the use of currently available antibiotics. In collaboration with primary care researchers, a study was initiated to investigate whether a five-day penicillin course for pharyngotonsillitis provides results that are comparable to the commonly recommended treatment for 10 days. Pharyngotonsillitis is one of the most common infections in primary health care and the reason for a large part of antibiotic prescribing.

The efficacy of penicillin is dependent on the time above the minimum inhibitory concentration (MIC). The most important determinants for time above MIC are dose and frequency. The hypothesis in this study was that more frequent dosing would be more effective and therefore the treatment duration could be shortened.

Intervention

Patients were randomly allocated to receive either penicillin V 800 mg four times daily for five days (a total of 16 grams) or penicillin V 1000 mg three times daily for 10 days (a total of 30 grams). The doses for children were adjusted according to bodyweight.

Method

The study was a randomised controlled, open label, non-inferiority study. The aim was to investigate whether the shorter treatment had comparable clinical efficacy to the 10-day treatment. The non-inferiority limit was set to minus 10 percentage points, which is customary for antibiotic studies. This means that with a probability of 95 percent, it can be shown whether the true difference in clinical cure between the two groups is less than 10 percentage points.

Inclusion criteria were patients from six years of age who had pharyngotonsillitis caused by group A streptococci, and three or four Centor criteria (fever ≥38.5°C, tender lymph nodes, coatings of the tonsils, and absence of cough) were included in the study. For children coatings of the tonsils was not required; inflamed tonsils was sufficient.

Patients eligible for inclusion were assigned to treatment with penicillin V as an oral tablet. The physicians' clinical judgments of throat status at inclusion were recorded and throat swabs for rapid antigen detection test and culture were performed.

One week after the end of penicillin treatment, patients came for an evaluation visit. The clinical outcome of the treatment was evaluated by a physician and a rapid antigen detection test and culture were performed. The patients were asked to fill in a diary from inclusion until this visit. In the diary they reported, among other things, the degree of sore throat, fever, intake of analgesics, and side effects. After one and three months respectively, a research nurse contacted the patients by telephone for follow-up.

Primary outcome was clinical cure five to seven days after the end of antibiotic treatment.

Secondary outcomes were bacteriological eradication, time to relief of symptoms, frequency of relapses, prevalence of complications, new tonsillitis or adverse events, and adherence to the study treatment.

Table 1. Primary and seconary outcomes.

	5 days	10 days	95% confidence interval (CI)
Clinical cure (n=397)	89,6% (181/202)	93,3% (182/195)	-3,7 (-9,7 to 2,2)
Bacteriological eradication (n=376)	80,4% (156/194)	90,7% (165/182)	-10,2 (-17,8 to -2,7)
Relapse within one month (n=359)	8/179	7/180	
Complications, three months (n=387)	0/198	4/189	
New tonsillitis, three months (n=386)	6/197	13/189	

Results

A total of 433 patients were included and randomised by 17 primary healthcare centres. Patients were recruited between September 2015 and February 2018.

The study showed that pencillin V, given four times daily for five days, had comparable clinical efficacy to penicillin V, given three times daily for 10 days. Fewer patients in the five-day treatment group achieved bacterial eradication at the evaluation visit. The number of relapses and complications did not differ between the two intervention groups, Table 1.

According to patient diaries, time to first day of relief of sore throat was slightly shorter in the five day group compared with the 10 day group (p<0,001, log-rank test), Figure 1.

Reported adverse events were mainly diarrhoea, nausea, and vaginal discharge or itching. For all three categories, the 10 day group had higher incidence and longer duration of adverse events, Figure 2.

Adherence to the study treatment, in terms of number of doses taken, was high according to patient diaries; median 100 percent in both groups.

During the telephone follow-up, a proportion of the study patients (n=43 in each treatment group) was asked which of the antibiotic treatments they would prefer if they had a choice. Irrespective of allocated treatment regimen, 63 percent of the patients would prefer the shorter treatment regimen, 22 percent would prefer the longer regimen and 15 percent had no preference.

Conclusion

The study demonstrated that penicillin V four times daily for five days was comparable (non-inferior) to three times daily for 10 days. The study showed no higher risk of relapses or complications with the shorter treatment regimen. A lower number of patients with bacteriological eradication can be weighed against the advantages shown in the study; shorter time to relief of symptoms, fewer adverse events and fewer antibiotics prescribed.

Figure 1. Time to first day without sore throat according to patient diary (n=381).

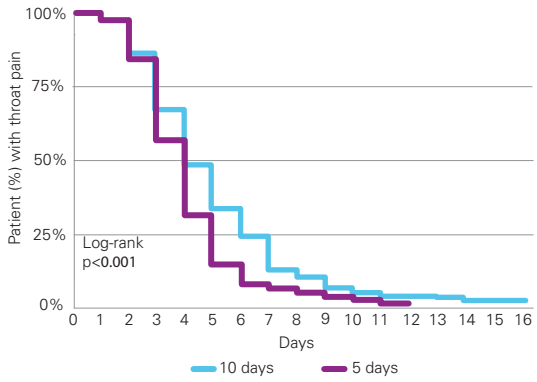
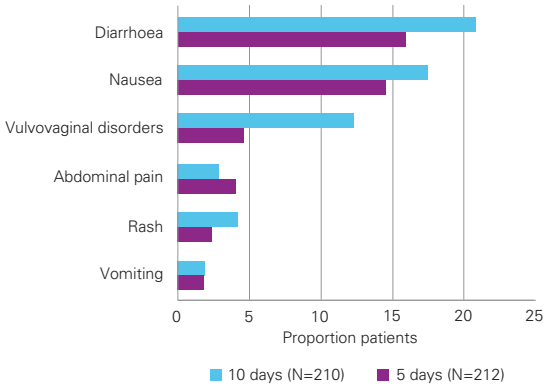


Figure 2. Adverse events with possible or probable relation to the study drug, registered by physician, (n=422, every patient who received at least one dose of study drug).



- Five days of treatment with penicillin V four times daily was non-inferior in clinical outcome for patients with pharyngotonsillitis caused by group A streptococci.
- The number of relapses and complications did not differ between the two intervention groups.
- The study shows that a five day treatment regimen might be an alternative to the currently recommended 10 day regimen.
- Changing from 10 days to five days of treatment could substantially reduce the total sales of penicillin V for this indication in countries that follow the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) guidelines.

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Success factors for implementation of antibiotic stewardship activities in Sweden

Antimicrobial stewardship is defined as *"a coherent set of actions which promote using antimicrobials responsibly"* (Dyar et al., 2017) and is one of the core strategies to combat AMR. Documents about antimicrobial stewardship and its implementation have been published within the EU-JAMRAI collaboration (EU-JAMRAI, 2018) and WHO (WHO, 2019).

During December 2019 and January 2020 the Public Health Agency of Sweden conducted an interview study regarding factors for success in stewardship activities in Sweden, within the framework of the EU-JAMRAI work package 7 collaboration. The study consisted of 14 interviews and three focus groups. To the interviews, professionals representing Strama groups (the Swedish strategic programme against antibiotic resistance) were recruited. In the focus groups, professionals representing different parts of the healthcare system participated.

The findings in this study show that many of the identified successful core components for antibiotic stewardship programs (Pulcini et. al., 2019, CDC, 2014, etc.) are implemented in Sweden and several of the described approaches are similar to activities initiated by Strama.

The results present success factors and examples of successful working methods at all levels of care:

- Sweden has functioning systems for *supporting technology* with data on antibiotic sales and resistance, which serve as a foundation for antibiotic stewardship work. Data from monitoring and surveillance of antibiotic sales and resistance are used for example to identify areas that need improvement. In primary care, antibiotic sales are monitored and reported regularly at healthcare centre level or for each prescriber. Antibiotic sales data linked to diagnose are mentioned as an important part of antibiotic stewardship activities in both hospitals and primary care. A successful approach is to appoint a physician responsible for antibiotics in each hospital clinic, whose tasks include to regularly follow up treatment outcomes.
- In response to questions about *rules and recommendations*, the national treatment recommendations were described as a success factor as well as targets, indicators and economic incentives. Supportive policy documents and legislation help to favor success.
- A central success factor for *good teamwork* in hospitals is mutual respect between professional groups. The Strama network, which stimulates collaboration within and among regional groups, is highlighted, e.g. being multi-professional and encouraging exchange of experiences regarding activities. The importance of involving different professions is also described as contributing to *good leadership*.
- Successful activities to promote responsible *antibiotic prescribing practices:*
  - *In hospitals:* antibiotic ward rounds was mentioned as one of the most successful activities. These have improved the use of antibiotics, highlighted the issue of antibiotic resistance and is a learning opportunity for the staff.
  - *In primary care:* regular feedback on prescription patterns and educational activities organised by Strama. Also involving the healthcare centres in performing self-assessments and identifying their own areas for improvement.
- Regarding successful strategies for *education and expertise*, a dialogue between and within different areas of healthcare and interaction between physician and patient were mentioned as tools to create an atmosphere of understanding. Media attention has also supported improvement.

In summary, this study describes good experiences and fruitful working models, which can support further antibiotic stewardship efforts. The results will be included in a publication by EU-JAMRAI.

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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, methodology and confidentiality

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

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

Sales for mixing into feed for aquaculture for food production are not included in the data referred to above, as such feed is traded from other countries. Data on prescriptions are collected through a separate system, and information is given under Comments by animal species, Aquaculture.

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

Updates of historical data

Data on sales of antibiotics for 2017 and 2018 have been recalculated, and some errors were discovered. Figures given in Table 2.1 have therefore been updated.

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 for data-collection has been adjusted and from 2015, it is assumed that the sales of this type of products are no less complete than before the reregulation.

Between 2010 and 2015, there has also been a lack of completeness in the sales of products with general marketing authorisation. For further information on the lack of completeness of data from recent years, see Swedres-Svarm 2015 p. 109. Data from 2016 and onwards are likely to be complete in this respect.

Trends in animal populations

Changes in the numbers of animals may affect trends in statistics on sales of antibiotics. Compared to 2010, the number of pigs slaughtered in 2019 has decreased by 12%, while the number of broilers has increased by 35%. The number of dairy cows decreased by 12% during the same period. The number of horses was estimated to 355 500 in 2016. The number of dogs was estimated to 784 000 in 2012 and 729 000 in 2006. Further details on animal numbers and data sources are found in the subchapter Demographics and denominator data in this report.

Overall sales

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

Of the overall sales expressed as kg active substance, more than 90% are products formulated for treatment of individual animals (injectables, tablets, intramammaries) and less than 10% for treatment of groups or flocks (premixes, oral powders, solutions for in water medication). In 2019, the total reported sales from Swedish pharmacies of antibiotics for animals were 9 601 kg, of which 58% was benzylpenicillin. The corresponding figures for 2010 were 14 117 kg and 53%, respectively.

Since 2010, sales of all classes of antimicrobials have decreased notably. In the past five years (since 2014), sales of aminopenicillins, aminoglycosides and macrolides and lincosmides have been relatively unchanged. Sales of other classes have decreased by more than 10%.

Since 2014, the total sales have been comparatively stable but sales in 2019 were 8% lower than sales in 2018 (Table 2.1). The decrease derives from all classes and in most cases a downward trend can be seen over time. But the decrease in benzylpenicillin (-6%), with the largest sales measured as kg active substance, warrants an explanation. Analysis of data by animal species given on prescriptions and sales for use in veterinary practice (where animal species is unknown) indicate that most of the decrease derives from cattle and use in veterinary practice. The dairy cow population decreased by 4% between 2018 and 2019. In Sweden, the summer of 2018 was exceptionally warm and dry, leading to a shortage of fodder. Thus, the decreased sales of penicillins may at least partly be explained by increased culling of cattle during the fall 2018 and spring 2019.

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

ATCvet code		2010	2011	2012	2013	2014	2015	2016	2017[b]	2018[b]	2019
QJ01AA, QG01A	Tetracyclines	1115	1073	881	935	787	685	515	529	516	522
QJ01CE, -R, QJ51	Benzylpenicillin[c]	7546	6696	6362	5954	5509	5861	5997	5921	5961	5579
QJ01CA, QJ01CR	Aminopenicillins	907	723	649	645	635	642	677	640	683	648
QJ01D	Cephalosporins	575	498	410	330	299	267	242	210	187	161
QA07AA, QJ01G, -R, QJ51R	Aminoglycosides	462	427	408	264	298	322	312	302	376	343
QA07AB, QJ01E	Sulphonamides	1998	1867	1812	1707	1699	1634	1643	1678	1539	1445
QJ01E	Trimethoprim & derivatives	357	338	329	320	314	313	318	326	297	281
QJ01F	Macrolides & lincosamides	739	648	632	564	484	485	472	515	578	486
QJ01MA	Fluoroquinolones	148	120	106	52	45	34	30	25	29	20
QA07AA,QJ01BA, QJ01XQ	Others[d]	270	216	174	205	201	224	337	147	237	115
	Total sales	**14 117**	**12 606**	**11 763**	**10 975**	**10 270**	**10 468**	**10 543**	**10 293**	**10 404**	**9 601**

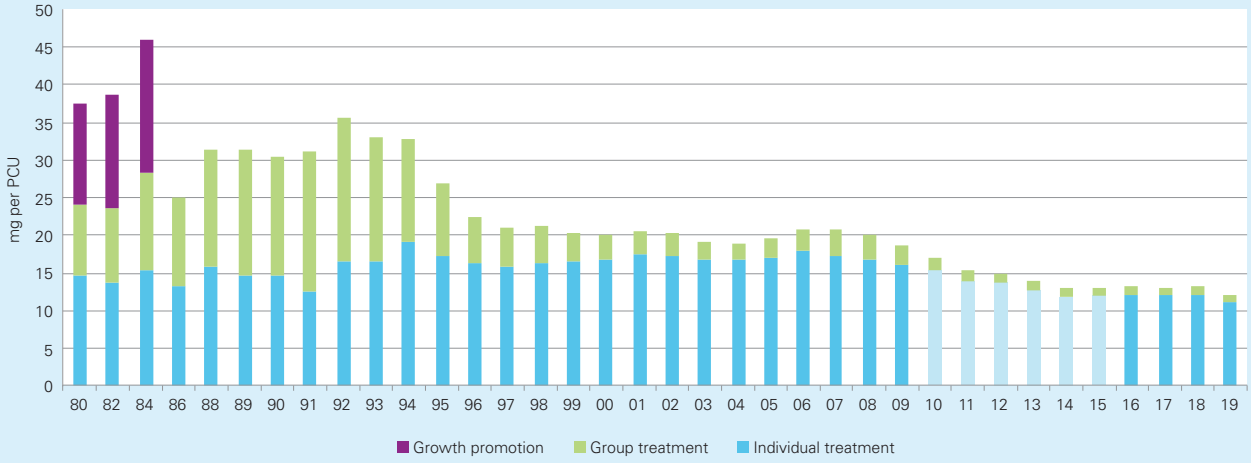
[a]Data from 2010-2015 are uncertain because of a lack of completeness mainly affecting injectable products. [b]Updated following the discovery of some errors in previous calculations. [c]Also includes small amounts of phenoxymethylpenicillin and penicillinase stable penicillins. [d]Others include: amphenicols, pleuromutilins and polymyxins, grouped for confidentiality reasons.

Population corrected sales

To correct for changes in the numbers of animals over time, the population correction unit (PCU) described in a publication from the European Medicines Agency was applied (EMA, 2011). The PCU is a purely technical term representing an approximation of the summed live weight of the major animal populations, excluding companion animals. In Figure 2.1, the total sales of antimicrobials for animals (including sales for companion animals) from 1980 and onward are presented as mg active substance per PCU, using figures for 2017 as a proxy for PCU in 2018 and 2019. As aquaculture is not included in the data presented, fish have been excluded from the PCU given in the reports from the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC).

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

Figure 2.1. Sales of antibiotics for animals expressed as mg per population correction unit (PCU)[a].



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

The Antimicrobial ad hoc expert group (AMEG) of the European medicines agency considers 3rd generation cephalosporins, quinolones and polymyxins as classes of antibiotics for which there should be special restrictions regarding their use in animals (category B, restrict) (EMA, 2019a). Since 2010, the sales of these antibiotics, expressed as mg/PCU, have decreased by 95%, 86% and 73%, respectively. For the 3rd generation cephalosporins and fluoroquinolones, the decrease is partly explained by a regulation that since 2013 is limiting veterinarians' rights to prescribe these types of antimicrobials (SJVFS 2019:32). As to polymyxins, the findings of transferable resistance to colistin were communicated to stakeholders during 2016 and onwards. An awareness among prescribers of the importance of this class of antimicrobials for public health, and of the potential consequences of transferable resistance, is a probable explanation for the observed decrease.

Comments on trends by animal species

Dairy cows

Växa Sweden (an organisation providing animal health services for dairy cattle) publishes a yearly report related to the livestock organisations' work to improve animal health and welfare in dairy cows (Växa Sverige, 2017). For statistics on incidence of antibiotic treatments of dairy cows enrolled in the Swedish milk recording scheme, data are retrieved from a database with veterinary reported disease events and treatments (Jansson Mörk, 2010).

According to Växa Sweden (2020), the by far most common indication for treatment of dairy cattle is mastitis. In Sweden, mastitis is generally treated systemically and any changes in treatment incidence, treatment length or choice of antibiotic for this condition will have a noticeable influence on the statistics on sales of antibiotics. The reported incidence of treatment of clinical mastitis in dairy cows has decreased over the last ten years and was 9.0 recorded treatments per 100 completed/interrupted lactations in 2018/2019. Of all recorded treatments, benzylpenicillin was by far the most common (around 90% of reported treatments). Treatment with fluoroquinolones for any indication in dairy cows has decreased from 2.38 recorded treatments per 100 completed/interrupted lactations in 2010 to 0.14 in 2018.

Pigs

Information on sales for pigs is given in In focus: sales of antibiotics for pigs.

In brief, in 2010 and 2019 the sales of antibiotics for pigs were 3 364 and 2 904 kg active substance, respectively, or 12.8 and 12.1 mg/kg slaughtered pig.

A shift from products for medication of groups of animals via feed or water towards medication of individual animals, preferably with narrow-spectrum substances such as benzylpenicillin is observed over the last ten years. This is well in line with guidance on appropriate use of antibiotics (Medical Products Agency, 2012).

Poultry

Antibiotics are rarely used for treatment of bacterial diseases in commercially reared *Gallus gallus*. Localised outbreaks can therefore have a major influence on the sales in a specific year. Over the last ten years, the yearly sales of fluoroquinolones for slaughter chickens and hens have been below or much below 1 kg, mostly below 0.25 kg. Mostly the types of products sold with chickens, hens or turkeys as recorded species are tablets or injectables and quantities very small, indicating that they were not used for treatment of commercially raised chickens. Cephalosporins or colistin are never used.

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

The use in 2019 corresponds to 0.41 mg active substance/kg slaughtered chicken. In most cases, the flocks were treated for necrotic enteritis with phenoxymethylpenicillin. A limited number of flocks were treated for colibacillosis with amoxicillin. In addition, grandparent and parent flocks were treated on 30 occasions, in most cases (22 occasions) with phenoxymethylpenicillin and the remainder with amoxicillin.

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

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

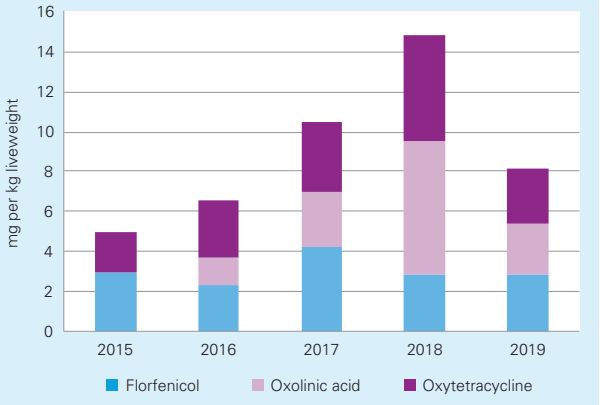
Year	Number of flocks treated	Total number of flocks
2011	6	3 185
2012	1	2 853
2013	4	3 133
2014	4	3 138
2015	28	3 191
2016	14	3 300
2017	1	3 300
2018	4	3 223
2019	54	3 368

Fish

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

The occurrence of bacterial disease in farmed fish is influenced by water temperatures in summer, and the amounts prescribed may therefore vary between the years. In 2019, a total of 123 kg of antibiotics were prescribed for fish for consumption, compared to 197 kg in 2018, a year with unusually high temperatures. Antibiotics prescribed in 2019 were florfenicol, oxolinic acid and oxytetracycline.

Figure 2.2. Prescription of antibiotics for fish as mg per kg live weight of slaughtered fish.



In figure 2.2, the prescription of antibiotics for farmed fish is shown as mg per kg liveweight fish slaughtered. Florfenicol is primarily used for treatment of flavobacteriosis (*Flavobacterium psychrophilum*), a disease mainly affecting juvenils (with a very low weight). Oxolinic acid and oxytetracycline are used to treat diseases caused by *Aeromonas salmonicida* and *F. columnare*, respectively. These are diseases affecting production fish, i.e. of a higher weight. Therefore, the relations between the antibiotics shown in figure 2.2 do not translate to treatment frequencies or actual exposure of individual fishes.

Horses

Around 65% of the sales of trimethoprim-sulphonamides are products for oral use in horses (paste or powder). Since 2010, there has been a decrease in sales of such products by 25%, measured as kg active substance. In 2013, guidelines for use of antibiotics in horses were published by the Swedish Veterinary Association and in 2015, this guidance was supplemented by guidance from the Medical products agency (Medical Products Agency 2015). It is possible that the guidance, together with an overall strong focus on the need for antibiotic stewardship in human and veterinary medicine has also contributed to the observed decrease.

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

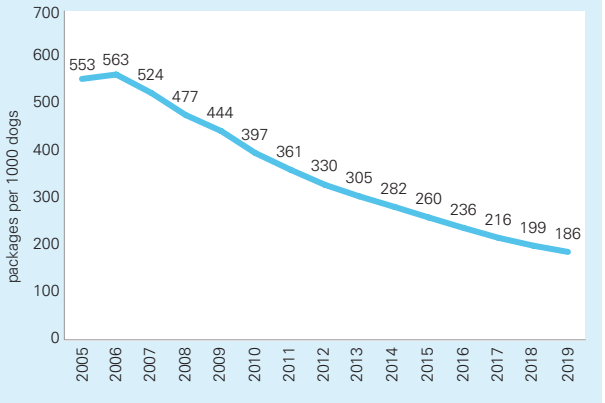
Dogs

In 2019, the overall sales of veterinary medicinal products for oral medication of dogs was 611 kg compared to 1 352 kg in 2010. Aminopenicillins (without clavulanic acid), first generation cephalosporins and lincosamides were by far the classes with largest sales in 2019.

The figures above refer to sales of veterinary products only. In 2006, the total number of packages of antibiotics dispensed for oral use in dogs, i.e. both veterinary antibiotics and those authorised for use in humans, corresponded to 563 packages per 1000 dogs. Since then, the number has decreased to 186 packages per 1000 dogs (-67%) (Figure 2.3). The most prominent changes relative to 2006 are noted for first generation cephalosporins (-91%), fluoroquinolones (-67%) and aminopenicillins with clavulanic acid (-76%).

As described in Svarm 2008, the emergence of infections with multiresistant methicillin-resistant *Staphylococcus pseudintermedius* and methicillin-resistant *S. aureus* triggered several national and local initiatives. This has most likely led to changes in prescribers' behaviour, which in turn explains the downward trends in sales of antibiotics for dogs shown in Figure 2.3.

Figure 2.3. Sales of the antibiotics for oral medication of dogs expressed as packages per 1 000 dogs. Data include antibiotics authorised for veterinary use as well as antibiotics for human use.



Sales of antibiotics for pigs in Sweden

In Sweden, veterinary medicinal products must be dispensed by pharmacies. All pharmacies are obliged to deliver data on sales of veterinary medicinal products, including target animal species as given on the prescription, to the eHealth Agency. In almost all commercial pig production herds, the owner has a contract with a veterinarian to provide the animal health services needed. In such circumstances, the veterinarian can delegate treatments of specified indications with specific veterinary medicines to the animal caretaker. This system is widely applied, and almost all antibiotics for treatment of animals on pig farms are acquired by veterinary prescription from the pharmacies.

To study trends in sales of antimicrobials for pigs, the sales of antibiotic products (ATCvet codes QJ01 and QA07AB) with pig specified on the prescriptions for the years 2010, 2015 and 2019 were selected. In addition, sales of products intended for group medication of pigs, but where no animal species was recorded at the pharmacy were included. Sales were calculated to kg active substance and to two different defined course doses (DCD): DCDvet as defined by ESVAC (EMA, 2019) and DCDse, defined on basis of Summary of product characteristics for products authorised in Sweden (see Background for more information). The total mass of slaughtered pigs (in kg) was chosen as denominator.

A comparison of the total output expressed in different units of measurement is shown in Figure 1. The results are indexed against year 2010 to allow comparability of trends. Between 2010 and 2015, the mass of pigs slaughtered decreased by 11%, but between 2015 and 2019 it was stable. This explains why outputs for kg active substance that are not corrected for population show a different pattern. As can be expected, the unit with kg slaughtered pigs as denominator corrects for this. Among the dose-based units, there was a decrease of 12% for DCDse/kg, while for DCDvet/kg the consumption appeared to be almost unchanged over time. The value for DCDvet is considerably lower than the value for DCDse for e.g. benzylpenicillin, the most sold substance during the period. Between 2010 and 2019 the sales of benzylpenicillin increased by 13-16% (Figure 2, Table), depending on the unit of measurement. Thus, the difference in trend-lines between DCDvet/kg and DCDse/kg is to a large extent explained by a high and increasing sales of benzylpenicillin.

The proportion of sales of products for treatment of groups of animals of the total sales has decreased over time for all units of measurement. Expressed in mg/kg, such sales were 35% of the total in 2010, compared to 18% in 2019 (Table). Decreases are seen for all classes or

Figure 1. Trends in sales of antibiotics for pigs from 2010 to 2019 with different units of measurement, indexed against year 2010.

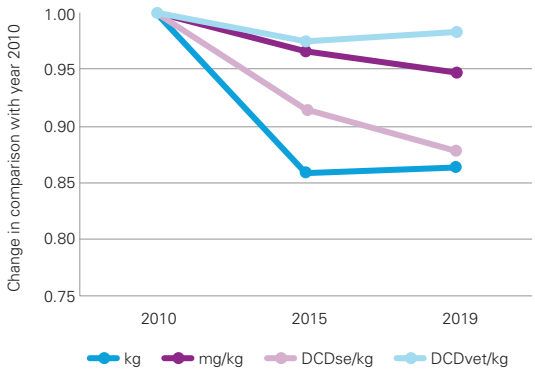


Table. Sales of antibiotics for pigs expressed as mg/kg slaughtered pigs by mode of administration.

	Individual treatment		Group treatment		Total	
	2010	2019	2010	2019	2010	2019
Tetracyclines	0.24	0.42	1.83	0.56	2.07	0.98
Benzylpenicillin[a]	4.86	6.17	0.00	0.00	4.86	6.17
Aminopenicillins	0.34	0.55	0.31	0.22	0.64	0.77
Trimethoprim & sulphonamides	1.85	1.51	0.00	0.00	1.85	1.51
Macrolides & lincosamides	0.33	0.48	1.41	0.94	1.74	1.42
Fluoroquinolones	0.07	<0.01	<0.01	0.00	0.07	<0.01
Others[b]	0.60	0.61	0.95	0.63	1.55	1.24
Total	**8.27**	**9.74**	**4.50**	**2.35**	**12.77**	**12.09**

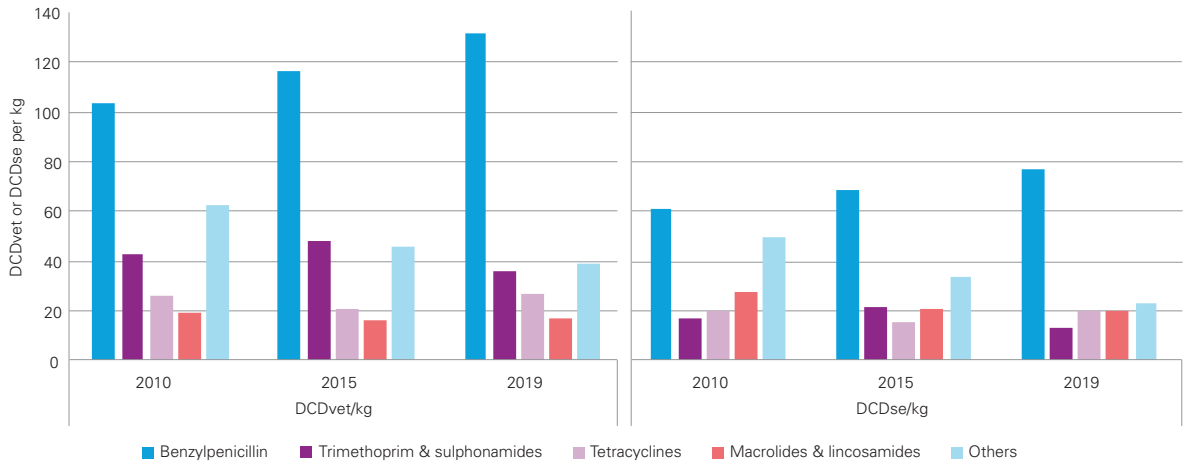
[a]Small amounts of benzylpenicillin in combination with dihydrostreptomycin are included under others.[b]Contains aminoglycosides, amhenicols, cephalosporins, pleuromutilins, polymyxins and combinaitons of bensylpenicillin and dihydrostreptomycin.

subclasses that are used for group medication. An especially prominent decrease is seen for polymyxins (-74%). Correspondingly, an increase is seen for most classes or subclasses of injectable products. Exceptions are products with trimethoprim-sulphonamides, of which there has been problems with availability on the market during 2019, and injectable products with aminopenicillins.

Changes over time for DCDvet/kg and DCDse/kg are shown in Figure 2. The above-mentioned difference for benzylpenicillin between DCDvet and DCDse is obvious, but there are differences also for e.g. trimethoprim-sulphonamides. Still, the changes over time by class or subclass are similar.

Taken together, the sales of antibiotics for pigs in Sweden have decreased between 2010 and 2019, and the proportion of sales for medication of groups of animals has decreased. Benzylpenicillin for medication of individual animals dominate and has increased. This is well in line with guidance on appropriate use of antibiotics (Medical Products Agency, 2012). In this situation, use of the unit DCDvet/kg underestimates overall changes in exposure, as there are major differences in the doses used nationally and those defined for DCDvet.

Figure 2. Sales of antibiotics for pigs expressed as DCDvet/kg slaughtered pigs and DCDse/kg slaughtered pigs.



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Medical Products Agency. 2012, Dosage of antibiotics for pigs – new treatment recommendation. In Swedish. *Information från Läkemedelsverket*, 23(suppl. 1):1-11. https://www.lakemedelsverket.se/sv/behandling-och-forskrivning/behandlingsrekommendationer/antibiotika-till-gris--behandlingsrekommendation

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 organisation support the implementation of EUCAST recommendations in the Nordic countries. The national resistance surveillance is based on data from different sources and collections (Table 3.1).

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

Species, group or type	Sampling
Mandatory reporting (SmiNet)	
Enterobacteriaceae with ESBL Enterobacteriaceae with $ESBL_{CARBA}$ *Staphylococcus aureus* resistant to methicillin *Streptococcus pneumoniae* non-susceptible to penicillin *Enterococcus faecium* or *faecalis* resistant to vancomycin *Mycobacterium tuberculosis*[a] *Neisseria gonorrhoeae*[a]	Samples of all types for clinical, screening or case finding purposes.
Neisseria meningitidis[a]	Invasive disease (blood, CSF, or other normally sterile sample).
Voluntary surveillance (Svebar)	
Escherichia coli	Clinical sampling from blood and urine.
Klebsiella pneumoniae	Clinical sampling from blood and urine.
Staphylococcus aureus	Clinical sampling from blood and skin and soft tissue infections.
Streptococcus pneumoniae	Clinical sampling from blood and nasopharynx.
Enterococcus faecalis *Enterococcus faecium*	Clinical sampling from blood.
Pseudomonas aeruginosa	Clinical sampling from blood and non respiratory infections.
Acinetobacter spp.	Clinical sampling from blood.
Haemophilus influenzae	Clinical sampling from blood and nasopharynx.
Streptococcus pyogenes *Streptococcus agalacticae*	Clinical sampling from blood.
Clostridioides difficile	Clinical sampling from faeces.
Salmonella spp[b]	Clinical sampling from blood, faeces and urine.
Campylobacter jejuni[b]	Clinical sampling from faeces.
Shigella spp[b]	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.
Acinetobacter spp. with $ESBL_{CARBA}$	All isolates resistant to meropenem
Pseudomonas spp. with $ESBL_{CARBA}$	All isolates resistant to imipenem/meropenem and ceftolozane-tazobactame
Staphylococcus aureus resistant to methicillin	All isolates from clinical samples.
Streptococcus pneumoniae non-susceptible to penicillin (MIC ≥ 0.5)	All isolates from clinical, screening or case finding samples.
Enterococcus faecium or *E. 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 with cephalosporin resistance	All isolates from clinical, screening or case finding samples.
Escherichia coli and *Klebsiella pnemoniae* resistant to cefadroxil	Consecutive samples from urine during one month every three years, 600-800 isolates

[a]All infections with these bacteria are mandatory to report. Antibiotic resistance data is acquired from these surveillance programs. [b]All infections with these bacteria are mandatory to report. However, the antibiotic resistance data is acquired through voluntary reporting in Svebar.

The national and international reference and development laboratory for phenotypic antimicrobial susceptibility testing (hosted by Clinical microbiology, Region Kronoberg, Sweden)

The availability of a national reference laboratory for phenotypic antimicrobial susceptibility testing (AST) promotes a national high quality of AST and surveillance of antibiotic resistance. Clinical microbiology in Region Kronoberg has throughout the period 1987 until today served as a national and since 2010 an important international hub in the field of susceptibility testing.

Background

For 25 years (1987-2012), the development of a Swedish national system for and harmonisation of AST was led by SRGA-M (RAF-M) chaired by Gunnar Kahlmeter and with Barbro Olsson-Liljequist (Institute for Communicable Disease Control) as the scientific secretary. For almost 20 years, the SRGA website (www.srga.org) created and run by SRGA-M, listed all recommendations from SRGA and SRGA-M. SRGA-M orchestrated the development and validation of methods, not only for antimicrobial susceptibility testing of bacteria, but also for internal and external quality assurance systems, the training of staff and national systems for AMR surveillance. Svebar, the current automated system which collects AMR data from routine laboratories in Sweden, emanated from the national reference laboratory (NRL) in Växjö. Throughout the years, all Swedish laboratories participated in the annual two-day workshop in practical methodology and all participated in the national initiative for harmonisation of AST and resistance monitoring. The other Nordic countries were invited to participate in the work and after a few years RAF-M was amicably closed down to create a Nordic substitute, NordicAST (www.nordicast.org).

National Reference Laboratory for phenotypic susceptibility testing

In 2000 the Director General of the Institute for Communicable Diseases, Erik Nordenfeldt, appointed clinical microbiology in Region Kronoberg to "national reference laboratory for phenotypic susceptibility testing". Ten years later, Ragnar Norrby confirmed the appointment and when the Swedish Laboratory Network in Microbiology (SLIM) was set up in 2017, the NRL role of the laboratory was affirmed.

Table 1. Requests to the reference laboratory for MIC determination and the most common reasons for referral in 2019.

Species	Number	Common reason for referral
Streptococcus pneumoniae	275	Beta-lactam resistance
Pseudomonas aeruginosa	106	Multiresistance – widened panel of antimicrobials
Haemophilus influenzae	60	Beta-lactam resistance
Staphylococcus epidermidis	30	MIC-determination for new glycopeptides
Escherichia coli	28	Multiresistance – request for wide MIC panels and test for colistin
Klebsiella pneumoniae	27	Multiresistance – request for wide MIC panels and test for colistin
Burkholderia cepacia-compelx	17	AST - Formal method and breakpoints lacking
Enterococcus faecalis	14	Glycopeptide resistance
Stenotrophomonas maltophilia	14	Formal method lacking, except for trimethoprim-sulphametoxazol. Interpretative difficulties concerning trimethoprim-sulfamethoxazole AST.
Enterococcus faecium	13	Glycopeptide resistance
Staphylococcus aureus	12	Linezolide- and daptomycin susceptibility
Salmonella species	10	Multiresistance and colistin resistance
Enterobacter cloacae-complex	10	Multiresistance and colistin resistance
Acinetobacter baumannii	8	Multiresistance and colistin resistance
Achromobacter xylosoxidans	6	Multiresistance and colistin resistance
36 other species (<5 of each)	47	Miscellaneous. Often due to the formal lack of method and breakpoints.

The national assignment gradually included offering other laboratories determination of MIC values with reference broth microdilution methodology of bacteria. Other tasks were to assist with the training of laboratory personnel, and to generally be prepared to help solve AST problems. The NRL procures custom made panels of antimicrobials, suited to each pathogen. Thus there is a panel for Enterobacterales, one for Pseudomonas, Staphylococci, Streptococci and several more (available panels are listed at http://www.mikrobiologi.org/referenslaboratorium). Since a common reason for assistance is multi- or panresistance, the NRL updates panels to include the most recent additions to the antimicrobial armamentarium. This sometimes includes antimicrobials where a formal method or breakpoints have not yet been determined. Table 1 lists 2019 requests to the reference laboratory for MIC determination and the most common reasons for referral.

The EUCAST Development Laboratory (EDL)

In 2001 Gunnar Kahlmeter was appointed chairman of the European Committee on Antimicrobial Susceptibility Testing (EUCAST) and in the following years, European countries agreed on common breakpoints for AST. Since then, European institutions such as the EMA, ECDC and EFSA and all European countries (and many overseas) have all adopted the EUCAST guidelines. Once a European system for determining breakpoints had been created (2002 - 2008), it became evident that to harmonise susceptibility testing in Europe and to implement the same breakpoints in all European countries, which at that time were using 7 different systems and methods, there must be a European AST method. After consultation inside EUCAST, it was agreed that the laboratory in Växjö had the necessary experience to take the responsibility for leading the work. A European standardised disk diffusion method was developed. Methods other than disk diffusion were dismissed early as unrealistic.

The development has been going on for more than 10 years and the commitment has gradually grown. New agents need methods, disk content, calibration of inhibition zone diameters to MIC-values and QC criteria. New methods and criteria need field testing and the EUCAST network of laboratories are tasked to help. The laboratory has become a concept and among international colleagues and laboratories goes by the name of "The EDL" (The EUCAST Development Laboratory). It employs 2-5 clinical and technical scientists and a clinical microbiologist. The number of staff on a given day depends on the number of assignments and ongoing projects as well as the availability of resources through the EU, ESCMID, ECDC and research grants.

All the work performed at the EDL and all raw data produced are channelled through and updated on the EUCAST website (www.eucast.org). The website also contains the annually updated tables of breakpoints, also administered through the EDL.

On the website, there is one page where you do not want to be listed – the "EUCAST warnings page" (http://www.eucast.org/ast_of_bacteria/warnings/). This shows failing manufacturers, materials and procedures. Examples of warnings are the recently issued warning against benzylpenicillin MIC determination in pneumococci using gradient tests and warnings regarding the lack of quality of resistance testing materials from some manufacturers.

EDL employees participate in the planning and implementation of annual EUCAST and NordicAST workshops and courses presenting news in the area of antibiotic resistance and AST.

These are examples of completed and ongoing EDL tasks and projects.

- Standard disc diffusion method for all antibiotics and species specific clinical breakpoints by EUCAST, continuous calibration, validation and updating (https://doi.org/10.1111/1469-0691.12373).
- Develop and validate substrates for AST of fastidious bacteria (Mueller-Hinton Fastidious (MH-F)) and of anaerobic bacteria (FAA medium).
- The ongoing development of disk diffusion for anaerobic bacteria.
- Methods and substrates to enable the setting of breakpoints and performance of routine AST for fastidious bacteria (Campylobacter, Kingella, Plesiomonas, Aeromonas, Aerococcus, Corynebacteria, etc.).
- Develop and maintain criteria for internal quality assurance.
- Develop systems for determining MIC reference distributions and ECOFFs (https://mic.eucast.org/Eucast2/).
- Develop reliable resistance screening systems (beta-lactam resistance in pneumococci and *H. influenzae*, methicillin resistance in staphylococci, quinolone resistance in Salmonella and in Gram-positive organisms, etc.).
- Rapid AST directly from positive blood culture bottles has now been available on EUCAST's website since November 2018. With this procedure AST results can be delivered in 4 – 6 hours for the most relevant pathogens. The method is published in the Journal of Antimicrobial Chemotherapy (https://doi.org/10.1093/jac/dkz548).
- The performance of available methods and materials for susceptibility testing of colistin (gradient tests, disc diffusion, broth dilution, etc.) was investigated and published in CMI (https://doi.org/10.1016/j.cmi.2017.11.020).

- The quality of material used in standard disk diffusion AST was investigated and published: discs from 9 suppliers (https://doi.org/10.1016/j.cmi.2018.05.021) and 21 commercially available Mueller Hinton media (https://doi.org/10.1016/j.cmi.2020.01.018).
- A recently completed project concerns *Burkholderia pseudomallei*, which causes melioidosis in areas around the equator, especially in Southeast Asia. On request we developed MIC distributions, ECOFFs and via EUCAST clinical breakpoints and subsequently disk diffusion criteria. For this project, we engaged a large number of laboratories in the region where mellioidosis occurs endemically. *Burkholderia pseudomallei* therefore has clinical breakpoints and method of disc diffusion in 2020 year breakpoint table.
- Develop a method and a system for determining appropriate disc strength for disc diffusion.
- Assist EUCAST and international industry in the development of new antibiotics, especially in the development and validation of AST methods and materials.
- Auscultations (EUCAST and ESCMID International Observerships): 1- 5 days of auscultation at EDL (India, Australia, Yemen, Croatia, Germany, South Africa and others).
- Courses for laboratory staff in basic resistance assessment (ESCMID Postgraduate courses, NordicAST workshops, practical courses for clinical and technical staff).

Much time is spent helping colleagues at other laboratories in Sweden and abroad. We answer many hundreds of questions every year via email and phone. Every year we receive many 1–5 day visits from colleagues in Sweden and abroad. Gunnar Kahlmeter is the head of the EDL and Erika Matuschek leads the everyday work.

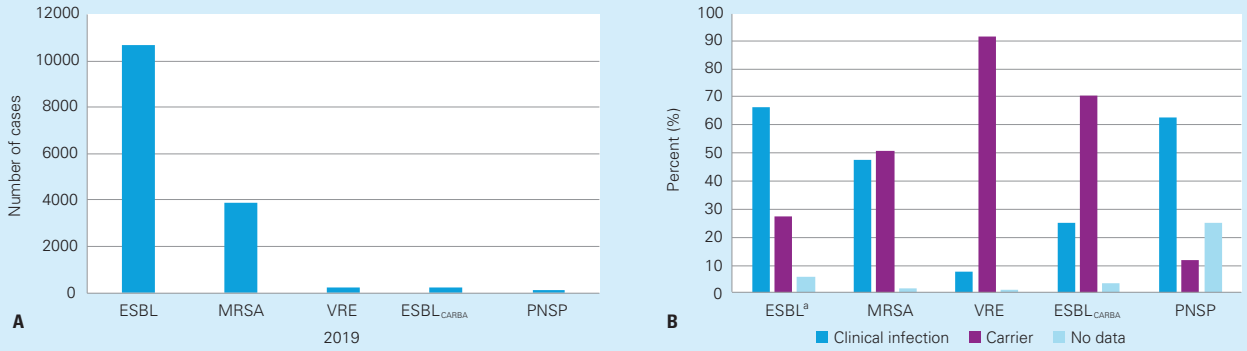
Abbreviations

National Reference Laboratory (NRL)
The EUCAST Development Laboratory (EDL)
The European Food Safety Agency (EFSA)
The European Society for Clinical Microbiology and Infectious Diseases (ESCMID)
Referensgruppen för Antibiotikafrågor (RAF) och dess metodgrupp (RAF-M)
Swedish Laboratory Network in Microbiology (SLIM)
Swedish Reference Group for Antibiotics (SRGA) and its subcommittee on methods (SRGA-M)

Notifiable diseases

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 (including AmpC) or $ESBL_{CARBA}$. As in previous years, the notifications of ESBL have outnumbered the other three manifold (Figure 3.1 and Table 3.2).

Figure 3.1 A, B. Number of mandatory reported cases during 2019 (A) and the proportion of clinical infection versus carriers (B).



[a]ESBL data, based on sample types, clinical infection (blood, urine, CSF), carrier (faeces, rectum, perineal), No data (other sample materials or not specified).
Source: The Public Health Agency of Sweden

Table 3.2. Summary of results for mandatory reported antibiotic resistance 2019.

	ESBL	$ESBL_{CARBA}$	MRSA	PNSP	VRE
Number of cases (inc)	10 717 (104)	201 (1.9)	3 858 (37)	118 (1.1)	232 (2.2)
Proportion clinical infection	67%	25%	47%	62%	8%
Gender	66% women	56% men	52% women	56% men	60 % men
Median-age (range)	56 year (0-100+)	53 year (0-100+)	31 year (0-100+)	54,5 year (0-91)	71 year (0-99)
Proportion of domestic cases	no information	22% (7% no data)	53% (7% no data)	66% (22% no data)	46%
Short epidemiological information	Community and health-care	Hospital abroad	Community	Community	Hospital, domestic spread
Bloodstream infections	835 (647 new cases 2019, 188 cases known from previous years)	6	72 (62 new cases 2019, 10 cases known from previous years)	9	10

Table 3.3. Number of laboratories used for antibiotic resistance calculations during 2015- 2019.

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

Voluntary surveillance based on clinical samples

This surveillance uses results collected from the local clinical microbiology laboratories. From 2015 and onwards, all data on clinical isolates from humans have been collected through Svebar. This is a system that automatically collects all culture results from participating clinical microbiology laboratories. Currently 20 laboratories deliver data to Svebar (March 2020). It is not possible to deduplicate data from Svebar since patient identification is not permitted in the system. Consequently, duplicate findings from blood and other samples will be reported. For unusual resistance types this can result in overestimation of the resistance, especially if these patients are sampled frequently. Large differences in resistance trends for these types of resistance should be interpreted with caution. Data analysed from the voluntary surveillance system (Svebar) are collected from laboratories with validated data (Table 3.3). All antibiotic resistance levels presented in this report are based on unselected susceptibility testing. For some pathogen/antibiotic combinations, a lower number of isolates with an AST result will be presented. Data from some laboratories are excluded when not all isolates are tested routinely. If data presented is based on selective testing, this will be indicatied in the grafs and tables. The number of AST isolates for each species and antibiotic combination is given in the attached file. The 95% confidence intervals are presented in figures showing resistance. The confidence intervals are only present from 2015 and onwards.

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

Microbiological characterisation program

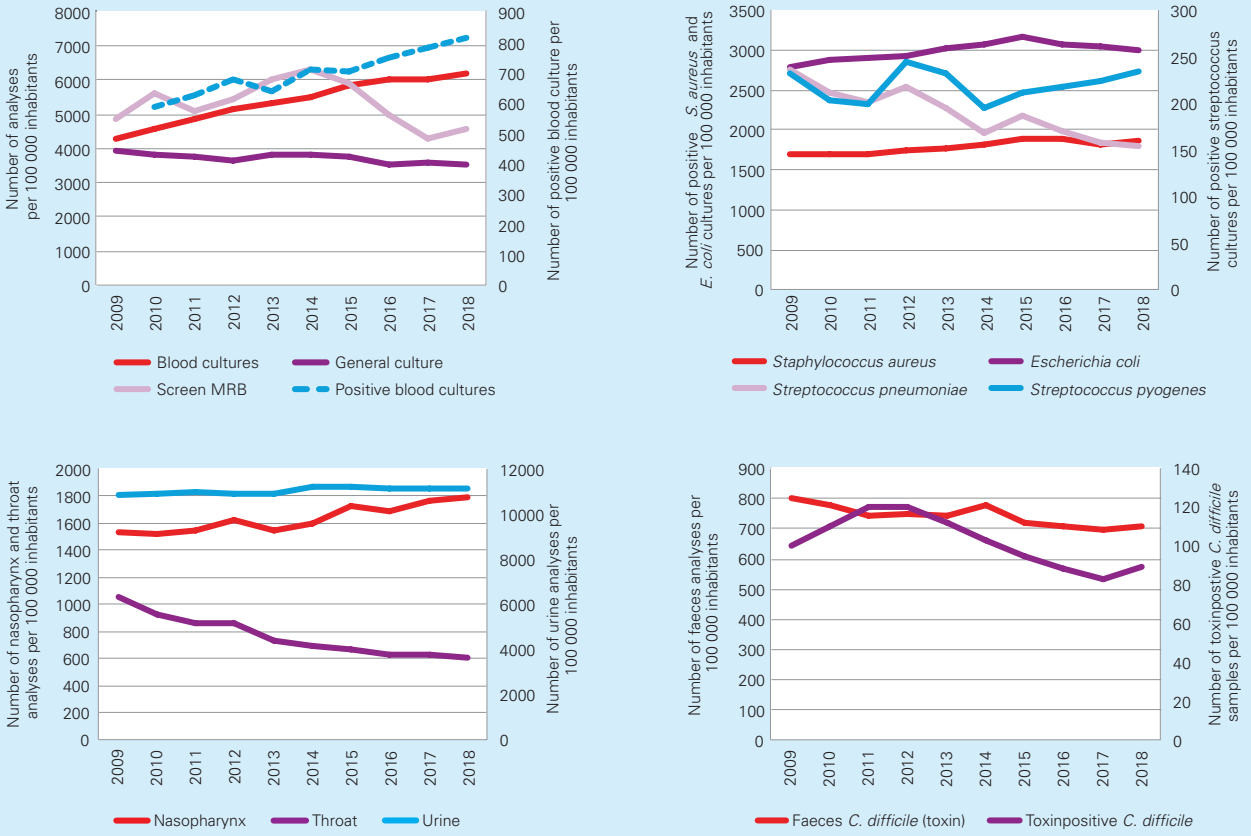
The Public Health Agency of Sweden provide microbiological characterisation programs for verification and characterisation of isolates that participating laboratories send in. Regarding antibiotic resistance there are currently programs for, *Clostridioides difficile*, Enterobacteriaceae with ESBL (including AmpC) and/or $ESBL_{CARBA}$, MRSA, PNSP, and VRE. In 2018, two additional programs were 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 indicator antibiotics. For Enterobacteriaceae with ESBL (including AmpC) 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. The collection for 2019 within this program was postponed. 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. An overwiev is summarised in Table 3.1.

Overview of sampling, culture results and reported antibiotic resistance

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. Since 2018 some of the data is derived from Svebar. No denominator was collected for 2019. Complete data for 2018 are given in the section Demographics and denominator data. In the following Figure 3.2 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*. Number of positive blood cultures per 100 000 inhabitants and 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. A downward trend is seen for MRB screening culture that could be a result of changes in sampling and screening practices. 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. Though for *S. pyogenes* there is an increased number of isolates the last three years.

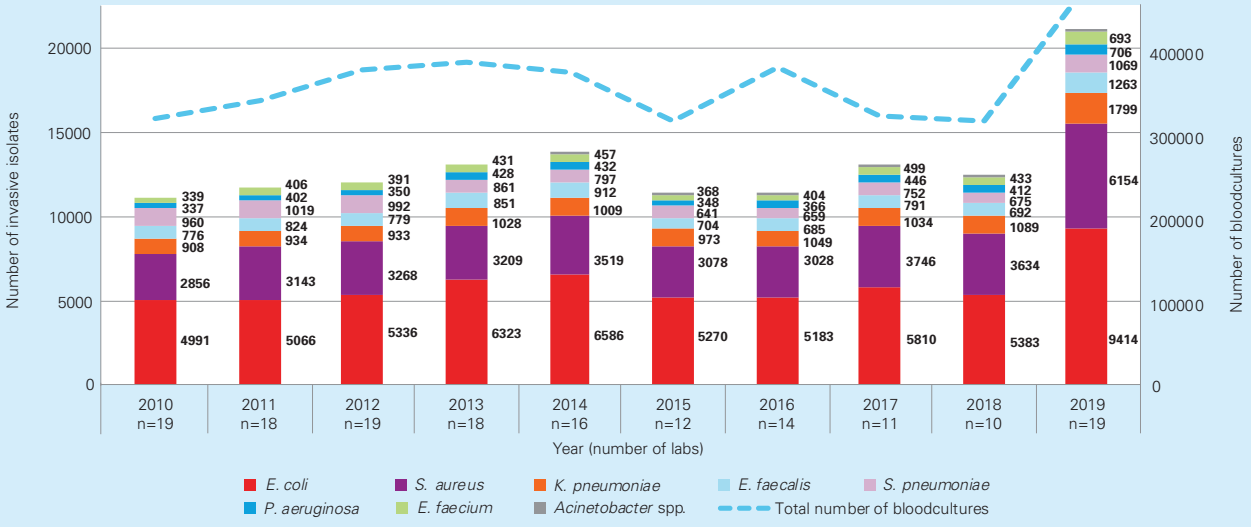
The number of bacteria reported to EARS-Net yearly, as well as the number of blood cultures taken, is shown in Figure 3.3.

Figure 3.2. Denominator data for humans, year 2009-2018. Number of requested analyses, and number of positive analyses or isolates. All per 100 000 inhabitants.



Source: The Public Health Agency of Sweden

Figure 3.3. Number of isolates, collected from blood during 2010-2019, reported to EARS-Net.



Source: The Public Health Agency of Sweden

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

Mandatory reporting of ESBL-producing Enterobacteriaceae

Results from 2019

- Number of reported cases: 10 717 (previous year 10 341), relative change +3.6%
- Number of bloodstream infections: 835 (previous year 703), relative change +19%

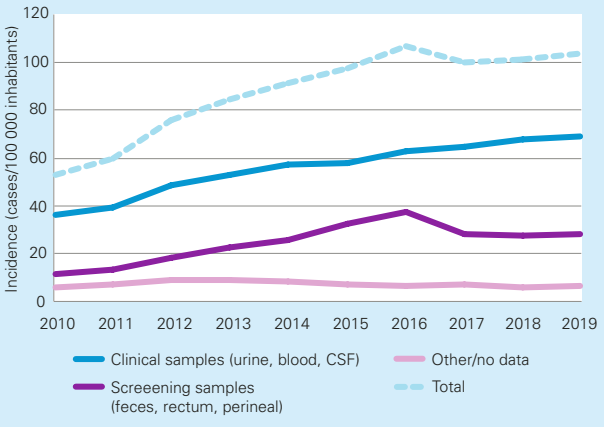
Trends

The incidence for ESBL has steadily increased over the years. A slight decrease were noted 2017. In 2019 the incidence was 104 new cases per 100 000 inhabitants, see Figure 3.4. The increase in recent years is mainly driven by cases with mostly clinical samples (urine, blood and cerebrospinal fluid (CSF)). While the incidence for samples taken for screening purposes (faeces, rectum and perineal) since 2017 has remained stable.

The number of bloodstream infections (BSI) with ESBL-producing Enterobacteriaceae has increased steadily since it became notifiable (Figure 3.5). In 2019, *E. coli* was the most common cause of BSI, 82% followed by *K. pneumoniae* 15%.

All 21 regions in Sweden reported ESBL-cases and a threefold difference in incidence was noted, from 62 to 177 cases per 100 000 inhabitants. The large variation could partly be explained by different local practices in sampling.

Figure 3.4. The incidence (cases/100 000 inhabitants) of cases with ESBL-producing Enterobacteriaceae in relation to type of infection, year 2010–2019.

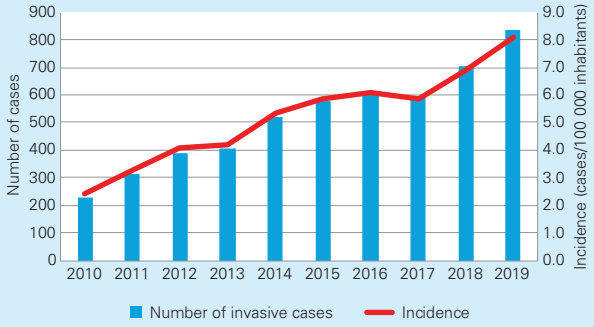


Source: The Public Health Agency of Sweden

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 (Table 3.2). Elderly, 85 years and older (n=911, incidence 346) followed by children under one year (n=382, incidence 331) had the highest incidence. The high incidence in neonates is probably a result of screening and contact tracing at neonatal units. Among the elderly urinary tract infection is a common bacterial infection explaining the high incidence in this group.

As in previous years, the most commonly reported species was *E. coli* found in 86% of all cases followed by *K. pneumoniae* with 10%. The remaining cases comprised of several other species of Enterobacteriaceae (for detailed information see attached file Figure 3.4).

Figure 3.5. Number and incidence (cases/100 000 inhabitants) of invasive cases with ESBL-producing Enterobacteriaceae, reported during year 2010–2019.



Source: The Public Health Agency of Sweden

Outbreaks

As in previous years small clusters with both ESBL-producing *K. pneumoniae* and *E. coli* have been noted at neonatal units and other units in different parts of Sweden during 2019. However, outbreaks with ESBL-producing Enterobacteriaceae are not consistently reported.

Comments

Differences in sampling, screening and contact tracing practices in the regions highly influences these results. Since 2016 the total incidence of ESBL-producing Enterobacteriaceae has not changed but the incidence for cases discovered in clinical samples has increased constantly during the years. The rise of bloodstream infections with ESBL-producing Enterobacteriaceae is particularly worrisome.

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

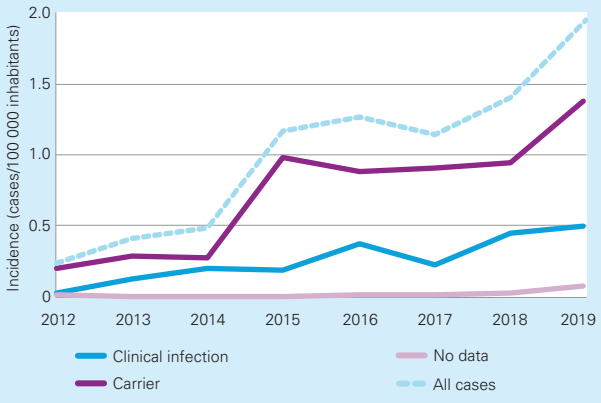
Results from 2019

- Number of reported cases: 201 (previous year 144), relative change +40%
- Number of bloodstream infections: 6 (previous year 7)

Trends

In 2019, the incidence for ESBL$_{CARBA}$ producing Enterobacteriaceae was 1.9 cases per 100 000 inhabitants, an increase with 40% (57 cases) compared to 2018. A majority, 71% of the cases, were carriers (Figure 3.6). Cases were reported from 20 of 21 regions in Sweden. The majority of cases were reported as acquired abroad (71%, n=143) and identified in targeted screening after hospitalisation abroad. Out of the 44 domestic cases, 19 were identified by investigation of clinical infection. The proportion of domestic cases with hospital acquired ESBL$_{CARBA}$ remained at the same level as previous year. For 23 domestic cases information of acquisition was missing. The ESBL$_{CARBA}$ cases were unequally distributed between women and men (44% women, 56% men) with median ages of 46 years for women and 59 years for men.

Figure 3.6. Incidence (number of cases/100 000 inhabitants) of notified cases with ESBL$_{CARBA}$ producing Enterobacteriacae, 2012-2019.

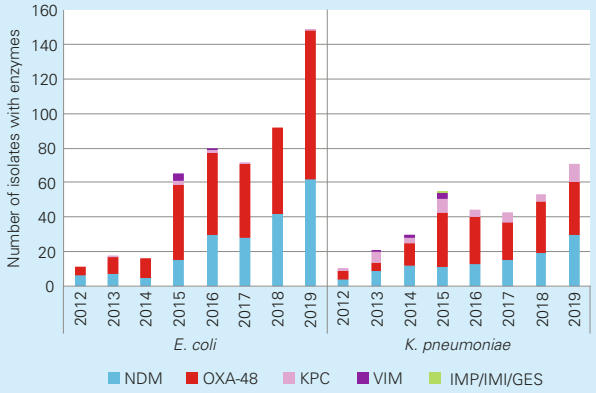


Source: The Public Health Agency of Sweden

Epidemiological typing of ESBL$_{CARBA}$

ESBL$_{CARBA}$ isolates from notified cases in 2019 have been characterised using whole genome sequencing (WGS). The most common carbapenemase-producing Enterobacteriaceae was *E. coli*, accounting for 64% of all cases, followed by *K. pneumoniae* (28%). Genes encoding for carbapenem resistance have also been detected in several other species of Enterobacteriaceae. The dominating enzyme type in 2019 was OXA-48 and this enzyme was detected in *E. coli* and *K. pneumoniae* isolates, in most cases together with CTX-M (=ESBL$_A$) (Figure 3.7.). The occurrence of ESBL$_{CARBA}$ producing Enterobacteriaceae with combinations of two carbapenemases (most commonly NDM + OXA-48) are still rare. Apart from the genotypic analysis, isolates have been tested for antibiotic susceptibility using broth microdilution (BMD) (since June 2019) or gradient test and disc diffusion (until June 2019), see Table 3.4. Colistin has only been tested with BMD and of the 56 isolates tested for colistin, seven *K. pneumoniae* were found to be resistant but none of the *E. coli* isolates.

Figure 3.7. Number of isolates and enzyme types of ESBL$_{CARBA}$ in Enterobacteriaceae in Sweden 2012-2019.



Source: The Public Health Agency of Sweden

Table 3.4. Antibiotic resistance in ESBL$_{CARBA}$ producing *E. coli* and *K. pneumoniae* 2019.

Antibiotic	*E. coli*		*K. pneumoniae*	
	OXA-48 group, % R (n=83)	NDM/KPC, % R (n=62)	OXA-48 group, % R (n=33)	NDM/KPC, % R (n=47)
Amikacin	7.2	16.1	24.2	68.1
Cefotaxime	74.7	95.2	84.8	100
Ceftazidime	60.2	95.2	81.8	100
Ciprofloxacin	16.9	32.3	36.4	51.1
Gentamicin	25.3	33.9	48.5	55.3
Imipenem	1.2	79.0	27.3	93.6
Meropenem	1.2	77.4	36.4	91.5
Meropenem Screen[a]	92.8	94.0	97.0	100
Nitrofurantoin	0.0	12.9	-	-
Piperacillin-tazobactam	100	93.5	36.4	34.0
Tobramycin	22.9	64.5	66.7	100

[a]Meropenem Screen (<28 mm or >0,125 mg/L).

Outbreaks

One observed cluster of ESBL$_{CARBA}$ occurred in Sweden at a neonatal unit, which included 3 patients.

In 2019, Germany identified an increasing number of cases with OXA-244-producing *E. coli* belonging to a cluster of *E. coli* with sequence type (ST) 38. In response to an urgent inquiry in ECDC's EPIS AMR-HAI, Sweden along with several other European Union/European Economic Area countries submitted WGS data on OXA-244 *E. coli* strains to ECDC. Sweden submitted data from 33 isolates of *E. coli* with OXA-244 (ST 38). A main cluster was identified containing 114 isolates from twelve countries. Nineteen of the Swedish isolates belonged to the main cluster when compairing MLST profiles (ECDC, 2020).

Another response to an urgent inquiry in ECDC's EPIS AMR-HAI was due to an outbreak of carbapenemase-producing (NDM-1 and OXA-48) and colistin-resistant *K. pneumoniae* with sequence type (ST) 307 in Germany. Sweden submitted WGS data from eight *E. coli* isolates with combined NDM-1 and OXA-48 enzymes. None of the Swedish isolates belonged to the outbreak identified in Germany (ECDC, 2019).

Comments

The number of ESBL$_{CARBA}$ cases is low but increasing in Sweden. The majority of cases are identified in screening programs after hospitalisation abroad. The lack of information on the way of acquisition for more than 50% of the domestic cases is worrisome. National surveillance is important in order to follow the development of ESBL$_{CARBA}$ among the Swedish population in the coming years, but also as a way to at an early stage, try to limit any possible spread.

Escherichia coli, from blood and urine cultures

Results from 2019

- Number of reported cases with ESBL$_{CARBA}$-producing *E. coli*: 144
- Number of reported cases with bloodstream infections caused by ESBL$_{CARBA}$-producing *E. coli*: 2
- Number of reported cases with ESBL-producing *E. coli*: 9 489
- Number of reported cases with bloodstream infections caused by ESBL-producing *E. coli*: 700

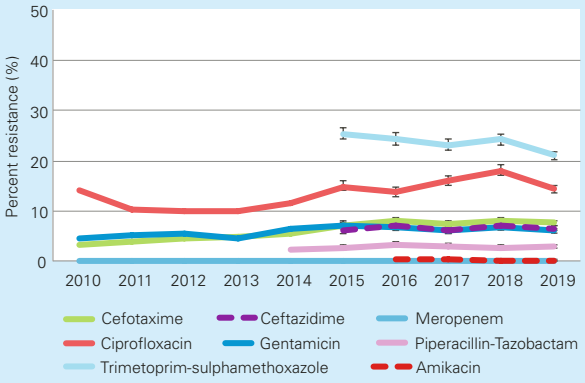
Table 3.5. Proportion (%) of antibiotic resistant *E. coli* from blood or urine 2019.

Antibiotic	Blood isolates, % R (n=9 414)	Urine isolates, % R (n=204 386)
Ampicillin	na	30.6
Cefadroxil	na	6.2
Cefotaxime	7.6	4.0
Ceftazidime	6.6	3.2
Flouroquinolone	14.3	10.9
Gentamicin	6.0	na
Mecillinam	na	4.8
Meropenem	0.0	na
Nitrofurantoin	na	1.2
Piperacillin-tazobactam	3.0	4.2[a]
Trimetoprim	na	20.4
Trimetoprim-sulphamethoxazole	21.4	na
Combined resistance to Cefotaxime/ceftazidime + Gentamicin/tobramycin	2.5	na
Combined resistance to both Piperacillin-tazobactam + Gentamicin/tobramycin	0.7	na

[a]Based on selective testing.

Trends

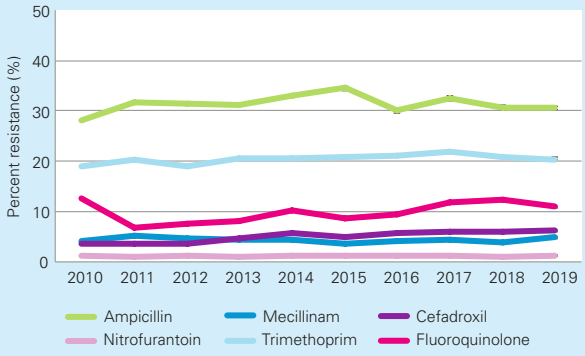
Figure 3.8. Antibiotic resistance in *E. coli* isolated from blood during the years 2010-2019. Prior to 2011, nalidixic acid was used for detection of fluoroquinolone resistance in Enterobacteriaceae. From 2011, ciprofloxacin was used. The numbers of AST isolates for all years and antibiotics ranges from 3 983 to 9 414. The exact numbers are given in the attached file.



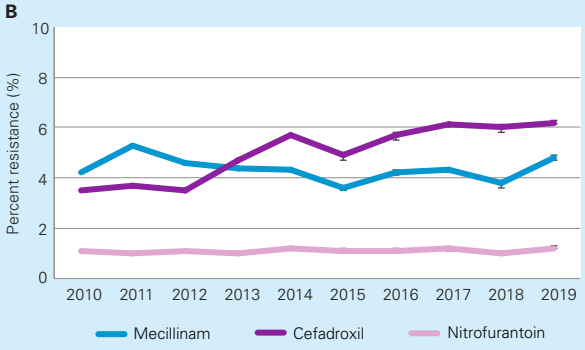
Source: The Public Health Agency of Sweden

Figure 3.9 A and B. Antibiotic resistance in *E. coli* isolates from urine during the years 2010-2019. Figure A shows all tested antibiotics and figure B shows more detailed data (below 10% resistance) for some antibiotics. Prior to 2011, nalidixic acid was used for detection of fluoroquinolone resistance in Enterobacteriaceae. From 2011, ciprofloxacin was used. The numbers of AST isolates for all years and antibiotics ranges from 5 892 to 204 386. The exact numbers are given in the attached file.

A

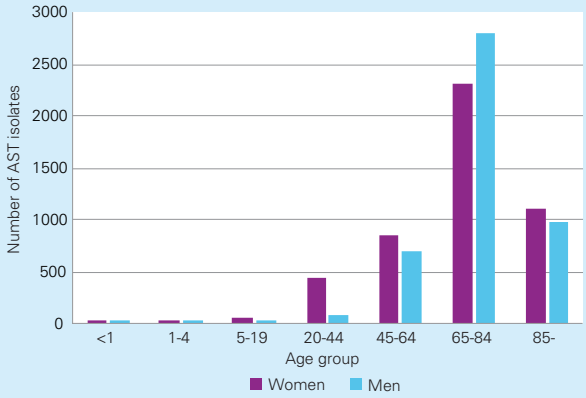


B



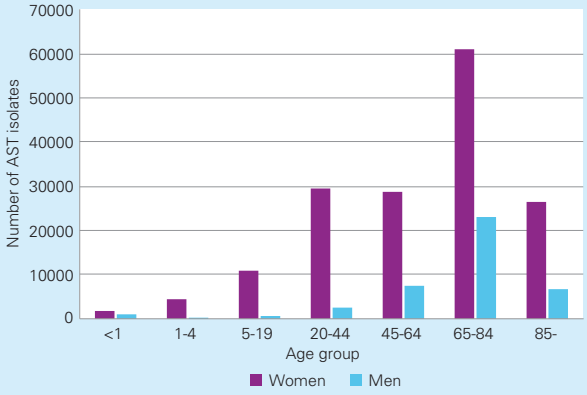
Source: The Public Health Agency of Sweden

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



Source: The Public Health Agency of Sweden

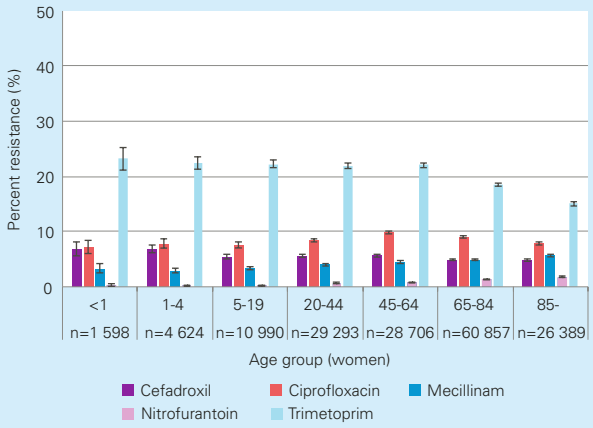
Figure 3.11. Age distribution among patients with *E. coli* isolated from urine. The number of isolates is based on ciprofloxacin AST.



Source: The Public Health Agency of Sweden

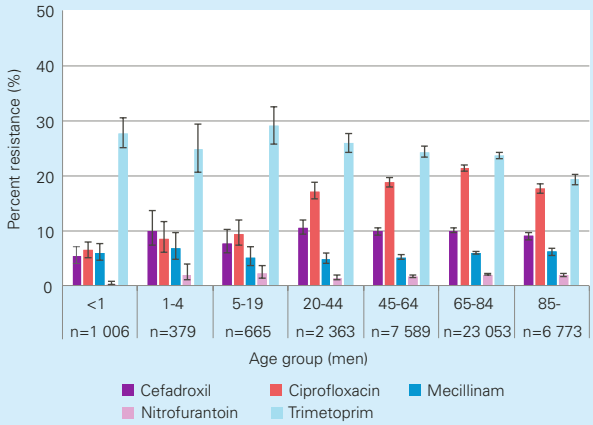
Resistance in *E. coli* causing urinary tract infections divided by age group and gender are shown in figures 3.12 and 3.13. Ciprofloxacin resistance was higher among men compared to women, especially in ages over 20 years. No other large difference in resistance was seen in relation to increasing age.

Figure 3.12. Antibiotic resistance in *E. coli* from urine in women divided in age groups, year 2019.



Source: The Public Health Agency of Sweden

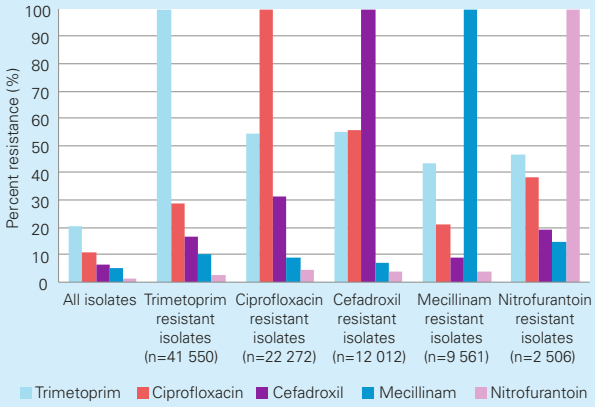
Figure 3.13. Antibiotic resistance in *E. coli* from urine in men divided in age groups, year 2019.



Source: The Public Health Agency of Sweden

In *E. coli* already resistant to one of the antibiotics commonly used to treat urinary tract infections, an increased resistance is observed for the other antibiotics as well (Figure 3.14).

Figure 3.14. Combined resistance based on *E. coli* from urine resistant to one selected antibiotic during 2019.



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 7.6%. The carbapenem resistance is still very low. Combined resistance to cefotaxime/ceftazidime and gentamicin/tobramycin or the combination piperacillin-tazobactam and gentamicin/tobramycin was 2.5% and 0.7% respectively (Table 3.5 and Figure 3.8).

Resistance to commonly prescribed oral antibiotics for treatment of urinary tract infections (UTI) caused by *E. coli* remained stable except for mecillinam. This increase in resistance is not a reason for any change of the recommended first-line treatment for uncomplicated UTIs (pivmecillinam and nitrofurantoin) (Figure 3.9). Cefadroxil resistance, which can be used as an indicator for production of ESBL, remained at 6%.

Resistance to fluoroquinolones is still high, but decreased slightly during 2019, and is now at approximately 14% and 11% for blood and urine isolates respectively (Table 3.4, Figure 3.8 and 3.9). The increasing flouroquinolone resistance seen during 2016-2017 can mostly be explained by a breakpoint change for ciprofloxacin. The high level of ciprofloxacin resistance must be considered when choosing empirical treatment for febrile UTI, especially among men in ages over 20 years (Figure 3.12 and 3.13).

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

Klebsiella pneumoniae, from blood and urine cultures

Results from 2019

- Number of reported cases with $ESBL_{CARBA}$-producing *K. pneumoniae*: 63
- Number of reported cases with bloodstream infections caused by $ESBL_{CARBA}$-producing *K. pneumoniae*: 4
- Number of reported cases with ESBL-producing *K. pneumoniae*: 1 110
- Number of reported cases with bloodstream infections caused by ESBL-producing *K. pneumoniae*: 125

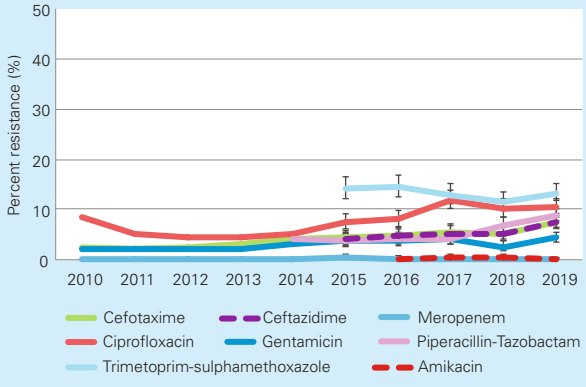
Table 3.6. Proportion (%) of antibiotic resistant *K. pneumoniae* from blood or urine 2019.

Antibiotic	Blood isolates, % R (n = 1 799)	Urine isolates, % R (n=21 089)
Ampicillin	Intrinsic resistance	Intrinsic resistance
Cefadroxil	na	5.9
Cefotaxime	7.3	4.1
Ceftazidime	7.4	4.4
Flouroquinolone	10.5	8.2
Gentamicin	4.4	na
Mecillinam	na	9.7
Meropenem	0.1	na
Nitrofurantoin	Intrinsic resistance	Intrinsic resistance
Piperacillin-tazobactam	8.9	11.9[a]
Trimetoprim	na	18.0
Trimetoprim-sulphamethoxazole	13.3	na
Combined resistance to Cefotaxime/ceftazidime + Gentamicin/tobramycin	3.8	na
Combined resistance to Piperacillin-tazobactam + Gentamicin/tobramycin	2.0	na

[a]Based on selective testing.

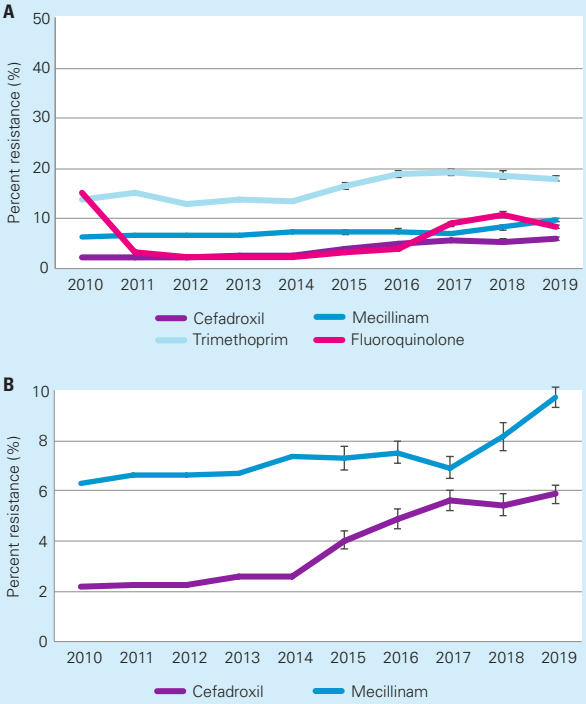
Trends

Figure 3.15. Antibiotic resistance in *K. pneumoniae* isolated from blood during the years 2010-2019. Prior to 2011, nalidixic acid was used for detection of fluoroquinolone resistance in Enterobacteriaceae. From 2011, ciprofloxacin was used. The numbers of AST isolates for all years and antibiotics ranges from 751 to 1 799. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Figure 3.16 A and B. Antibiotic resistance in *K. pneumoniae* isolates from urine during the years 2010-2019. Figure A shows all tested antibiotics and figure B shows more detailed data (below 10% resistance) for some antibiotics. Prior to 2011, nalidixic acid was used for detection of fluoroquinolone resistance in Enterobacteriaceae. From 2011, ciprofloxacin was used. The numbers of AST isolates for all years and antibiotics ranges from 2 030 to 21 089. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Comments

Among invasive isolates, the resistance levels increased for all antibiotics tested with the exception for carbapenems where the resistance remains low. The resistance to cefotaxime was 7.3%. Combined resistance to cefotaxime/ceftazidime and gentamicin/tobramycin or the combination piperacillin-tazobactam and gentamicin/tobramycin was 3.8% and 2.0% respectively (Table 3.6 and Figure 3.15).

Resistance to commonly prescribed oral antibiotics for treatment of urinary tract infections caused by *K. pneumoniae* remained stable except for mecillinam. This increase in resistance is not a reason for any change of the recommended first-line treatment for uncomplicated UTIs (pivmecillinam and nitrofurantoin). Cefadroxil resistance, which can be used as an indicator for production of ESBL, was 5.9%. 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.

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

Shorter time to antimicrobial susceptibility testing results in sepsis with new EUCAST methodology

A recently published method and breakpoints from the European Committee on Antimicrobial Susceptibility Testing (EUCAST) aim to improve the time to an antimicrobial susceptibility testing (AST) result for the most common bacteria found in bloodstream infections and sepsis. After implementing this new method in our clinical laboratory the number of AST results reported the same day or by afternoon rounds increased dramatically.

Background

Bloodstream infections and sepsis are associated with high morbidity and mortality, in particular if antibiotic treatment is delayed or ineffective. It is also recommended that the empirical antimicrobial therapy is narrowed as soon as antimicrobial susceptibility testing (AST) results are complete.

EUCAST has developed a rapid antimicrobial susceptibility testing (RAST) methodology based on disk diffusion to be used directly from blood culture bottles for species commonly involved in bloodstream infections. There are specific breakpoints for each combination of species, antibiotic and incubation time (4, 6 and 8 hours).

The RAST methodology was introduced in our routine clinical laboratory in May 2018 and replaced a non-standardised method for AST directly from blood cultures.

Direct species identification with matrix-assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF MS) was already routinely performed on all new positive clinical blood culture bottles but several other changes had to be made before RAST could be implemented:

- Reading exercises to standardise reading of RAST inhibition zones
- Automatic interpretation of RAST results (custom spreadsheet in Microsoft Excel)
- Ensuring sufficient number of technicians working with blood cultures during peak work load
- Inform recipients of the meaning of RAST results

Evaluation

Clinical blood cultures from 25 May 2018 to 22 October 2019 were included. Only species with RAST breakpoints were tested. One blood culture bottle per patient and sampling time was included in the analysis. Polymicrobial cultures and follow-up cultures to previously positive blood cultures were excluded (79 and 16 bottles respectively). Laboratory open hours were weekdays 07:30-17:00 and weekends 08:00-13:00. All work was performed by routine laboratory staff.

Table 1. Percentage of isolates with RAST breakpoints reported the same day and in time for afternoon rounds (at 15:00) on the day of the positive signal from the blood culture instrument. Averages across species in bold.

	Before RAST (n = 100)		**RAST 2018-05 – 2019-05** (n = 945)		**RAST 2019-05 – 2019-10** (n = 351))	**All RAST 2018-05 – 2019-10** (n = 1 296)
E. coli	50%	→	79%	→	84%	80%
K. pneumoniae	67%	→	86%	→	80%	84%
S. aureus	40%	→	75%	→	85%	78%
P. aeruginosa	13%	→	52%	→	86%	59%
S. pneumoniae	0%	→	63%	→	67%	63%
E. faecalis	33%	→	77%	→	82%	78%
E. faecium	33%	→	67%	→	60%	65%
Average	**44%**	→	**76%**	→	**82%**	**78%**
By afternoon rounds (15:00)	**22%**	→	**45%**	→	**71%**	**52%**

Before the introduction of RAST both the EUCAST standard 18 hour disk diffusion and a locally developed non-standardised rapid AST method was used in parallel. After the introduction of RAST the non-standardised rapid method was replaced with RAST. In both cases the standard disk diffusion method was used as the only AST method if not enough time was left in the work day to perform a rapid AST on a specific sample.

Time started when the first positive bottle was removed from the blood culture instrument (BACTEC FX, BD) and ended when the first AST result was delivered, regardless of AST method used (non-standardised rapid AST, RAST or EUCAST standard disk diffusion). The control group consisted of the last 100 positive consecutive blood culture isolates with RAST breakpoints immediately prior to the introduction of RAST. To further shorten reporting times reading RAST after 4 hours of incubation was prioritised from 28 May 2019 to 22 October 2019 (separate column in Table 1).

Results

On average more than 78% of all isolates with RAST breakpoints were reported the same day and 52% before 15:00 (approximate time for afternoon rounds) (Table 1). After May 2019 this was further improved to 82% and 71%, respectively, by insisting on the 4 hour read.

Median time to first AST result regardless of AST method decreased from 19 hours and 3 minutes (before RAST) to 7 hours and 13 minutes (all RAST) and even further to 5 hours and 56 minutes after May 2019 (Table 2). Species distributions before and after RAST were almost identical. The most frequent reason why RAST was not performed was a positive signal from the instrument late in the workday making even the 4 hour read impossible (60% of the no-shows).

Table 2. Time to first AST result, regardless of method used. The control group used both the non-standardised rapid AST method and EUCAST standard disk diffusion. Data from after the introduction of RAST includes RAST and EUCAST standard disk diffusion.

	Median (hh:mm:ss)
Control group, before RAST (n=100)	19:03:18
After introduction of RAST (n=1 297)	7:12:45
After May 2019 (n=333)	5:55:51

Conclusions

RAST delivers a reliable and rapid way of dramatically shortening the average and median time to AST results compared to before its introduction.

References

European Committee on Antimicrobial Susceptibility Testing. Rapid AST in blood cultures. 2020. http://www.eucast.org/rapid_ast_in_blood_cultures/breakpoints_for_short_incubation/

Jonasson E, Matuschek E, Kahlmeter G. 2020, The EUCAST rapid disc diffusion method for antimicrobial susceptibility testing directly from positive blood culture bottles. J Antimicrob Chemother 75.4, 968–978.

Rhodes A, Evans LE, Alhazzani W et al. 2017, Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock. Intensive Care Med 43, 304–377.

Staphylococcus aureus including MRSA

Mandatory reporting of methicillin resistant *Staphylococcus aureus*

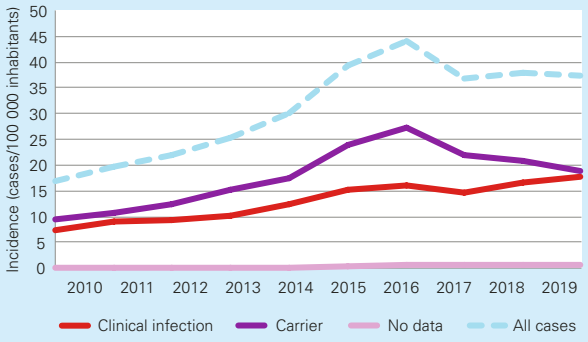
Results from 2019

- Number of reported cases: 3 858 (previous year 3 864), relative change -0.2%
- Number of bloodstream infections: 72 (previous year 64), relative change +13%

Trends

In 2019, a total of 3 858 cases of MRSA were notified. The incidence was 37 cases per 100 000 inhabitants compared to 38 cases per 100 000 inhabitants in 2018 (Figure 3.17). The number of cases reported with clinical infections were 1 830 (47%) while 1 958 cases (51%) were listed as carriers. MRSA-cases were reported from all 21 regions in Sweden with incidences varying from 23 to 63 cases per 100 000 inhabitants. These differences could likely be explained by differences in screening and contact tracing practices between the regions.

Figure 3.17. The incidence (cases/100 000 inhabitants) of cases with MRSA in relation to type of infection, year 2009–2019.

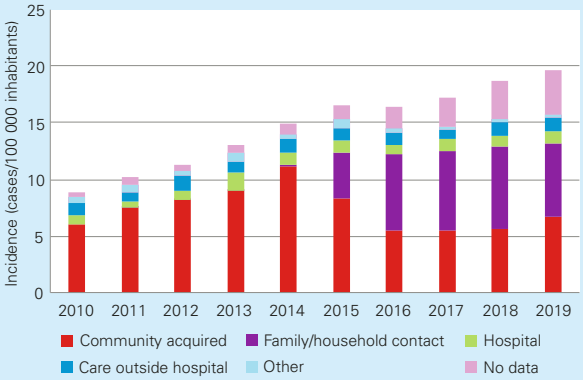


Source: The Public Health Agency of Sweden

There were almost equal distribution between women and men, as 52% (n=2 011) were women and 48% (n=1 847) men, with a median age of 30 and 33 years respectively. Among the domestic MRSA cases (n=2 035), the incidence was highest for children below one year of age (n=199, 172 cases/100 000 inhabitants) followed by the elderly, 85 years or older (n=139, 53 cases/100 000 inhabitants). The high incidence of MRSA among the young children is likely due to screening practices at neonatal- and maternal care units in combination with contact tracing around new cases.

Community-acquired infections continue to be most prominent route of acquiring MRSA (Figure 3.18). A change in the clinical notification form was made in 2015, where community-acquired infections were divided into family/household-acquired or community-acquired. Among cases with MRSA acquired in Sweden, 33% (n=681) were reported as community-acquired while 33% (n=668) were reported as acquired from family/household contacts. The proportion of domestic cases with MRSA acquired in hospital as well as healthcare/care outside hospital was six percent respectively (n=119 and n=126). Twenty percent (n=403) of the domestic cases, lacked information on acquisition.

Figure 3.18. Epidemiological classification of notified cases with MRSA acquired in Sweden, year 2010-2019. Presented as incidence (cases/100 000 inhabitants).

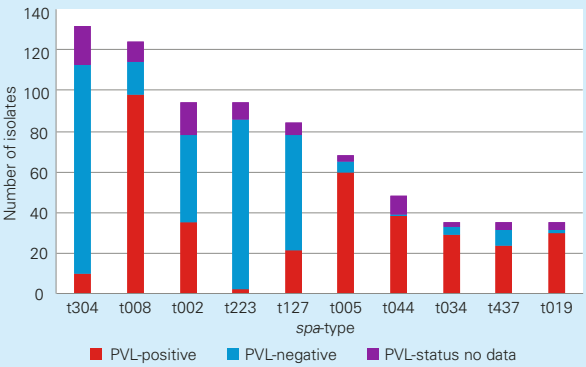


Source: The Public Health Agency of Sweden

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. In addition to the surveillance program, typing data is also obtained from regional microbiological laboratories. Typing data were available for isolates from 1 659 (91%) of the clinical cases and for 1 008 isolates (51%) sampled from asymptomatic carriers. Among the isolates from clinical cases, a total of 321 *spa*-types were identified. The ten most common *spa*-types were seen in 41% of the clinical cases (Figure 3.19).

Figure 3.19. The ten most common *spa*-types (with PVL status) for MRSA from clinical infections, 2019.



Source: The Public Health Agency of Sweden

Outbreaks

Several minor healthcare associated transmissions of MRSA were reported from the regions during 2019. Of importance were a spread among patients cared for at a national facility for burn victims. A cluster with a MRSA, *spa*-type t315, including seven patients from five regions were identified using WGS analysis.

Comments

After many years of gradual increase of MRSA, the number of reported cases declined between 2016 and 2017 and have since remained stable. The decline is most prominent among carriers. No major change is seen in the proportions of domestic cases acquiring MRSA in hospitals or other care facilities. However, the proportion of domestic cases with missing information on where the infection was aquired has increased from 6 to 20% since 2012.

Antibiotic resistance in voluntary reported clinical isolates of MRSA

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.

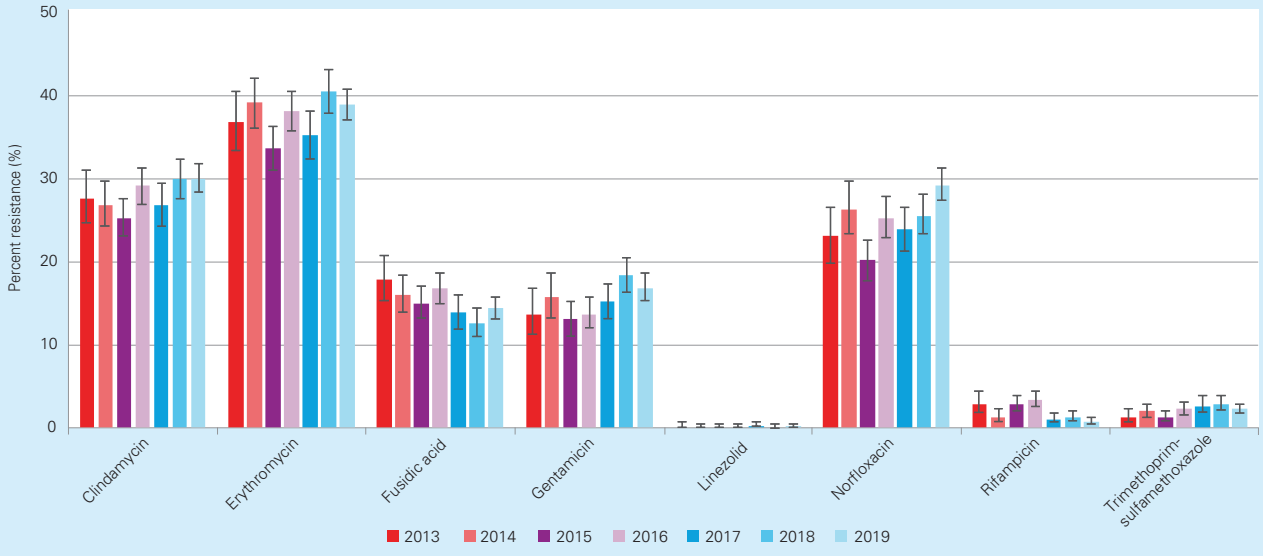
Comments

The proportion of MRSA among clinical *S. aureus* isolates were 2.0% in 2019 and has almost doubled compared with 2013 (Table 3.7). The resistance in MRSA to other antibiotics remained stable (Figure 3.20).

Table 3.7. Number of *S.aureus* and MRSA from clinical isolates and proportion of MRSA 2013-2019.

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

Figure 3.20. Antibiotic resistance in clinical MRSA isolates 2013-2019. The numbers of AST isolates for all years and antibiotics ranges from 576 to 2 685. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Staphylococcus aureus, from blood and skin and soft tissue cultures

Results from 2019

- Number of cases of MRSA reported: 3 858.
- Number of cases with bloodstream infections caused by MRSA: 72.

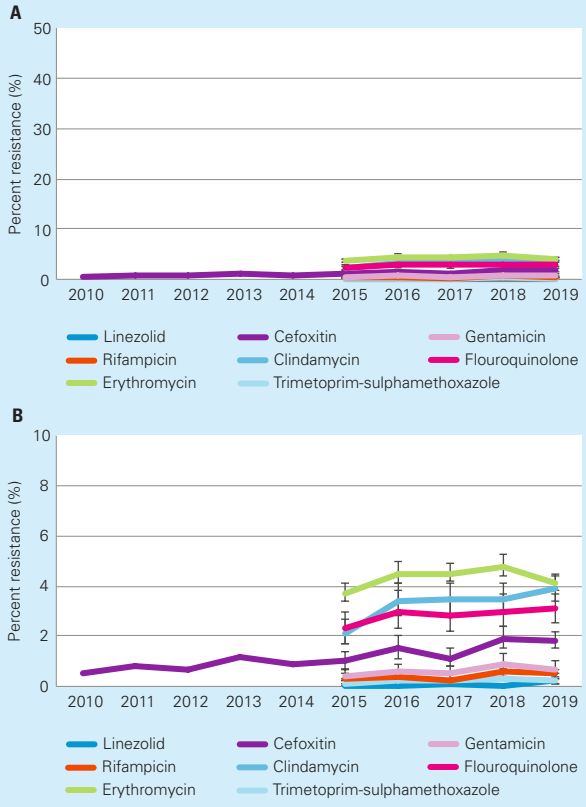
Table 3.8. Proportion (%) of antibiotic resistant *S. aureus* from blood or skin and soft tissue infections 2019.

Antibiotic	Blood isolates, % R (n=6 154)	Skin and soft tissue isolates, % R (n=79 904)
Cefoxitin	1.8	1.9
Clindamycin	3.9	4.9
Erythromycin	4.1	5.5
Gentamicin	0.7	0.5
Flouroquinolone[a]	3.7	2.5[b]
Fusidic acid	na	2.7
Linezolid	0.2	na
Rifampicin	0.5	na
Trimetoprim-sulphamethoxazole	0.2	na

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

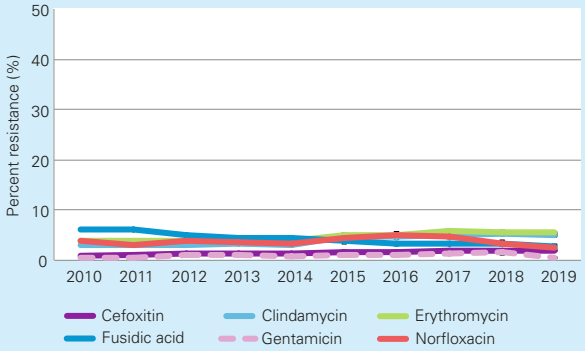
Trends

Figure 3.21 A and B. Antibiotic resistance in *S. aureus* from blood during the years 2010-2019. Figure A shows all tested antibiotics and figure B shows more detailed data (below 10% resistance) for some antibiotics. The numbers of AST isolates for all years and antibiotics ranges from 2 387 to 6 154. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Figure 3.22. Antibiotic resistance for *S. aureus* from skin and soft tissue samples 2010-2019. The resistance for norfloxacin is based on results from less than five laboratories in 2018 and 2019. The numbers of AST isolates for all years and antibiotics ranges from 5 343 to 79 904. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Comments

MRSA isolated from blood has slowly increased and is now 1.8% of isolated *S. aureus* (indicated by cefoxitin resistance) and the same proportion is seen for skin and soft tissue infections (Figure 3.21 and 3.22, Table 3.8). Susceptibility testing to vancomycin is not routinely performed on cefoxitin-susceptible *S. aureus*. In 2019, 325 out of 6 154 (5%) 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 2019

- Total number of reported cases: 232 (previous year: 444), relative change -48%
- Number of reported cases of *E. faecium* with vancomycin resistance: 221 (previous year: 438), relative change -50%
- Number of reported cases of *E. faecalis* with vancomycin resistance: 11 (previous year: 6)
- Number of bloodstream infections: 10 (previous year: 9)

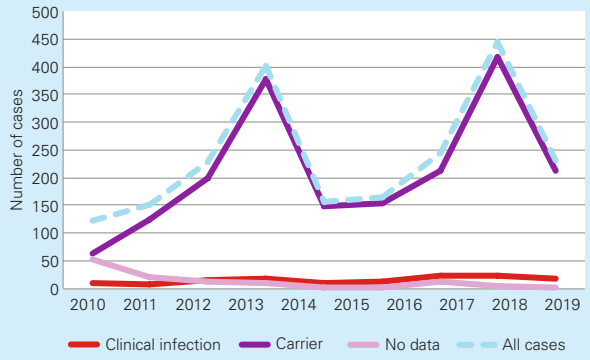
Trends

The national incidence decreased from 4.3 to 2.2 cases per 100 000 inhabitants between 2018 and 2019. Seventeen out of twenty-one regions reported cases of VRE during 2019. Out of these cases, 184 (79%) were healthcare related. A majority of the isolates (n=201, 87%) were from faeces, and only 9% from urine, wound or other clinical samples (Figure 3.23). Ten invasive VRE infections were reported in 2019.

In 2019, half of the cases were reported as acquired abroad. Most domestic cases were found through contact tracing (58%) in contrast to cases acquired abroad, which were detected through screening (87%) (Figure 3.24).

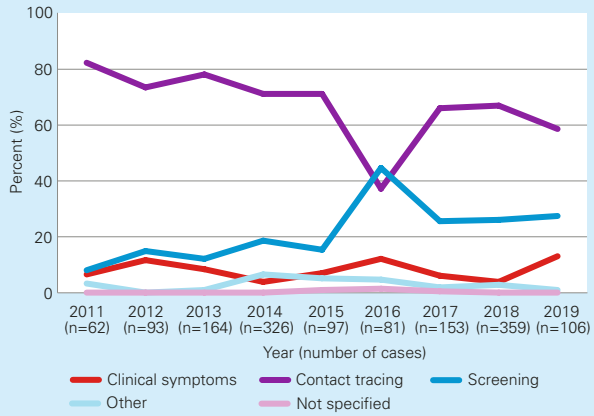
The median age for VRE was 71 years and it is still most common among men, 60%. In 2019, 221 *E. faecium* cases and 11 *E. faecalis* cases were reported. The vanA genotype was most commonly found (n=167) (Figure 3.25).

Figure 3.23. Number of cases of reported VRE based on type of infection 2011-2019.



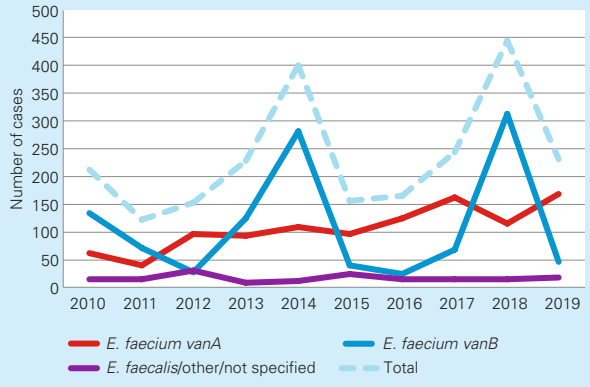
Source: The Public Health Agency of Sweden

Figure 3.24. Acquisition of VRE in Sweden during 2011-2019.



Source: The Public Health Agency of Sweden

Figure 3.25. Number of VRE cases and their corresponding *van*-type.



Source: The Public Health Agency of Sweden

Epidemiological typing

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

In 2019, twenty hospital-related outbreaks of *E. faecium* were reported. Out of these were five small outbreaks (5-15 cases each) and fourteen small clusters with two to four cases each. Seventeen cases belonged to the large national outbreak seen in 2018 with totally 279 cases, denoted SE-EfmB-1707. Two small outbreaks occurred in a hospital in region Uppsala (SE-EfmA-1902, n=10 and SE-EfmA-1904, n=6) and two small outbreaks were reported from region

Table 3.9. Epidemiological typing of VRE 2019.

Epidemiological typing *E. faecium*	Sequence type (ST)	Number of epidemiological typed VRE
EfmA unique	26 different sequence types	104
EfmB unique	6 different sequence types	20
SE-EfmB-1707	80	17 (total 279 isolates)
SE-EfmA-1811	80	3 (total 7 isolates)
SE-EfmB-1901	117	2
SE-EfmA-1902	80	10
SE-EfmA-1903	117	2
SE-EfmA-1904	80	6
SE-EfmA-1905	761	3
SE-EfmA-1906	761	2
SE-EfmA-1907	80	3
SE-EfmB-1908	17	2
SE-EfmA-1909	559	2
SE-EfmA-1911	80	15
SE-EfmA-1912	117	2
SE-EfmA-1913	80	2
SE-EfmA-1915	375	2
SE-EfmB-1916	17	8
SE-EfmA-1917	323	7
SE-EfmB-1918	80	2
SE-EfmA-1919	375	4
SE-EfmA-1920	80	2
SE-EfmA-1921	1495	3
VVE[b]	1421	4
Total number of epidemiological typed VRE	30 different sequence types	**227[a]**
Epidemiological typing *E. faecalis*	**Sequence type (ST)**	**Number of epidemiological typed VRE**
EfsA unique	3 different sequence types	7
SE-EfsB-1910	6	2
SE-EfsB-1914	72	2
Total number of epidemiological typed VRE	4 different sequence types	**11**

[a]The total number of isolates varies compared to the number of cases reported, since some patients have more than one isolate of *E. faecium/E. faecalis* and and not all cases are sent to the Public Health Agency of Sweden for epidemiological typing. [b]Vancomycin-variable enterococci (VVE), phenotypically vancomycin susceptible *E. faecium* with the *vanA*-gene.

Stockholm (SE-EfmA-1911, n=15 and SE-EfmB-1916, n=8) and the fifth small outbreak was reported from region Örebro (SE-EfmA-1917, n=7). There were also two small clusters of *E. faecalis* with *vanB* reported with two cases each (Table 3.9).

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

Eight out of ten invasive cases had *E. faecium* harbouring *vanA* and two cases had *E. faecium* harbouring *vanB*. Seven of the invasive cases were part of different outbreaks/clusters and only three cases were unique (Table 3.9).

Comments

The number of VRE cases decreased with over 52% during 2019 due to that the large national outbreak was contained and only smaller outbreaks were seen. Of note is that the number of invasive cases increased from nine to ten cases and that seven of them 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.

Enterococcus faecalis and *Enterococcus faecium*, from blood cultures

Results from 2019

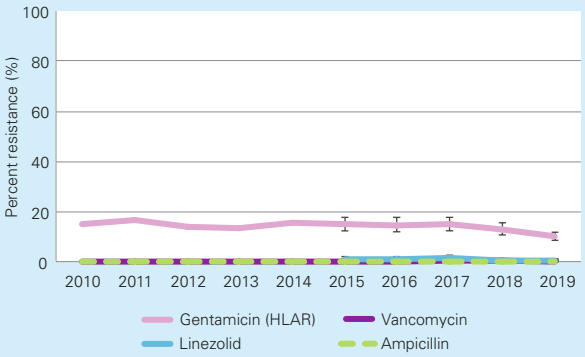
- Total number of VRE cases reported: 232 (previous year: 444), relative change -48%
- Number of reported cases of *E. faecium* with vancomycin resistance: 221 (previous year: 438), relative change -50%
- Number of reported cases of *E. faecalis* with vancomycin resistance: 11 (previous year: 6)
- Number of bloodstream infections caused by VRE: 10 (previous year: 9)

Table 3.10. Proportion (%) of antibiotic resistant *E. faecalis* and *E. faecium* isolated from blood 2019.

Antibiotic	Blood isolates *E. faecalis*, % R (n = 1 269)	Blood isolates *E. faecium*, % R (n = 693)
Ampicillin	0.0	83.8
Gentamicin (HLAR)	10.4	10.8
Linezolid	0.4	0.5
Piperacillin-tazobactam	0.2	84.1
Vancomycin	0.1	1.2

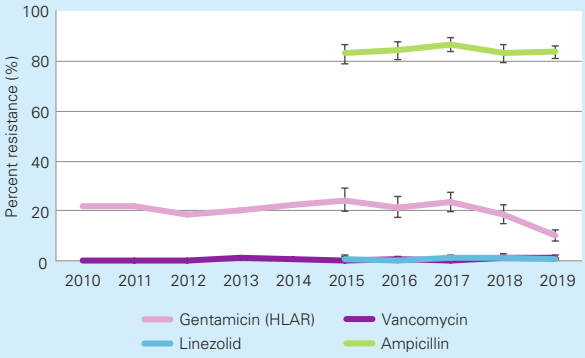
Trends

Figure 3.26. Antibiotic resistance in *E. faecalis* isolated from blood during the years 2010-2019. The numbers of AST isolates for all years and antibiotics ranges from 545 to 1 263. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Figure 3.27. Antibiotic resistance in *E. faecium* isolated from blood during the years 2010-2019. The numbers of AST isolates for all years and antibiotics ranges from 331 to 693. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Comments

The vancomycin resistance among invasive isolates remains low and was 0.1% for *E. faecalis* and 1.2% for *E. faecium* in 2019. The decrease in high-level aminoglycoside resistance (HLAR) could possibly be explained by the reduced use of aminoglycosides and difference in the clonality of the enterococci that resides within hospitals (Table 3.10 and Figures 3.26 and 3.27).

Streptococcus pneumoniae including PNSP

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

Results from 2019

- Number of reported cases: 118 (previous year 91), relative change +30%
- Number of bloodstream infections: 9 (previous year 3)

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

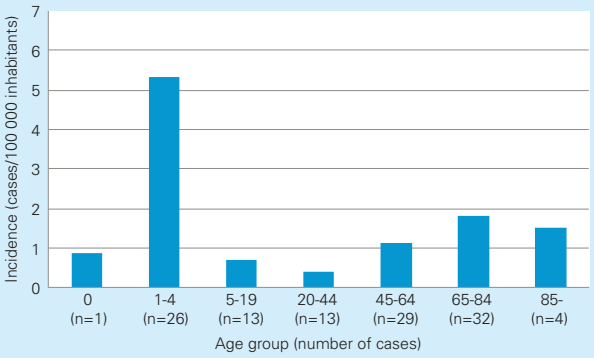
Trends

The national incidence increased from 0.9 cases per 100 000 inhabitants to 1.1 cases per 100 000 inhabitants between 2018 and 2019. The incidence for PNSP acquisition was highest among children under five years of age (4.5 cases per 100 000 inhabitants) representing 23% of all cases. Most cases were found in the age group over 65 years (31%) (Figure 3.28). Of all cases, 57% were men and 44% women.

PNSP was most often found in cultures from the nasopharynx (52%). Thirty-one isolates were found in sputum/bronchoalveolar lavage (26%). In 74 cases (62%) the detection of PNSP was due to clinical symptoms (Figure 3.29).

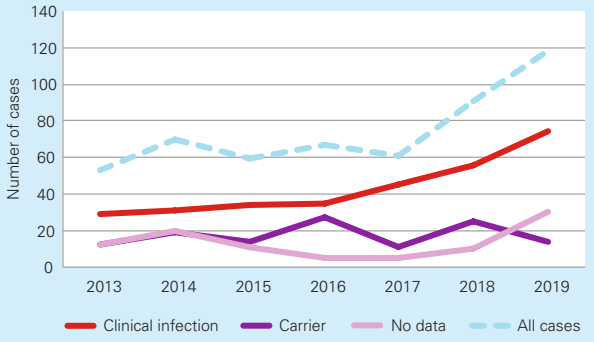
A majority of the cases had been acquired in Sweden (66%) and twelve percent of the cases abroad. For the remaining cases, no country of acquisition was given (22%).

Figure 3.28. Incidence per age group for PNSP acquisition 2019.



Source: The Public Health Agency of Sweden

Figure 3.29. Number of cases of reported PNSP based on type of infection 2013-2019.

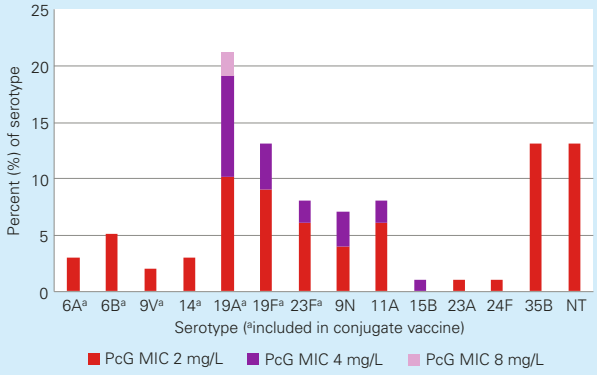


Source: The Public Health Agency of Sweden

Epidemiological typing

A total of 108 isolates with PcG MIC > 1 mg/L were sent to PHAS for serotyping during 2019 (92% of notified cases). Of these, 64 isolates (60%) belonged to serotypes included in the conjugate vaccines (PCV10 or PCV13) used for children in the national vaccination programme. Isolates with high PcG MIC (n=23) were found in six serotypes (Figure 3.30). The nine invasive cases were caused by vaccine serotypes 9V (n=1), 14 (n=1), 19A (n=3), 23F (n=2) and non-vaccine serotypes 9N (n=1), and 23A (1).

Figure 3.30. Distribution of MICs among PNSP with PcG MIC > 1 mg/L (n=100).



Source: The Public Health Agency of Sweden

To follow and evaluate the effect of vaccination against pneumococcal disease and to identify spread of antibiotic resistant clones, PHAS collects PNSP isolates with PcG MIC ≥ 0.5 mg/L for serotyping. In 2019, 320 isolates were collected (including the 108 cases of PNSP). The serotype distribution were, in decending order: NT (16%), 19A (13%), 35B (11%), 19F (10%), 11A (7%), 23F (6%), 9N (5%) and 6B (4%). Of these, 44 % constituted types included in the conjugate vaccines used for children in the national vaccination programme.

Outbreaks

During 2019, there was a small spread (<10 cases) with a resistant *S. pneumoniae* of serotype 19A, found through contact tracing, connected to a childrens day care center.

Streptococcus pneumoniae, from blood and nasopharynx

Results from 2019

- Number of reported cases of PNSP: 118 cases
- Cases with bloodstream infections caused by PNSP: 9
- Cases of cases of invasive pneumococcal disease: 1 345

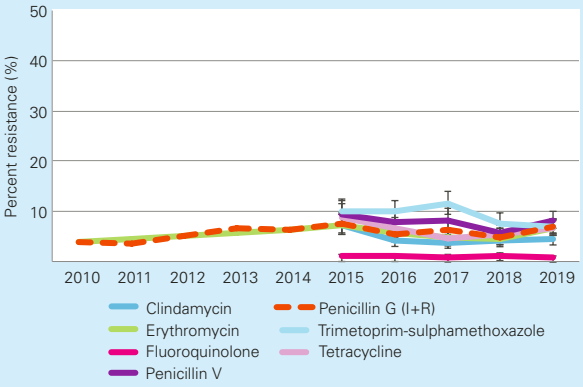
Table 3.11. Proportion (%) of antibiotic resistant *S. pneumoniae* isolated from blood and nasopharynx 2019.

Antibiotic	Blood isolates, % R (n=1 069)	Nasopharynx isolates, % R (n=5 904)
Clindamycin	4.4	5.5
Erythromycin	6.5	8.4
Fluoroquinolone	0.8	1.6
Penicillin G (I+R)	6.9	12.1
Penicilln V	8.2	14.0
Tetracycline	6.7	7.8
Trimetoprim-sulphamethoxazole	6.9	11.6

Trends

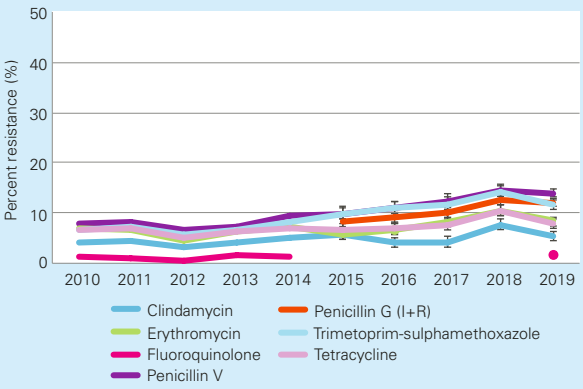
The methodological problem with underestimation of benzylpenicillin (PcG) MIC when using gradient tests does not influence the resistance proportions since I and R are reported together.

Figure 3.31. Antibiotic resistance in *S. pneumoniae* isolated from blood during the years 2010-2019. Penicillin V resistance is based on susceptibility testing using oxacillin. The numbers of AST isolates for all years and antibiotics ranges from 582 to 1 069. The exact numbers are given in the attached file.



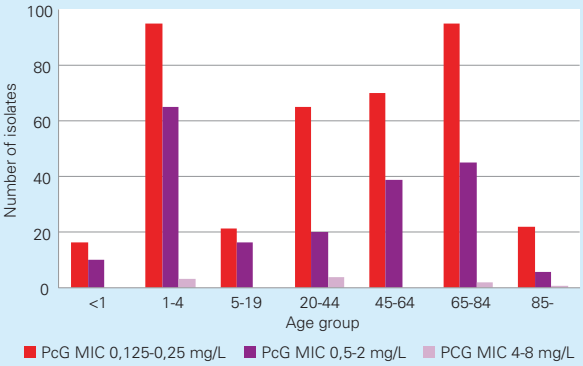
Source: The Public Health Agency of Sweden

Figure 3.32. Antibiotic resistance in *S. pneumoniae* isolated from nasopharynx during the years 2010-2019. Penicillin V resistance is based on susceptibility testing using oxacillin. The numbers of AST isolates for all years and antibiotics ranges from 456 to 5 904. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Figure 3.33. Distribution of *S. pneumoniae* with reduced susceptibility to penicillin G from nasopharynx 2019. Benzylpenicillin MIC values above 0.06 mg/L are categorised as susceptible, increased exposure (I) or resistant (R>2 mg/L).



Source: The Public Health Agency of Sweden

Comments

Among invasive infections, the proportion of PcG non-susceptible isolates was 6.9% in 2019 (Table 3.11 and Figure 3.31). Since 2012, there has been a slow increase in resistance for all tested antibiotics for respiratory tract infections (Figure 3.32). The methodological problems regarding gradient tests results in difficulties when interpreting MIC. Some isolates interpreted as I (purple bars) are probably incorrect and would be interpreted as R if BMD was used (Figure 3.33). In the current Svebar data, both methods are reported, making the proportion of R hard to follow. The total resistance proportion (I+R) is not influenced.

Haemophilus influenzae, from blood and nasopharynx cultures

Results from 2019

- Number of reported cases of invasive *H. influenzae*: 259

Table 3.12. Proportion (%) of antibiotic resistant *H. influenzae* from blood or nasopharynx 2019.

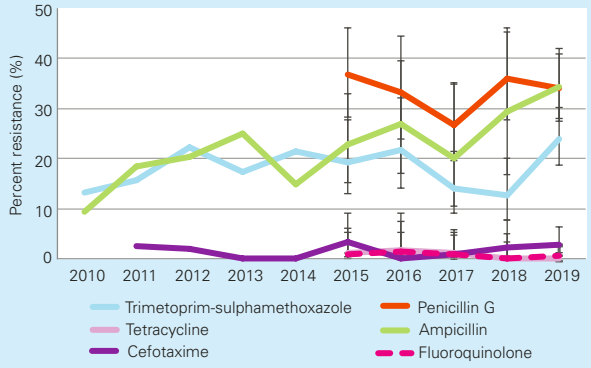
Antibiotic	Blood isolates, % R (n = 209)	Nasopharynx isolates, % R (n = 13 332)
Ampicillin/ Amoxicillin	34.4	37.4
Amoxicillin-Clavulanic acid	nd	16.2
Cefotaxime	2.8	nd
Fluoroquinolone[a]	0.0	1.1
Penicillin G	34.1	42.9
Tetracycline	0.6	0.5
Trimetoprim-sulphamethoxazole	23.9	29.6
Cefaclor	30.6	nd

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

Trends

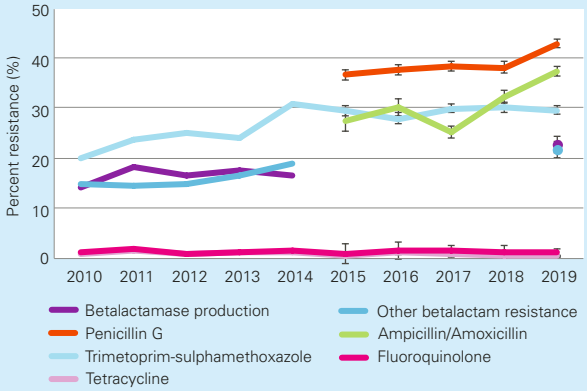
During 2019, 54 isolates were received within the microbiological characterisation program for cephalosporin resistance in *H. influenzae* at PHAS. The majority of these, 47 isolates, showed high-level resistance to extended-spectrum cephalosporins, caused by alterations in penicillin-binding protein 3 (PBP3). The remaining 7 isolates showed lower level resistance to cephalosporins. One large (5-15 cases), still ongoing spread with high-level cephalosporin resistant *H. influenzae*, as well as five small clusters with two cases each were seen during 2019.

Figure 3.34. Antibiotic resistance in *H. influenzae* isolated from blood during the years 2010-2019. The numbers of AST isolates for all years and antibiotics ranges from 40 to 209. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Figure 3.35. Antibiotic resistance in *H. influenzae* isolated from nasopharynx during the years 2010-2019. The numbers of AST isolates for all years and antibiotics ranges from 1 421 to 13 332. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Comments

Invasive isolates of *H. influenzae* are notifiable according to the Communicable Disease Act regardless of antibiotic resistance. The cefotaxime resistance among invasive isolates is still low (Figure 3.34). The variation in resistance should be interpreted with caution since there is a small number of tested isolates. Among respiratory isolates, the resistance levels are relatively stable (Figure 3.35).

Pseudomonas aeruginosa, from blood and non-respiratory cultures

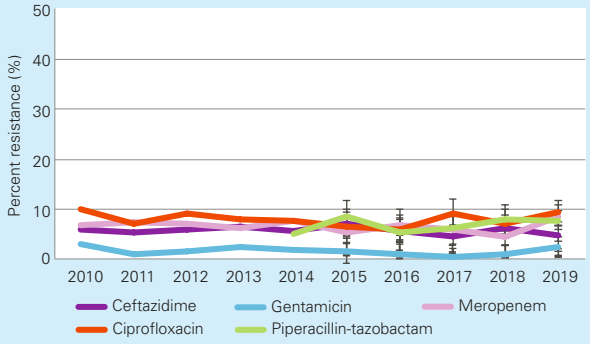
Results from 2019

Table 3.13. Proportion (%) of antibiotic resistant *P. aeruginosa* isolated from blood or non-respiratory specimens 2019.

Antibiotic	Blood isolates, % R (n = 706)	Non-respiratory isolates, % R (n=16 486)
Ceftazidime	4.8	4.8
Ciprofloxacin	9.3	10.6
Gentamicin	2.4	1.7
Meropenem	8.4	5.2
Piperacillin-tazobactam	7.6	6.2

Trends

Figure 3.36. Antibiotic resistance in *P. aeruginosa* isolated from blood during the years 2010-2019. The numbers of AST isolates for all years and antibiotics ranges from 337 to 706. The exact numbers are given in the attached file.

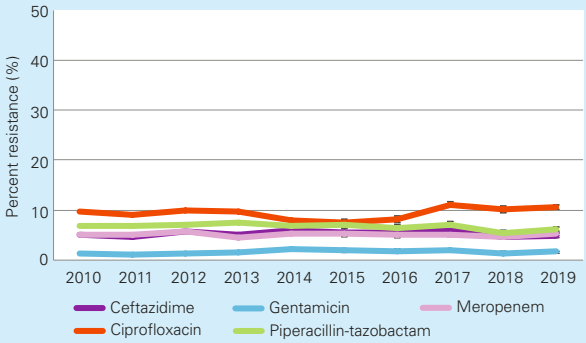


Source: The Public Health Agency of Sweden

Comments

Resistance to ceftazidime is most often due to efflux pumps and porin loss, not ESBL production. The resistance for all antibiotics is stable for both blood isolates and non-respiratory isolates (Figure 3.36 and 3.37). Colistin resistance is occasionally seen in *E. coli*, *K. pneumoniae*, *P. aeruginosa* and *Acinetobacter*. This occurs only in multiresistant isolates and basically only in isolates where there is a connection with healthcare abroad. In multiresistant isolates, it is important to determine colistin susceptibility and only broth microdilution is recommended for AST (MIC determination).

Figure 3.37. Antibiotic resistance in *P. aeruginosa* from non-respiratory isolates 2010-2019. The numbers of AST isolates for all years and antibiotics ranges from 1 980 to 16 486. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Acinetobacter spp, from blood cultures

Results from 2019

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

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

Comments

During 2019, a total of 113 isolates of *Acinetobacter* spp. from blood was reported to Svebar. The carbapenem resistance was 3.5% (Table 3.14). Bloodstream infections caused by *Acinetobacter* spp. are still rare in Sweden compared to other countries in Europe where multiresistant *Acinetobacter* is a problematic pathogen in hospitals. Colistin resistance is occasionally seen in *E. coli*, *K. pneumoniae*, *P. aeruginosa* and *Acinetobacter*. This occurs only in multiresistant isolates and basically only in isolates where there is a connection with healthcare abroad. In multiresistant isolates, it is important to determine colistin susceptibility and only broth microdilution is recommended for AST (MIC determination).

Streptococcus pyogenes, from blood cultures

Results from 2019

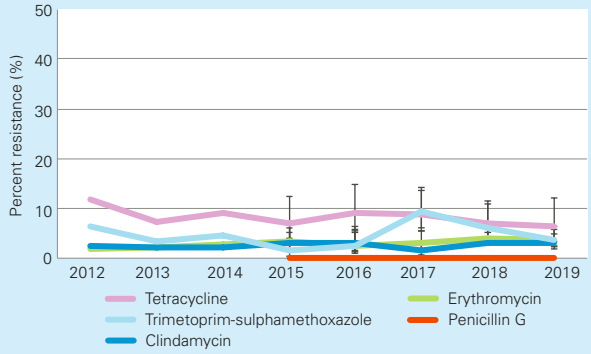
- Number of reported cases of invasive *S. pyogenes*: 768

Table 3.15. Antibiotic resistance in *S. pyogenes* isolated from blood 2019.

Antibiotic	Blood isolates, % R	Number
Penicillin G	0.0	539
Erythromycin	3.7	539
Clindamycin	3.0	536
Tetracycline	6.4	125
Trimetoprim-sulphamethoxazole	3.8	338

Trends

Figure 3.38. Antibiotic resistance in *S. pyogenes* isolated from blood during the years 2012-2019. The numbers of AST isolates for all years and antibiotics ranges from 77 to 539. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Comments

Invasive cases of *S. pyogenes* are notifiable according to the Communicable Disease Act and in 2019 a total of 768 cases were reported. This is a small decrease compared with previous year (n=823). AST results from 539 isolates were available from Svebar (Table 3.15). Some laboratories did not test susceptibility for trimethoprim-sulphamethoxazole and tetracycline. Resistance remained stable and similar or higher levels of resistance have been reported both in Denmark, and in the US (Figure 3.38) (DANMAP 2018 and CDC's Bact Facts Interactive).

Streptococcus agalactiae, from blood cultures

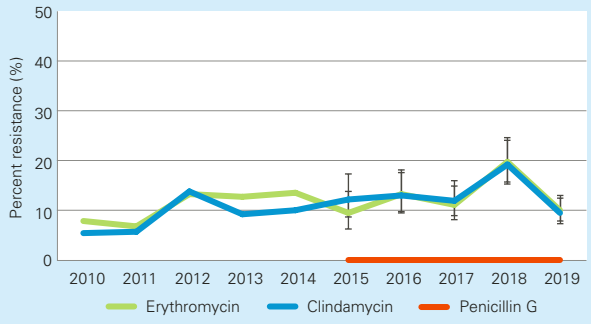
Results from 2019

Table 3.16. Proportion of resistant *S. agalactiae* isolated from blood 2019.

Antibiotic	Blood isolates, % R	Number
Penicillin G	0.0	491
Erythromycin	10.1	441
Clindamycin	9.6	444

Trends

Figure 3.39. Antibiotic resistance in *S. agalactiae* (GBS) from blood during the years 2009-2019. The numbers of AST isolates for all years and antibiotics ranges from 166 to 491.The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Comments

S. agalactiae is not included in the Communicable Disease Act, but it is an important pathogen in the context of pregnancy and child birth. Resistance to both erythromycin and clindamycin decreased compared to 2018, and is now approximately 10% (Table 3.16 and Figure 3.39). Similar or higher levels of resistance have been reported in Denmark, Norway and in the US (DANMAP 2018, NORM/NORM-VET 2018 and CDC's Bact Facts Interactive).

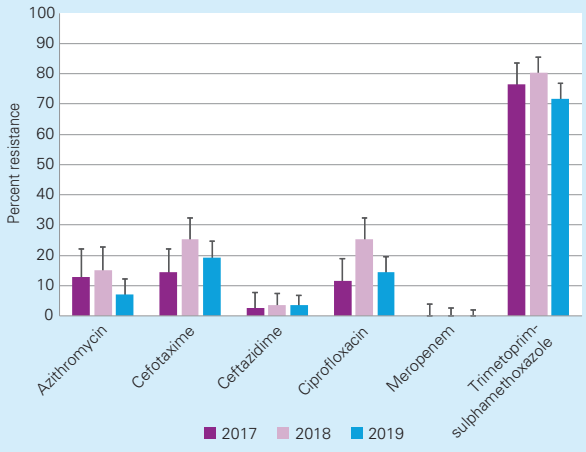
Shigella spp, from faecal samples

Mandatory reporting of *Shigella*

A total of 524 cases with shigellosis were notified in 2019. Two cases had reports of invasive infections. In almost 80% of all cases the infection were acquired abroad. Species identification were available for 337 of the cases. *S. sonnei* were identified in 63% of the isolats, followed by *S. flexneri* (31%). *S. boydii* and *S. dysenteriae* were reported in ten or less cases. The number of cases have increased the last years. In 2017 and 2018, a total of 213 and 317 cases were notified respectively. The increase of cases can partly be explained by a shift in the microbiological method of detection used, where nucleic acid amplification tests are more utilised.

In 2019, 54 cases with *Shigella* were also mandatory notified as ESBL-producing Enterobacteriaceae. Twenty-four cases, out of 25 with known ESBL-type, had $ESBL_A$. No cases with *Shigella* have been reported with $ESBL_{CARBA}$.

Figure 3.40. Antibiotic resistance in *Shigella* spp. from faecal samples 2017-2019. The numbers of AST isolates for all years and antibiotics ranges from 74 to 242. The exact numbers are given in the attached file.

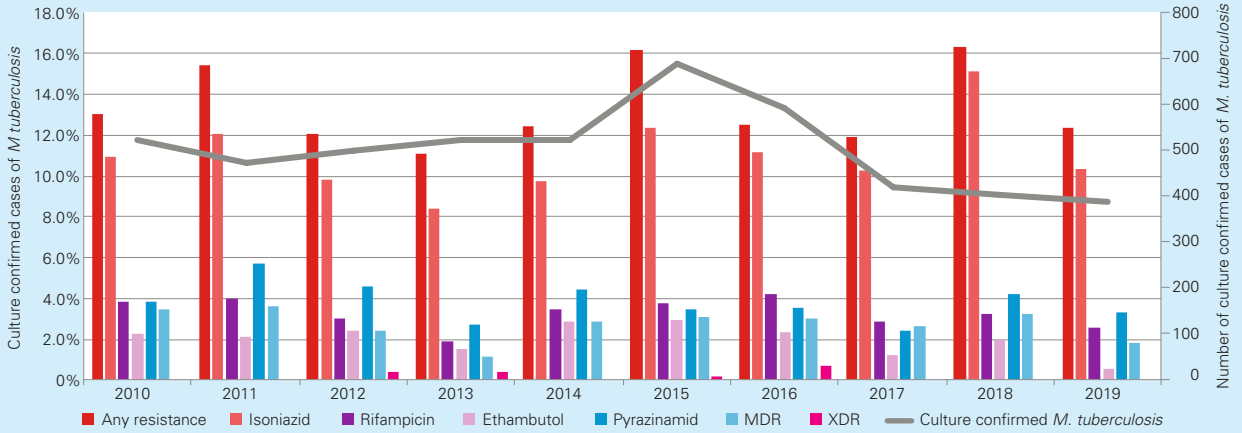


Source: The Public Health Agency of Sweden

Comments

In 2019, 283 isolates of *Shigella* were reported and AST results were available from 242 isolates. None of the isolates were carbapenem resistant (Figure 3.40). The difference in resistance to cefotaxime (19%) and ceftazidime (3%) indicates carriage of $ESBL_A$. The data on antibiotic resistance cannot be separated according to origin of infection, but according to the mandatory reporting of shigellosis four out of five notified cases in 2019 were infected abroad.

Figure 3.41. Drug resistant *M. tuberculosis* in Sweden 2009-2019.



Mycobacterium tuberculosis, mandatory reporting

During 2019, a total of 491 cases of tuberculosis (TB) were reported compared to 506 cases during 2018 which is a decrease of 3%. Out of the 491 cases, 12 was already on TB treatment when arriving in Sweden.

The number and proportion of culture confirmed cases were 396 (81%) compared to 408 (81%) in 2018. *Mycobacterium bovis* was identified in three cases, *Mycobacterium africanum* in five cases and *Mycobacterium tuberculosis* in 388 cases. The proportions of cases diagnosed with MDR-TB decreased, 3.2% (13/404) to 1.8% (7/388). 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 48 patients corresponding to 12.4% of the 388 with culture confirmed *M. tuberculosis*, see Figure 3.41. As previously, the most common resistance found was isoniazid resistance.

Among the cases born in Sweden one out of 53 cases with culture confirmed diagnosis had multidrug resistant TB and one case was TB monoresistant to isoniazid. Of all the TB cases reported in Sweden 2019, 87% were born in another country. In total, 335 cases in this group had a culture confirmed TB and 46 (14%) had some kind of resistance out of which six had MDR-TB.

TB isolates has been typed genetically 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 14% (69/491) were considered as infected in Sweden and of the 396 cases analysed with whole genome sequencing 79% were unique isolates not belonging to any cluster.

The proportion of patients with *M. tuberculosis* resistant to any antibiotics has decreased in 2019 including the proportion of MDR-TB and the total number of cases have continued to decrease.

Neisseria gonorrhoeae, mandatory reporting

Gonorrhoea is a notifiable infection and in 2019, 3 245 cases (31 cases per 100 000 inhabitants) of gonococcal infections were reported to the Public Health Agency of Sweden. This is an increase with approximately 20% compared to 2018 (2 715 cases) and the incidence has increased by a mean of 15% per year since 2009. Most of these cases were identified in the three largest regions 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. Compiled antimicrobial resistance data from Stockholm and Skåne regions are not available at current date. In 2019, 1 035 clinical *N. gonorrhoeae* isolates (multiple isolates from some patients) were fully characterised at the Swedish Reference Laboratory for Sexually Transmitted Infections.

TABLE 3.17. Antibiotic resistance rates (%) of Swedish clinical *Neisseria gonorrhoeae* isolates 2010-2019.

	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)	2019 (n=1 035)
Cefixime	6	8	10	4	2	2	1	1 (0.6)	1 (1.2)	1 (0.8)
Ceftriaxone	2	2	1	<1 (0.3)	<1 (0.3)	0	0	0	0	0
Azithromycin	12	11	10	13	9	10	3	5	5[a]	12[a]
Ciprofloxacin	56	55	62	53	60	53	53	47	57	60
Spectinomycin	0	0	0	0	0	0	0	0	0	0

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

Antimicrobial susceptibility testing was performed according to standardised and quality assured methodology using Etest for MIC determination of ceftriaxone, cefixime, azithromycin, spectinomycin, and ciprofloxacin. The used clinical resistance breakpoints have been determined by EUCAST. Since January 2019, EUCAST does not state any clinical resistance breakpoint for azithromycin and in this report the Epidemiological Cutoff (ECOFF), distinguishing strains with azithromycin resistance mechanisms, is instead used for azithromycin.

In Table 3.17, the antimicrobial resistance in clinical gonococcal isolates cultured in 2019 are compared with those from 2010 to 2018. Briefly, the level of resistance to ciprofloxacin, which previously was used as first-line treatment for gonorrhoea, remains very high, i.e. 60% in 2019. The proportion of isolates above the azithromycin ECOFF was 12%, which represents a significant increase since 2018 (5%). The resistance to cefixime has significantly decreased since 2012 (10%), and in 2019 it was 0.8%, which is similar as in 2016-2018 (~1%). Furthermore, as in 2015-2018 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.

Neisseria meningitidis, mandatory reporting

Invasive meningococcal disease is a notifiable disease, and in 2019 a total of 66 cases (0.6 cases per 100 000 inhabitants) of the disease were reported. In total, 57 clinical invasive isolates from blood, cerebrospinal fluid and/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 standardised and quality assured methodology using Etest for determination of MIC values for penicillin G, cefotaxime, meropenem, chloramphenicol, ciprofloxacin and rifampicin. The used clinical resistance breakpoints have been determined by EUCAST. Production of β-lactamase was examined by nitrocefin discs.

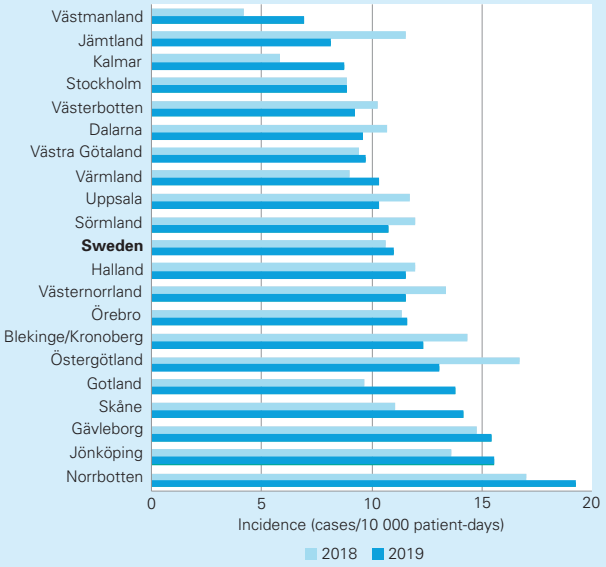
Fifteen (26%) isolates had an intermediate susceptibility to penicillin G (MIC>0.064 mg/L), and two of these isolates were resistant (MIC>0.25 mg/L). All isolates (100%) were susceptible to cefotaxime (MIC values of <0.002-0.016 mg/L), meropenem (MICs: <0.002-0.032 mg/L), chloramphenicol (MICs: 0.125-2 mg/L), ciprofloxacin (0.002-0.008 mg/L), and rifampicin (MICs: 0.002-0.125 mg/L). None of the isolates obtained in 2019 produced β-lactamase, and in fact no β-lactamase-producing meningococcal isolate has ever been identified in Sweden.

Clostridioides difficile

Incidence of CDI

In 2019, 6 536[a] 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 2019 was 11 cases/10 000 patient-days (patient-days data are from 2018) (Figure 3.42). The incidence has decreased by 25% between 2009 and 2016 and has since 2016 remained stable.

Figure 3.42. Incidence of new cases of CDI[a] (cases per 10 000 patient-days) distributed per Swedish regions 2018-2019. (Incidence of cases 2019 is calculated using patient-days for 2018).



[a]The number of inhabitants in the region has been used as denominator data in the incidence calculation. Where information on the region in which the sample was taken was missing, the region commonly reported by the laboratory has been used in the calculations. For region Jönköping, own figures used by the region's infection control unit are used. Stockholm Unilab has not reported data for the entire year, mean of reported cases per week times 52 has been used for full-year data. A case is considered new if at least eight weeks have elapsed since the previous positive test, otherwise it is counted as an ongoing illness episode or recurrence. It is in line with the European case definition of *C. difficile*.

Source: The Public Health Agency of Sweden

Antibiotic resistance in *Clostridioides difficile* isolates 2018

In 2019, susceptibility to four indicator antibiotics (erythromycin, tetracycline, moxifloxacin and clindamycin) and two antibiotics used for treatment of CDI (metronidazol and vancomycin) were tested on a subset of isolates, from ribotypes that have historically shown high level of resistance (001, 012, 027, 046, 078/126 and 106) or are most common (014, 002). Tetracycline resistance was clearly associated with ribotype 012 and 078/126, with 50% and 68% resistance respectively. Ribotype 012 showed also high levels of resistance against erythromycin and clindamycin 88% and 75% respectively.

High levels of resistance were observed for ribotype 027 as previously known. Resistance levels within the most common ribotypes were low but it is worth noting that we found 6% and 5% resistance against moxifloxacin in ribotype 014 and 002 respectively. The resistance was encoded by intrinsic mutations in the DNA gyrase genes.

All isolates tested were susceptible to metronidazol and vancomycin.

Zoonotic pathogens: *Campylobacter* and *Salmonella*

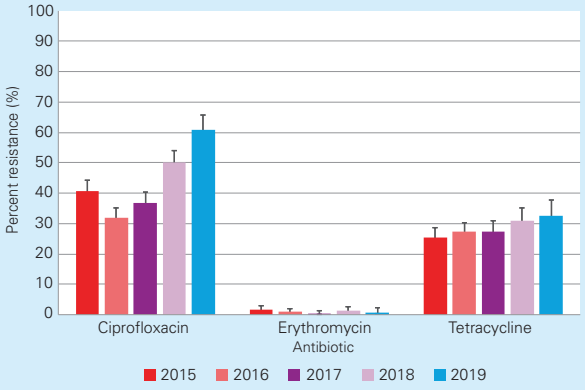
Mandatory reporting of *Campylobacter* spp.

A total of 6 693 cases were reported in 2019, the lowest number of reported cases since 2006. Fifty-five percent of cases were considered to be infected abroad. 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 using whole-genome sequencing, is species identification and cluster analysis to identify potential outbreaks. Antibiotic susceptibility data, collected via Svebar, can not be separated according to origin of infection.

Campylobacter jejuni, from faecal samples

A total of 4 481 *Campylobacter* species were found in faecal sampling. Half of the isolates were reported as the combination of *C. jejuni/C. coli*, 40% *C. jejuni* and four percent as *C. coli*. The presence of AST data was highest for *C. jejuni* (22% of all isolates).

Figure 3.43. Antibiotic resistance in *Campylobacter jejuni* from faecal samples 2015-2019. The numbers of AST isolates for all years and antibiotics ranges from 352 to 816. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Comments

For *C. jejuni* the resistance to ciprofloxacin was 61% and 33% for tetracycline in 2019. Less than one percent were resistant to erythromycin (Figure 3.43). The proportion of isolates fully susceptible or fully resistant were 38% and 0.6%, respectively (Table 3.18). The decrease of notified cases in 2019, according to the Communicable disease act, is reflected in the decreasing number of isolates with an AST.

TABLE 3.18. Combined suceptibility and resistance to erythromycin, ciprofloxacin and tetracycline in *Campylobacter jejuni* from faecal samples 2015-2019.

	2015	2016	2017	2018	2019
Number of isolates with combined AST for erythromycin, ciprofloxacin and tetracycline	659	793	697	544	352
Proportion fully suseptitible to erythromycin, ciprofloxacin and tetracycline, %	53.9	60.9	59.8	47.4	38.4
Proportion fully resistant to erythromycin, ciprofloxacin and tetracycline, %	1.4	0.8	0.4	0.9	0.6

During 2018-2019, the majority of notifiable *Campylobacter* infections were acquired abroad (55%). In 2016 and 2017, there was a large outbreak of *Campylobacter* in humans, linked to domestic poultry production. During these two years the proportions of isolates with Swedish origin were higher. It can be noted that the resistance to ciprofloxacin were lower 2016-2017 (Figure 3.43) and a higher percentage of isolates were fully suscepible as well (Table 3.18).

Salmonella

Results from 2019

A total of 1 953 *Salmonella enterica* isolates were reported in Svebar, 80% were from faecal samples, 13% from blood and 6% from urine.

TABLE 3.19. Antibiotic resistance in *Salmonella enterica* (*S.* Typhi and *S.* Paratyphi excluded) isolated from blood or from faeces and urine samples in 2019.

Antimicrobial	Blood isolates, %R (n = 125)	Faeces/urine isolates, %R (n= 754)
Azithromycin	0.0	0.7
Cefotaxime	1.6	1.5
Ceftazidime	1.6	1.7
Fluoroquinolone	27.4	20.2
Meropenem	0.0	0.0
Piperacillin-tazobactam	0.0	1.1
Trimethoprim-sulfamethoxazole	6.4	4.9

Mandatory reporting of *Salmonella*

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

In 2019, a total of 1 993 cases were notified with *Salmonella* infections (*S.* Typhi and *S.* Paratyphi excluded), 29 cases with typhoid fever and 14 cases with paratyphoid fever. Almost all cases with typhoid fever and all cases with paratyphoid fever were infected abroad and the majority were epidemiologically

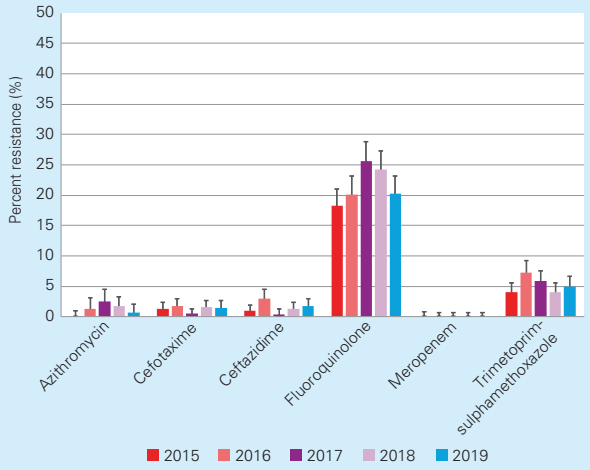
linked to South Asia. For the remaining *Salmonella* infections, 62% of the cases were infected abroad. The national surveillance program using whole-genome sequencing, focus on epidemiological typing of domestic isolates in order to identify potential outbreaks. During 2019, isolates from 868 cases were analysed in the program (90% of the domestic cases). The three most prevalent serotypes in the domestic cases, of the 65 identified, were monophasic *S. typhimurium* (24%), *S. enteritidis* (18%) and *S. typhimurium* (10%). In the 14% of investigated isolates from cases infected abroad, *S. enteritidis* were the most prevalent serotype (46%).

A total of 11 cases in 2019 were reported having *Salmonella* with ESBL. In eight cases with known ESBL-type, six had $ESBL_A$. No cases with *Salmonella* species have been reported with $ESBL_{CARBA}$.

Invasive infections were reported for 119 cases in the mandatory reporting, 88 cases with Salmonella infection (*S.* Typhi and *S.* Paratyphi excluded), in 20 with typhoid fever and 11 of the cases with parathyphoid fever.

Salmonella spp., from faecal and urine samples

Figure 3.44. Antibiotic resistance in *Salmonella enterica* from faecal and urine samples 2015-2019. Results from *S.* Typhi and *S.* Paratyphi have been excluded. The numbers of AST isolates for all years and antibiotics ranges from 304 to 875. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Comments

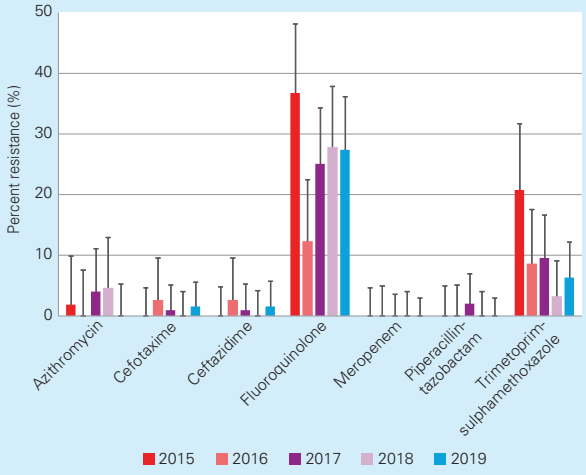
No significant changes in antibiotic resistance is seen between 2015- 2019 (Figure 3.44). During this period no carbapenem-resistent *Salmonella* have been reported. The highest resistance was against fluoroquinolones in isolats from faeces and urine, 20% in 2019. Almost 80% of the *Salmonella* from faecal and urine samples are fully susceptible to azithromycin, cefotaxime and ciprofloxacin (Table 3.20).

TABLE 3.20. Combined suceptibility and resistance to azithromycin, ciprofloxacin and cefotaxime in *Salmonella enterica* from faecal and urine samples 2015-2019. Results from *S.* Typhi and *S.* Paratyphi have been excluded.

	2015	2016	2017	2018	2019
Number of isolates with combined AST for azithromycin, cefotaxime and ciprofloxacin	424	328	426	454	404
Proportion fully suseptitible to azithromycin, cefotaxime and ciprofloxacin, %R	79.5	75.0	74.4	75.8	79.2
Proportion fully resistant to azithromycin, cefotaxime and ciprofloxacin, %R	0.0	0.6	0.0	0.2	0.3

Salmonella spp., from blood

Figure 3.45. Antibiotic resistance in *Salmonella enterica* from blood samples 2015-2019. Results from *S.* Typhi and *S.* Paratyphi are excluded. The numbers of AST isolates for all years and antibiotics ranges from 47 to 125. The exact numbers are given in the attached file.



Source: The Public Health Agency of Sweden

Comments

In 2019, there were 125 isolats of *Salmonella* reported in blood with an AST (Figure 3.45). Previous years the number of isolats, with an AST, have ranged between 47-107 per year and antibiotic. The data may contain duplicates and there is a risk of overestimation of the resistance. Hence, results should be interpreted with some caution. Similar recistance rates are seen in isolates from blood as in faeces and urine (Table 3.19). No carbapenem resistance was detected.

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 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

Escherichia coli

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

During 2019, samples of intestinal contents from healthy fattening pigs (n=301) and broilers (n=101) as well as samples of pig meat (n=293) and bovine meat (n=294) at retail were screened for *E. coli* resistant to ESCs and carbapenems using selective media. The meat samples comprised of fresh meat originating both from Sweden (pig meat=254 and bovine meat=264) and other countries or with unknown origin (pig meat=39 and bovine meat=30). 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 39 (13%) of the samples of intestinal contents from fattening pigs and a transferable gene coding for ESC resistance was detected in 8 isolates, i.e. 3% of the samples. All of these were $ESBL_A$ and carried $bla_{CTX\text{-}M\text{-}14}$ (n=4), $bla_{CTX\text{-}M\text{-}15}$ (n=3), or $bla_{CTX\text{-}M\text{-}55}$ (n=1). The remaining 31 isolates had an AmpC phenotype and genome sequencing of these isolates revealed mutations causing hyperproduction of AmpC beta-lactamases. Carbapenem resistant *E. coli* was not isolated from any sample.

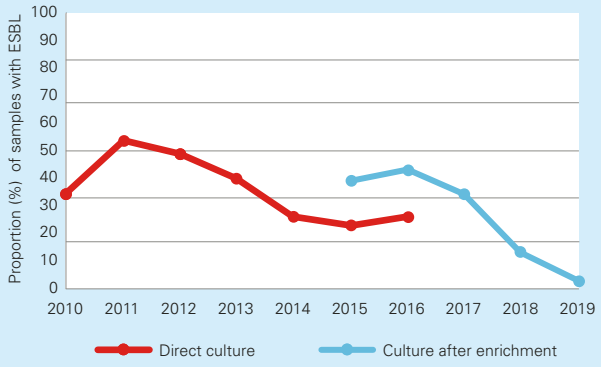
Apart from resistance against beta-lactams, including ESCs, 23 (59%) of the tested isolates were also resistant to at least two other antibiotics, i.e. multiresistant. The most common traits were resistance to sulphonamides (87% of the multiresistant isolates), tetracycline (83% of the multiresistant isolates), and trimethoprim (78% of the multiresistant isolates). Resistance to quinolones was also a common trait (43% of the multiresistant isolates).

Escherichia coli with ESC-resistance was isolated from 8 (8%) of the samples of intestinal contents from broilers and a transferable gene coding for ESC resistance was detected in 3 isolates, i.e. 3% of the samples. All of these were $ESBL_A$ and carried the genes $bla_{CTX\text{-}M\text{-}1}$. The remaining five isolates had an AmpC phenotype and genome sequencing of these isolates revealed mutations causing hyperproduction of AmpC beta-lactamases. Carbapenem resistant *E. coli* was not isolated from any sample.

The three isolates with transferrable ESC-resistance were the only resistant also to other substances than beta-lactams, including ESCs. Two of these were resistant to at least two other antibiotics, i.e. multiresistant. Both of them were resistant to sulphonamides and tetracycline.

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 $ESBL_M$ since 2016 is statistically significant ($p<0.01$, X^2; Figure 4.1). This decrease is most likely explained by decreased occurrence of such bacteria in the breeding pyramid.

FIGURE 4.1. Proportion (%) of samples from broilers positive for *Escherichia coli* with $ESBL_A$ or $ESBL_M$ from 2010 to 2019. The number of samples each year varies (n=100-302, 2019 n=101).



Escherichia coli with ESC-resistance was isolated from 2 (<1%) of the samples of pig meat. One of the isolates originated from a meat sample of Swedish origin (Table 4.1) and the other from a sample originating from another country. A transferable gene coding for ESC resistance was detected in both of them. Both isolates were $ESBL_A$ and carried the genes $bla_{CTX\text{-}M\text{-}1}$ (n=1), or $bla_{SHV\text{-}12}$ (n=1). Carbapenem resistant *E. coli* was not isolated from any sample.

Apart from resistance against beta-lactams, including ESCs, the two isolates were resistant to three and four substances respectively, i.e. multiresistant. Both were resistant to sulphonamides, tetracycline, and trimethoprim. One of the isolates was also resistant to quinolones.

Escherichia coli with ESC-resistance was isolated from 3 (1%) of the samples of bovine meat. One of the isolates with ESC-resistance originated from a meat sample of Swedish origin (Table 4.1) and the other two from samples originating from other countries. A transferable gene coding for ESC resistance was detected in 1 isolate, i.e. <1% of the samples. The isolate was $ESBL_A$ and carried the gene $bla_{CTX\text{-}M\text{-}1}$. The remaining two isolates had an AmpC phenotype and genome sequencing of these isolates revealed mutations causing hyperproduction of AmpC beta-lactamases. 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. multiresistant. This isolate was resistant to chloramphenicol, sulphonamides, tetracycline, trimethoprim, and quinolones. No transferable genes coding for ESC resistance were detected in this isolate.

Salmonella

Within the official *Salmonella* control programme in poultry, *Salmonella* Kisii with resistance to cefotaxime was isolated from an environmental sample taken at a farm. The isolate had an $ESBL_A$ phenotype and carried the $bla_{CTX\text{-}M\text{-}2}$ gene.

Apart from resistance to extended spectrum cephalosporins, the isolate was resistant to seven other antibiotics including fluoroquinolones. It was however susceptible to carbapenems. It is unknown how the flock became contaminated, but other studies have suggested that exotic serovars like *S.* Kisii are often feed contaminants.

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 clinical isolates of Enterobacteriaceae free of charge for referring laboratories. During 2019, 35 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=4), dogs (n=17) and horses (n=14).

Apart from resistance against beta-lactams, including ESCs, 57% of the investigated isolates were also resistant to at least two other antibiotics, i.e. multiresistant. The most common resistances were against trimethoprim-sulphonamides (57%) and streptomycin (64%). Resistance to gentamicin (40%), tetracycline (31%) and enrofloxacin (20%) were also common traits.

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

Animal species	Matrix	Year	No. of samples	No. of samples with ESC resist-ance	No. of samples with $ESBL_A$ or $ESBL_M$	% samples with $ESBL_A$ or $ESBL_M$	Beta-lactamase (No. of isolates)								
							CTX-M-1	CTX-M-3	CTX-M-14	CTX-M-15	CTX-M-27	CTX-M-55	TEM-52	SHV	CMY-2
Broilers	Intestine	2019	101	8	3	3	3								
Broilers	Intestine	2018	300	42	38	13	13							1	24
Broilers	Meat	2018	242	35	28	12	8								20
Broilers	Intestine	2017	100	40	34	34	14								20
Broilers	Intestine	2016	302	130	127	42	93[a]								34[b]
Broilers	Meat	2016	243	109	107	44	66[a]			1					40[b]
Broilers	Intestine	2015	100	40	39[c]	39[c]	18[c]								22[c]
Broilers	Intestine	2014	200	72	71	36	1								70[d]
Broilers	Intestine	2013	100	45	40	40							2		38[d]
Broilers	Meat	2013	59	31	30	51									30[d]
Broilers	Intestine	2012	200	102	97	49									97[d]
Broilers	Meat	2012	97	41	40	41									40[d]
Broilers	Intestine	2011	100	57	54	54	3								51
Broilers	Intestine	2010	200	77	68	34	12								56
Broilers	Meat	2010	100	49	44	44	4								40
Cattle	Meat	2019	264	1	0	0									
Cattle[e]	Intestine	2017-18	67	3	2	3	1			1					
Cattle	Meat	2017	249	3	2	<1				1	1				
Cattle[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	2019	301	39	8	3			4	3		1			
Pigs	Meat	2019	254	1	1	<1								1	
Pigs	Intestine	2017	241	29	9	4			6	2		1			
Pigs	Meat	2017	228	0	0	0									
Pigs	Intestine	2015	303	35	4	1				1		2			1
Pigs	Meat	2015	286	1	1	<1						1			
Pigs	Intestine	2011	184	9	3	2		1		1			1		
Pigs	Meat	2011	100	0	0	0									
Pigs	Intestine	2008	452	9	0	0									
Pigs	Meat	2008	50	0	0	0									
Turkeys	Intestine	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 $bla_{CTX\text{-}M\text{-}1}$. [b]CIT-group, five caecal and three meat isolates were sequenced and possessed the gene $bla_{CMY\text{-}2}$. [c]One isolate carried both an $ESBL_A$ and an $ESBL_M$ gene. [d]CIT-group, all isolates from broilers or broiler meat with a CIT-group enzyme in other years possessed the gene $bla_{CMY\text{-}2}$. [e]Cattle under 1 year, in 2012 calves 1-4 weeks of age.

TABLE 4.2. Clinical isolates of different bacterial species of Enterobacteriaceae, producing $ESBL_A$ or $ESBL_M$, from companion animals and horses, 2008-2019.

Animal species	Beta-lactamase group	Beta-lactamase gene	Bacterial species	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
CATS	**All**	**All**	**Enterobacteriaceae**		**1**	**3**	**3**			**1**	**2**	**2**	**5**	**3**	**4**
	CIT	CMY-2	*Escherichia coli*		1	1						1			1
		CMY-16	*Escherichia coli*							1					
		CMY-2 + CTX-M-65	*Escherichia coli*										1	1	
	CTX-M-1	CTX-M-15	*Enterobacter cloacae* group								1				
			Escherichia coli			1						1	2	1	2
			Klebsiella pneumoniae			1	1								
		CTX-M-3	*Escherichia coli*										1		
	CTX-M-9	CTX-M-14	*Escherichia coli*											1	1
			Kluyvera sp.				1								
	SHV	SHV-12	*Escherichia coli*										1		
	TEM	TEM-52	*Escherichia coli*								1				
	unknown	unknown	*Escherichia coli*				1								
DOGS	**All**	**All**	**Enterobacteriaceae**	**1**	**3**	**5**	**18**	**12**	**14**	**22**	**24**	**31**	**17**	**22**	**17**
	CIT	CMY-2	*Escherichia coli*			1	9	4	5	5	6	5	4	9	6
			Klebsiella pneumoniae								1				
			Proteus mirabillis				1				2	2			
		CMY-2 + CTX-M-27	*Escherichia coli*										1		
		CMY-4	*Escherichia coli*												2
	CTX-M-1	CTX-M-1	*Enterobacter cloacae* group							4					
			Escherichia coli			1		1	1	3			3	2	2
		CTX-M-15	*Enterobacter cloacae* group								2	2	1	1	
			Enterobacter sp.		1	2	1	2	1	6					
			Escherichia coli	1			2	3	2		2	7	1	6	2
			Klebsiella pneumoniae		1						1	2			1
			Morganella morganii									1			
		CTX-M-3	*Enterobacter* sp.						1						
			Escherichia coli						2		1	2			
		CTX-M-55	*Escherichia coli*								1	1			
		CTX-M-57	*Escherichia coli*								1				
	CTX-M-2	CTX-M-2	*Escherichia coli*				1								
	CTX-M-9	CTX-M-14	*Escherichia coli*								5	5	2	1	1
			Klebsiella pneumoniae								1			1	
		CTX-M-27	*Escherichia coli*				3		1	1	1	1	3		2
		CTX-M-9	*Escherichia coli*				1	2	1	1					
	DHA	DHA-1	*Escherichia coli*											1	
	SHV	SHV-12	*Escherichia coli*							2		3	2		
			Klebsiella oxytoca												1
	TEM	TEM-52-like	*Escherichia coli*											1	
	unknown	unknown	*Escherichia coli*		1	1									
HORSES	**All**	**All**	**Enterobacteriaceae**	**2**	**5**	**24**	**16**	**6**	**9**	**8**	**14**	**18**	**32**	**22**	**14**
	CIT	CMY-2	*Escherichia coli*												1
	CTX-M-1	CTX-M-1	*Enterobacter cloacae* group								1		2		
			Enterobacter sp.						1						
			Escherichia coli		2	9	8	3	3	2	3	5	13	6	1
			Klebsiella oxytoca							1					
			Serratia odorifera			1									
		CTX-M-15	*Escherichia coli*		1	1						1			4
			Klebsiella pneumoniae		1						3			1	
	CTX-M-9	CTX-M-14	*Escherichia coli*				1				1				
		CTX-M-9	*Escherichia coli*							1					
	SHV	SHV-12	*Citrobacter braakii*			1									
			Citrobacter sp.											1	
			Enterobacter aerogenes									1			
			Enterobacter amnigenus							1					
			Enterobacter cloacae group							1	2	5	8	8	3
			Enterobacter sp.		1	3	5	3	3						
			Escherichia coli	2		2	2					3	6	6	1
			Escherichia hermannii			1									
			Escherichia sp.												1
			Klebsiella oxytoca						2		1	1	3		1
			Klebsiella pneumoniae							1					1
			Leclercia adecarboxylata									1			
			Pantoea agglomerans									1			
		SHV-12 like	*Klebsiella pneumoniae*												1
	unknown	unknown	*Enterobacter cloacae* group							1	3				
			Escherichia coli			1									
			Klebsiella pneumoniae			5									

Multiresistant ESBL-producing Enterobacteriaceae from horses

As of 2010, the National Veterinary Institute (SVA) has encouraged Swedish veterinary laboratories to submit presumptive extended-spectrum β-lactamase (ESBL)- and plasmid-encoded AmpC β-lactamase (pAmpC)-producing Enterobacteriaceae for verification and genotypic characterisation. From 2017 all at SVA identified ESBL- and pAmpC-producing Enterobacteriaceae are subjected to genome sequencing. In a retrospective *in silico* detection of antimicrobial resistance genes in such isolates, an *Escherichia coli* with bla_{SHV-12} isolated from a horse in 2018 was found to also carry *mcr-9*. The *mcr-9* gene is a homologue to the *mcr-1* gene that may confer reduced susceptibility to colistin (Carroll et al, 2019). As a result of this random finding, additional ESBL/pAmpC-producing Enterobacteriaceae clinical isolates for which WGS data were available were investigated for the presence of *mcr-9*, or other *mcr* genes. Detailed results of these investigations have recently been published (Börjesson et al, 2020).

In summary, isolates of Enterobacteriaceae carrying bla_{SHV-12} and *mcr-9* from 29 different horses were found among 102 investigated clinical isolates from cats, dogs and horses. The isolates belonged to the species *Enterobacter cloacae* group (n=15), *Escherichia coli* (n=9), *Klebsiella oxytoca* (n=4) and *Citrobacter freundii* (n=1). Different sequence types were present among isolates within the different species. However, all the isolates were positive for plasmids of the replicon types incHI2 and incHI2A, and in some isolates these were the only replicon types identified. Taken together, this indicates that the spread of Enterobacteriaceae carrying bla_{SHV-12} and *mcr-9* among horses in Sweden has probably mainly been by plasmid dissemination, with incHI2 and incHI2A being the likely plasmids. Nonetheless, there were also cases of suspected clonal spread within and between different premises (i.e. stud farm, equine hospitals).

All the isolates carrying *mcr-9* were subjected to renewed phenotypic susceptibility testing for colistin by broth microdilution (MICRONAUT MIC-Strip Colistin, Merlin Diagnostika). For all the isolates, the MIC was below the EUCAST epidemiological cut-off values (http://www.mic.eucast.org, Table 1). This is in concordance with previous studies which showed that isolates carrying *mcr-9* generally would be defined as susceptible to colistin. However, increased MIC have been linked to the presence of two regulatory genes, *qse*B och *qse*C (Kieffer et al, 2019) but these genes were not present in any of the investigated Swedish isolates.

Phenotypic susceptibility testing of the isolates carrying *mcr-9* for a number of relevant substances had been performed previously by broth microdilution (VetMIC CLIN GN). The results for isolates of *Enterobacter cloacae* group and *E. coli* are shown in Table 2. All the isolates were resistant to three or more substances, i.e. multiresistant. The phenotypic traits were in accordance with the results of the *in silico* detection of antimicrobial resistance genes.

Table 1. Distribution of MICs (No. of isolates) of colistin in Enterobacteriaceae carrying *mcr-9*, separated by bacterial species.

	Distribution (%) of MICs (mg/L)										
Bacterial species	**0.06**	**0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**
C. freundii						1					
E. cloace group			7	5	3						
E. coli			4	5							
K. oxytoca			2	2							

In Focus

Benzylpenicillin, gentamicin, streptomycin and trimethoprim-sulfonamides are the only classes authorised in Sweden for systemic treatment of bacterial infections in horses. As seen in the different resistance profiles occurring among the isolates of *E. cloacae* group and *E. coli* (Table 2), all isolates are resistant to the above-mentioned substances. Or with other words, for infections in horses caused by these isolates the only alternatives if treatment is needed would be off-label treatment with fluoroquinolones or tetracyclines. For some isolates, also these two alternatives were void.

In 2019, an additional seven isolates of Enterobacteriaceae (three *E. cloacae* group, one *E. coli*, one *Escherichia* species, one *Klebsiella oxytoca*, and one *Klebsiella pneumoniae*) carrying bla_{SHV-12} and *mcr-9* have been confirmed. All of these were multiresistant and had similar resistance profiles as the isolates from previous years.

Table 2. Resistance phenotypes of isolates from the *Enterobacter cloacae* group and *Escherichia coli*.

Bacterial species	No. of isolates	Ampicillin	Gentamicin	Strepto-mycin	Trim-Sulph.	Tetracycline	Neomycin	Enrofloxacin
E. cloacae group	1	R	R	R	R	R	S	R
	5	R	R	R	R	R	S	S
	1	R	R	R	R	S	R	S
	6	R	R	R	R	S	S	S
	1	R	R	R	R	R	S	S
	1	R	R	R	R	S	S	S
E. coli	1	R	R	R	R	R	R	R
	1	R	R	R	R	R	S	S
	1	R	R	R	R	S	R	S
	3	R	R	R	R	S	S	S
	2	R	R	R	R	S	S	S
	1	R	R	R	R	R	S	S

References

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Börjesson S, Greko C, et al. 2020, A link between the newly described colistin resistance gene *mcr-9* and clinical Enterobacteriaceae isolates carrying bla_{SHV-12} from horses in Sweden. *J Glob Antimicrob Resist*, 20:285-289.

Kieffer N, Royer G, et al. 2019, *mcr-9*, an inducible gene encoding an acquired phosphoethanolamine transferase in *Escherichia coli*, and its origin. *Antimicrob Agents Chemother*, e00965-19.

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 horses) and Table 4.4 (companion animals).

Farm animals

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

In dairy cattle, active monitoring of selected isolates of beta-lactamase producing *S. aureus* from milk samples has been ongoing since 2010, and about 1300 isolates have been tested up to and including 2019. The monitoring is performed on isolates with anonymised origin. No MRSA was detected in 2019 of the 57 isolates screened for occurrence for *mecA* and *mecC*, but during previous years 6 MRSA with *mecC* and 3 MRSA with *mecA* were detected.

In 2016 and early 2017 there was an outbreak of MRSA with *mecC* among goats and sheep connected to a zoo. In addition, MRSA with *mecC* was found in 8 out of 21 sampled goats in a herd in 2017 and in one goat sold from the same herd. In 2019 an additional goat herd with MRSA was identified. The farm had an epidemiological link to the herd in 2017 and shared the same *spa*-type, t373. In total 6 goats were sampled and samples were pooled two and two for cultivation with all pools being positive for *mecC*-MRSA.

Companion animals and horses

Up to and including 2019, a total of 126 cases of MRSA in companion animals and horses have been confirmed. These include 54 dogs, 22 cats, 2 rabbits and 48 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.

In 2019, MRSA was detected in clinical samples, from wound infections, ears and skin lesions, from eight dogs and three cats. Since the first finding of MRSA in companion animals, *spa*-type t032 has been most common, but during the most recent years the identified *spa*-types have varied (Table 4.4). In 2018 two of the MRSA-positive cats from the same household were screened for MRSA as a rabbit in the same family previously was diagnosed with MRSA. The rabbit was sampled again in 2019 and was still positive.

In 2019, MRSA was isolated from five horses with wound infections, of which four of them were after surgery. (Table 4.3). In isolates from horses, *spa*-type t011, CC398, has dominated historically. In 2019, three isolates were of *spa*-type t011, one was t1971 and one was t1257.

Wild animals

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

TABLE 4.3. Farm animals and horses. Isolates of methicillin-resistant *Staphylococcus aureus* (MRSA) in Swedish horses, pigs, cows, goats and sheep up to and including 2019. 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*
Horse	2019	1	R	≤0,12	0,5	>16	≤0.5	>16	>8	>32	8	2	t011	*A*
Horse	2019	1	R	≤0,12	≤0.25	>16	≤0.5	>16	>8	>32	8	2	t011	*A*
Horse	2019	1	R	≤0,12	0,5	>16	≤0.5	>16	>8	>32	≤4	2	t011	*A*
Horse	2019	1	R	0,25	>8	>16	≤0.5	>16	>8	>32	8	2	t1971	*A*
Horse	2019	1	R	≤0,12	>8	>16	≤0,5	>16	>8	>32	8	2	t1257	*A*
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*
Goat	2019	1	R	0.25	0.5	≤0.5	≤0.5	≤0.1	0.5	≤2	8	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 2019. 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 four from dogs in 2017, 2018 and 2019 respectively were not available for further testing and are not included in the table.

				Antibiotic, MIC (mg/L)										
Animal species	**Year**	**No. of isolates**	**Beta-lactams**	**Cli**	**Ery**	**Tet**	**Fus**	**Gen**	**Cip**	**Tmp**	**Chl**	**Lin**	***spa*-type**	***mec*-gene**
Dog	2006-14	13	R	≤0.25	≤0.25-1	≤0.5	≤0.06-0.5	≤0.5-1	>4	1-2	8		t032	*A*
Dog	2007	1	R	0.5	0.5	2	-	1	>4	2	4		t032	*A*
Dog	2008	1	R	0.5	>32	≤0.5	0.5	32	>4	>32	16		t127	*A*
Dog	2009	1	R	0.5	1	1	0.5	1	>4	4	16		t032	*A*
Dog	2010	1	R	>32	>32	≤0.5	0.5	1	>4	2	16		t002	*A*
Dog	2010	1	R	≤0.25	>32	≤0.5	0.5	≤0.5	>4	8	4		t020	*A*
Dog	2010	1	R	≤0.25	≤0.25	≤0.5	8	1	0.5	2	8		t002	*A*
Dog	2013	1	R	≤0.25	>32	16	0.25	2	0.25	2	8		t127	*A*
Dog	2013	1	R	≤0.25	1	≤0.5	0.5	≤0.5	0.5	4	8		t304	*A*
Dog	2013	1	R	≤0.25	1	≤0.5	0.25	≤0.5	0.5	2	8		t127	*A*
Dog	2013	1	R	0.5	1	1	1	1	>4	4	8		t032	*A*
Dog	2013	1	R	≤0.25	0.5	≤0.5	0.5	≤0.5	0.5	>32	8		t223	*A*
Dog	2014	1	R	≤0.25	1	16	0.5	1	0.5	4	8		t325	*A*
Dog	2014	1	R	≤0.25	>32	≤0.5	≤0.06	≤0.5	0.25	1	8		t002	*A*
Dog	2015	1	R	0.5	≤0.25	≤0.5	0.5	≤0.5	0.25	≤0.5	8		t373	*C*
Dog	2015	3	R	≤0.25	>32	16-32	≤0.06-0.5	≤0.5	0.12-0.25	1-2	4-8		t127	*A*
Dog	2015	1	R	≤0.25	≤0.25	≤0.5	0.12	≤0.5	0.25	1	8		t843	*C*
Dog	2015	1	R	≤0.25	>32	16	0.25	≤0.5	0.5	2	8		t948	*A*
Dog	2015	1	R	≤0.25	>32	16	0.12	≤0.5	0.25	1	4		t177	*A*
Dog	2016	1	R	16	≤0.25	32	0.5	16	>4	>32	64		t034	*A*
Dog	2016	1	R	≤0.25	>32	8	4	≤0.5	0.5	4	8		t044	*A*
Dog	2017	1	R	≤0.25	≤0.25	≤0.5	>4	0.25	>4	0.5	8	2	t032	*A*
Dog	2017	1	R	8	≤0.25	64	≤0.25	0.5	>4	>8	4	≤1	t034	*A*
Dog	2017	1	R	≤0.25	≤0.25	≤0.5	≤0.25	0.25	0.5	1	4	2	t2734	*A*
Dog	2017	1	R	≤0.25	≤0.25	≤0.5	≤0.25	0.5	0.25	>8	8	2	t5634	*A*
Dog	2017	1	R	>32	>32	≤0.5	≤0.25	0.5	1	2	8	≤1	t127	*A*
Dog	2017	1	R	≤0.25	≤0.25	≤0.5	≤0.25	0.25	>4	0.5	4	2	t022	*A*
Dog	2017	1	R	≤0.25	2	≤0.5	≤0.25	0.25	>4	0.5	4	≤1	t008	*A*
Dog	2017	1	R	≤0.25	≤0.25	≤0.5	≤0.25	8	>4	>8	8	2	t891	*A*
Dog	2018	2	R	≤0.12-0.25	>8	>16	≤0.5	≤1	≤0.25-0.5	≤2	≤4-8	≤1-2	t127	*A*
Dog	2018	1	R	0.25	0.5	≤0.5	≤0.5	≤1	≤0.25	>32	8	2	t223	*A*
Dog	2019	1	R	>4	>8	≤0.5	≤0.5	≤1	>8	≤2	16	2	t003	*A*
Dog	2019	1	R	>4	>8	>16	≤0.5	≤1	≤0,25	>32	8	2	t034	*A*
Dog	2019	1	R	≤0,12	≤0.5	≤0.5	≤0.5	≤1	≤0,25	≤2	8	4	t10893	*C*
Dog	2019	1	R	≤0,12	>8	>16	≤0.5	≤1	≤0,25	≤2	8	2	t127	*A*
Dog	2019	1	R	≤0,12	≤0,25	≤0.5	≤0.5	≤1	0,5	≤2	8	≤1	t1339	*A*
Dog	2019	1	R	≤0,12	0,5	≤0.5	≤0.5	≤1	≤0,25	≤2	8	2	t18886	*C*
Dog	2019	1	R	≤0,12	≤0,25	≤0.5	≤0,5	≤1	≤0,25	>32	8	2	t790	*A*
Dog	2019	1	R	0,25	0,5	≤0,5	≤0,5	≤1	≤0,25	≤2	8	2	t843	*C*
Cat	2009	1	R	≤0.25	0.5	≤0.5	0.25	≤0.5	>4	4	4		t032	*A*
Cat	2009-2012	3	R	≤0.25	≤0.25-0.5	≤0.5	0.25-0.5	≤0.5-1	>4	1-2	8		t032	*A*
Cat	2010	1	R	≤0.25	0.5	≤0.5	1	≤0.5	>4	1	8		t032	*A*
Cat	2011	1	R	≤0.25	≤0.25	≤0.5	0.25	≤0.5	>4	1	8		t022	*A*
Cat	2012	1	R	0.5	1	1	1	1	>4	2	16		t032	*A*
Cat	2014	2	R	≤0.25	≤0.25	≤0.5	≤0.06-0.25	≤0.5	0.25	0.5	8		t978	*C*
Cat	2015	1	R	≤0.25	≤0.25	≤0.5	≤0.06	≤0.5	0.25	1	8		t843	*C*
Cat	2015	1	R	≤0.25	0.5	≤0.5	0.12	≤0.5	0.25	1	8		t933	*A*
Cat	2016	1	R	≤0.25	>32	≤0.5	0.5	≤0.5	2	2	8		t008	*A*
Cat	2016	1	R	≤0.25	≤0.25	≤0.5	≤0.06	≤0.5	0.12	≤0.5	4		t304	*A*
Cat	2017	1	R	≤0.25	≤0.25	≤0.5	≤0.25	0.5	0.25	>8	4	≤1	t786	*A*
Cat	2018	2	R	0.25	0.5	≤0.5	>4	≤1	≤0.25	≤2	8	2	t132	*A*
Cat	2018	2	R	0.25	0.5	≤0.5	≤0.5	≤1	>8	≤2	8	2	t032	*A*
Cat	2018	1	R	≤0.12	0.5	≤0.5	≤0.5	≤1	≤0.25	≤2	8	2	t12236	*A*
Cat	2019	1	R	≤0.12	0,5	≤0,5	≤0,5	≤1	0,5	≤2	8	8	t002	*A*
Cat	2019	1	R	>4	0,5	>16	≤0,5	≤1	≤0,25	>32	8	4	t034	*A*
Cat	2019	1	R	≤0.12	0,5	≤0,5	≤0,5	≤1	0,5	≤2	8	2	t373	*C*
Rabbit	2017	1	R	≤0.25	≤0.25	≤0.5	4	0.5	0.25	0.5	4	≤1	t132	*A*
Rabbit	2019	1	R	≤0.12	≤0.25	≤0.5	>4	≤1	≤0.25	≤2	8	2	t132	*A*

Methicillin-resistant *Staphylococcus pseudintermedius* (MRSP)

In 2019, there were 48 MRSP cases reported to the Swedish Board of Agriculture (Figure 4.2). This number is around the same level as in previous years. Isolates from 42 cases (38 dogs, 3 cats and 1 horse) were available for further susceptibility testing and genome sequencing. Information on the sampling site was available for 38 cases; skin (including external ear canal) 14 cases, wounds (including surgical wounds) 20 cases and the remaining four were isolated from various other sites. All isolates were defined as multi-resistant. For resistance phenotypes, see Table 4.5.

The results of the genome sequencing divided the isolates into 23 different multi-locus sequence types, of which ST551 was the most common type with 13 isolates (twelve from dogs and one from a horse; Table 4.5). The ST551 was first detected in 2016 and was also the most common ST in 2018 with 11 out of 49 genome sequenced isolates. In earlier years, ST71 (a sequence type spread in Europe and described by Perreten et al. 2010), was dominating among Swedish isolates. In 2019, only 5 out of 42 isolates were of this type. Now the epidemiology of MRSP is more diverse with several sequence types occurring.

FIGURE 4.2. Number of cases of methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) in Sweden 2006-2019. In 2006-2007 the numbers represent the isolates that were sent to SVA and confirmed as *mecA*-positive and from 2008 number of cases notified to the Swedish Board of Agriculture.

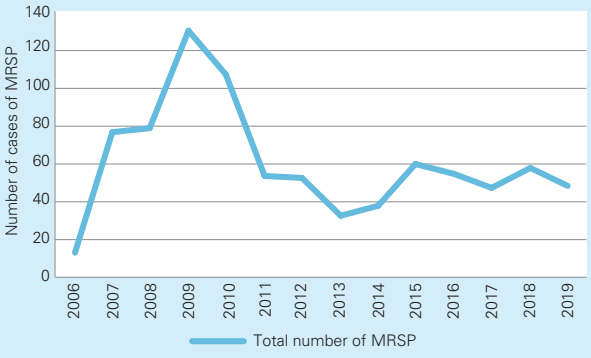


TABLE 4.5. Resistance phenotypes (beta-lactams excluded) and multilocus sequence types of isolates of methicillin resistant *Staphylococcus pseudintermedius* (MRSP) in 2019. All isolates were positive for the *mecA* gene. Shaded areas indicate resistance.

Antibiotic MIC (mg/L)									MLST						
Beta-lactams	Ery	Cli	Tsu[a]	Tet	Enr	Fus	Gen	Nit	ST71	ST551	ST566	ST258	ST265	Single ST:s[b]	Sum
R	>2	>2	4->4	>4	>1	>2	4->4	<=16		1					1
R	>2	>2	4->4	>4	>1	<=0.5	4->4	<=16	2	11				2	15
R	>2	>2	4->4	>4	>1	<=0.5	<=1	<=16						1	1
R	>2	>2	4->4	>4	<=1	<=0.5	4->4	<=16						1	1
R	>2	>2	4->4	>4	<=0.25	2	<=1	<=16				1			1
R	>2	>2	4->4	>4	<=0.25	<=0.5	4->4	<=16		1		1	2		4
R	>2	>2	4->4	>4	<=0.25	<=0.5	<=1	<=16						2	2
R	>2	>2	4->4	<=0.25	>1	>2	4->4	<=16	1						1
R	>2	>2	4->4	<=0.25	>1	<=0.5	<=1	<=16	2					1	3
R	>2	>2	1	>4	>1	<=0.5	4->4	<=16						1	1
R	>2	>2	0.5	<=0.25	>1	<=0.5	4->4	<=16			2				2
R	>2	>2	0.5	<=0.25	<=0.25	<=0.5	<=1	<=16						1	1
R	>2	>2	<=0.250	<=0.25	<=0.25	<=0.5	<=1	<=16						1	1
R	>2	2	0.5	>4	<=0.25	<=0.5	<=1	<=16						1	1
R	>2	1	4->4	>4	<=0.25	<=0.5	<=1	<=16				1			1
R	>2	<=0.5	4->4	>4	<=0.25	<=0.5	4->4	<=16						1	1
R	>2	<=0.5	1	<=0.25	<=0.25	<=0.5	4->4	<=16						1	1
R	>2	<=0.5	0.5	>4	>1	<=0.5	4->4	<=16						1	1
R	>2	<=0.5	0.5	<=0.25	<=0.25	<=0.5	<=1	32						1	1
R	1	>2	4->4	<=0.25	1	1	4->4	>64						1	1
R	<=0.500	<=0.500	4->4	>4	<=0.25	<=0.5	<=1	<=16						1	1
								Sum	**5**	**13**	**2**	**3**	**2**	**17**	**42**

[a]Concentration of trimetoprim given, tested in concentration ration 1/20 (trimetoprim/sulphamethoxazole); [b]Single ST:s include ST45, ST84, ST181, ST337, ST343, ST934, ST1095 and ST1620-1629.

Zoonotic pathogens

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

Salmonella

Findings of *Salmonella* in animals are notifiable in Sweden. In Svarm, antibiotic susceptibility is determined in one isolate from each notified incident in farm animals or horses each year. Isolates from incidents previously notified but still under restrictions are also included. In incidents involving more than one serovar, one isolate of each serovar is tested. In the case of poultry, one isolate from each infected flock is included. More than one flock can be affected on the same farm, in that case one isolate from each of the infected flocks is included. From incidents in companion animals and wild animals a selection of isolates is tested. The majority of *Salmonella* from wild birds are from cases of salmonellosis among passerines during the winter season, while *Salmonella* from cats are cases when cats have eaten these birds lying dead or diseased on the ground. Such isolates are almost invariably *S.* Typhimurium susceptible to all tested antibiotics. Therefore, only the first 5 and 25 index cases of *Salmonella* from sparrows 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 2019

A total of 86 *Salmonella* isolates were tested in 2019, all belonging to the species *S. enterica* and with two subspecies represented, subsp. *enterica* (81 isolates) and subsp. *diarizonae* (5 isolates). The isolates were shared into 15 different serovars with *S.* Typhimurium as the clearly dominant serovar with 58 isolates, including 6 isolates belonging to the monophasic *S.* Typhimurium variant type 4,[5],12:i:- (Table 4.6). Some isolates belonged to exotic and unusual serovars, such as *S.* Kisii and *S.* Bukavu.

One isolate from cattle had the antigenic formula *S.* 9,12:-:-, which is congruent with the antigenic formula for *S.* Gallinarum. However, this serovar is host adapted to poultry and is not considered pathogenic to mammals. It is therefore likely that this isolate was not a *S.* Gallinarum but an aphasic mutant of another serovar with related formula, such as *S.* Enteritidis, however, no further investigations were made on this isolate.

The subspecies *diarizonae* is usually associated with reptiles, however, the serovar *S. enterica* subsp. *diarizonae* 61:-:1,5 is present in sheep in both Sweden and several other countries, such as Norway, Iceland, Switzerland, UK, Spain, Germany, and the USA. It is considered a serovar host adapted to sheep where it may cause both intestinal and extraintestinal infections, but in most cases the animals are healthy carriers of the bacterium in the intestine, vagina, tonsils, or nose. Although it is still notifiable in Sweden, it has for this particular serovar been decided not to follow up with backtracing and eradication. Four isolates from sheep and one from a young, five months old dog belonged to this serovar. It is uncertain how the dog became infected with this serovar or whether there was any connection to sheep. All of these isolates were susceptible to all tested antibiotics.

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 18 of the isolates (21%) were categorised as resistant to colistin. Three of these isolates were *S.* Dublin, which had an MIC of 4 µg/ml. It has previously been described that this serovar may have slightly higher colistin MICs. One *S.* Enteritidis isolate had an

TABLE 4.6. Serovar distribution and number of *Salmonella* isolates (n=86) tested for antimicrobial susceptibility, 2019.

Serovar	Cattle	Pig	Poultry	Sheep	Horse	Cat	Dog	Wild birds	Wild mammals	Total
S. Agona	1	1					1			**3**
S. Bukavu			1							**1**
S. Derby							1			**1**
S. Dublin	4									**4**
S. Duesseldorf	2		1							**3**
S. enterica subsp. *diarizonae* 61:-:1,5				4			1			**5**
S. enterica subsp. *enterica* 9,12:-:-	1									**1**
S. Enteritidis					1				1	**2**
S. Hessarek						1		1		**2**
S. Kisii			1							**1**
S. London		1								**1**
S. Monchaui	1									**1**
S. Newport						1				**1**
S. Reading	1		1							**2**
S. Typhimurium	9	10	2		2	16	6	7		**52**
S. Typhimurium monophasic 4,[5],12:i:-	5	1								**6**
Total	**24**	**13**	**6**	**4**	**3**	**18**	**9**	**8**	**1**	**86**
% of total	**28**	**15**	**7**	**5**	**3**	**21**	**10**	**9**	**1**	**100**

MIC for colistin of 8 µg/ml. The remaining colistin resistant isolates (n=14) were *S.* Typhimurium, all with a colistin MIC of 4 µg/ml. All the colistin resistant *S.* Dublin and *S.* Typhimurium isolates were susceptible to all other compounds, whereas the *S.* Enteritidis isolate was also resistant to the quinolones, nalidixic acid and ciprofloxacin. The reason for this increased colistin MIC is currently not known. All the isolates were tested by PCR for presence of *mcr-1 – mcr-5* genes, which are known to confer resistance to colistin, but all isolates were negative for these genes.

The majority of the isolates (57 of 86; 66%) were susceptible to all antibiotics tested, however a relatively large proportion (29 of 86, 34%) displayed resistance to one or more compound (Table 4.7). Seventeen of these, however, showed only resistance to colistin while the remaining 12 were multiresistant, i.e. resistant to three or more compounds.

TABLE 4.7. Distribution of MICs and resistance (%) in *Salmonella enterica* (n=86) from all animals, 2019.

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	13							84.9	2.3						12.8				
Azithromycin	NA[a]								4.7	72.0	22.1	1.2							
Cefotaxime	1					98.8					1.2								
Ceftazidime	1						98.8					1.2							
Chloramphenicol	5										95.3				4.7				
Ciprofloxacin	2	69.8	27.9			1.2	1.2												
Colistin	21							53.5	25.6	19.8	1.2								
Gentamicin	1						89.5	9.3				1.2							
Meropenem	0		100																
Nalidixic acid	1									97.7		1.2			1.2				
Sulphamethoxazole	13										8.1	20.9	58.1						12.8
Tetracycline	12								88.4				4.7	1.2	5.8				
Tigecycline	0					100													
Trimethoprim	6					76.7	17.4							5.8					

[a]NA not applicable. No approved breakpoints exist for *Salmonella*.

TABLE 4.8. Distribution of MICs and resistance (%) in *Salmonella* Typhimurium, including six monophasic variants (n=58) from all animals, 2019.

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	17							79.3	3.4						17.2				
Azithromycin	NA[a]								3.4	82.8	13.8								
Cefotaxime	0					100													
Ceftazidime	0						100												
Chloramphenicol	7										93.1				6.9				
Ciprofloxacin	0		36.2	63.8															
Colistin	24							39.7	36.2	24.1									
Gentamicin	0						87.9	12.1											
Meropenem	0		100																
Nalidixic acid	0									100									
Sulphamethoxazole	17										6.9	12.1	63.8						17.2
Tetracycline	15								84.5				6.9		8.6				
Tigecycline	0					100													
Trimethoprim	9					74.1	17.2							8.6					

[a]NA not applicable. No approved breakpoints exist for *Salmonella*.

All multiresistant *S.* Typhimurium isolates were resistant to both ampicillin (aminopenicillins) and sulphametoxazole (sulphonamides) while all, except one were resistant to tetracyclines and all, except one to trimethoprim (Table 4.9). Four isolates were resistant to chloramphenicol.

A single isolate, *S.* Kisii, was resistant to eight different compounds including fluoroquinolones and cephalosporins (Table 4.9). This was the only isolate that was resistant to the cephalosporins, cefotaxime and ceftazidime, and also the only isolate that was resistant to gentamicin.

No isolate was resistant to meropenem (carbapenems).

In the subset of *S.* Typhimurium, resistance was overall low in 2019 but has varied over the years (Figure 4.3). The variation is largely due to differences in occurrence of multiresistant strains between the years. However, the resistance to all four compounds, ampicillin, chloramphenicol, sulphamethoxazole, and tetracycline, increased compared to 2018, which is largely due to an increased number of monophasic isolates and isolates with chloramphenicol resistance (DT104 resistance profile).

A single *Salmonella* isolate was from a wild mammal, a *S.* Enteritidis from a hedgehog. 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.

Farm animals 2000–2019

From a public health perspective, resistance in *Salmonella* from farm animals is of greater concern than resistance in isolates from wild animals or companion animals. 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 2000-2019, isolates from the vast majority of notified incidents in major farm animals were tested in

FIGURE 4.3. Resistance to ampicillin, chloramphenicol, sulphamethoxazole, and tetracycline in *Salmonella* Typhimurium in all animals, 2000-2019.

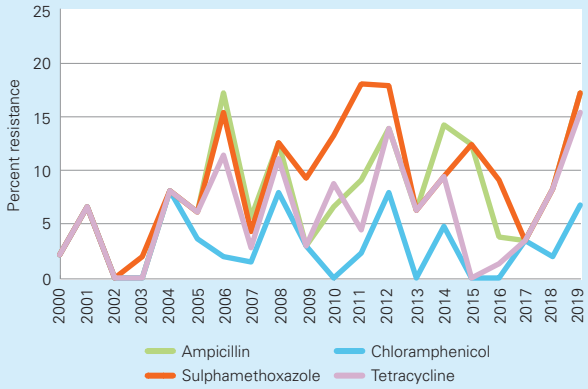


TABLE 4.9. MICs (mg/L) in the 29 isolates of *Salmonella enterica* resistant to one or more antibiotics, 2019. Shaded fields indicate resistance.

Source	Serovar	Sul	Tmp	Cip	Tet	Mero	Azt	Nal	Ctx	Chl	Tgc	Caz	Col	Amp	Gen
Cattle	Dublin	16	0.5	≤ 0.015	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Cattle	Dublin	16	≤ 0.25	≤ 0.015	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Cattle	Dublin	16	≤ 0.25	≤ 0.015	≤ 2	≤ 0.03	≤ 2	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Horse	Enteritidis	32	0.5	0.25	≤ 2	≤ 0.03	4	>128	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	8	≤ 1	≤ 0.5
Poultry	Kisii	>1024	≤ 0.25	0.5	64	≤ 0.03	16	16	> 4	≤ 8	≤ 0.25	> 8	≤ 1	>64	16
Pig	Monophasic	>1024	≤ 0.25	0.03	>64	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	≤ 1	>64	≤ 0.5
Cattle	Monophasic	>1024	>32	≤ 0.015	>64	≤ 0.03	8	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	≤ 1	>64	≤ 0.5
Cattle	Monophasic	>1024	>32	≤ 0.015	>64	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	≤ 1	>64	≤ 0.5
Cattle	Monophasic	>1024	>32	≤ 0.015	>64	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	≤ 1	>64	≤ 0.5
Cattle	Monophasic	>1024	>32	≤ 0.015	>64	≤ 0.03	8	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	≤ 1	>64	≤ 0.5
Cattle	Monophasic	>1024	>32	≤ 0.015	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	≤ 1	>64	≤ 0.5
Cat	Typhimurium	32	0.5	≤ 0.015	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Cat	Typhimurium	32	≤ 0.25	≤ 0.015	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Cat	Typhimurium	32	0.5	≤ 0.015	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Cat	Typhimurium	32	≤ 0.25	0.03	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	2	≤ 0.5
Cat	Typhimurium	32	0.5	0.03	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	2	≤ 0.5
Cat	Typhimurium	32	≤ 0.25	0.03	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Dog	Typhimurium	32	≤ 0.25	0.03	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Dog	Typhimurium	32	0.5	0.03	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Dog	Typhimurium	32	0.5	≤ 0.015	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Cattle	Typhimurium	>1024	0.5	≤ 0.015	32	≤ 0.03	8	≤ 4	≤ 0.25	>128	≤ 0.25	≤ 0.5	≤ 1	>64	≤ 0.5
Pig	Typhimurium	>1024	0.5	0.03	32	≤ 0.03	8	≤ 4	≤ 0.25	>128	≤ 0.25	≤ 0.5	≤ 1	>64	≤ 0.5
Dog	Typhimurium	32	0.5	0.03	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Pig	Typhimurium	32	≤ 0.25	0.03	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Pig	Typhimurium	>1024	≤ 0.25	≤ 0.015	32	≤ 0.03	8	≤ 4	≤ 0.25	>128	≤ 0.25	≤ 0.5	≤ 1	>64	≤ 0.5
Pig	Typhimurium	32	≤ 0.25	0.03	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Cattle	Typhimurium	>1024	≤ 0.25	≤ 0.015	32	≤ 0.03	4	≤ 4	≤ 0.25	>128	≤ 0.25	≤ 0.5	≤ 1	>64	≤ 0.5
Cat	Typhimurium	16	≤ 0.25	≤ 0.015	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5
Wild bird	Typhimurium	32	≤ 0.25	≤ 0.015	≤ 2	≤ 0.03	4	≤ 4	≤ 0.25	≤ 8	≤ 0.25	≤ 0.5	4	≤ 1	≤ 0.5

Svarm, in total 772 isolates. About half of the isolates, 381 (49%), were *S.* Typhimurium and of these 37% were from pigs, 33% from cattle, 29% from poultry and 1% from sheep.

In 2019, 29 *S.* Typhimurium were isolated from farm animals. Of these 12 were resistant to one or more compounds (Table 4.9), and 10 of these were multiresistant. All phenotypic resistance combinations for *S.* Typhimurium during the period 2000-2019 are shown in Table 4.10 while the combinations for the 2019 isolates can be deducted from Table 4.9.

Four isolates from 2019 – two from pigs and two from cattle – were resistant to ampicillin, sulphonamides, tetracycline, and chloramphenicol. This was the typical profile of the *S.* Typhimurium DT104 clone, which was widespread during the 1990'ies but now is less prevalent. The present isolates were not investigated further to determine whether they were indeed DT104. It should be noted that in 2019, 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 49 multiresistant isolates of *S.* Typhimurium in the period 2000-2019 were from 48 separate notified incidents

TABLE 4.10. Resistance phenotypes of *Salmonella* Typhimurium (n=381) from notified incidents in farm animals, 2000-2019.

		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**																						3	3
AmpSulTetChl	**Pigs**																						2	2
AmpSulTetTm	**Cattle**																					4		4
AmpStrSul	**Cattle**													1								1	1	3
AmpSulTet	**Pigs**																					1		1
AmpSulTm	**Cattle**																					1		1
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
Col	**Pigs**																						**2**	**2**
Susceptible	**Sheep**	1																					3	4
Susceptible	**Cattle**	4			2		1	1	1	6		2		5	1	1				27	1	1	24	77
Susceptible	**Pigs**	1	1			2			33	5	1	1		8					1	18	2		31	104
Susceptible	**Poultry**	1		1		1			5	1			1	2				1	1	43	4		34	95
Sum		**7**	**1**	**1**	**2**	**4**	**3**	**1**	**44**	**19**	**1**	**22**	**1**	**20**	**1**	**2**	**1**	**1**	**2**	**104**	**11**	**15**	**118**	**381**

of which 32 involved cattle, 11 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. Three of the isolates from 2019 were from the same farm but collected at different timepoints. There were no known links between the other incidents.

In 2019, six of the notified incidents in farm animals involved monophasic *S.* Typhimurium, five from cattle and one from pigs. Since this variant was first found in 2006, only nine incidents of monophasic *S.* Typhimurium had been confirmed in farm animals in Sweden up till 2018. Three incidents had involved only cattle, three only pigs, one only ducks, and one incident involved both cattle and poultry. In six of these incidents the isolates were multiresistant, while all six isolates from 2019 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. 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 *S.* Typhimurium. Monophasic *S.* Typhimurium has spread over the last decade in many European countries and become one of the most prevalent strains. Most of these isolates display resistance to ampicillin, streptomycin, sulphonamides, and tetracycline which was also the case for five of the isolates from 2019.

Two isolates from poultry belonged to the exotic serovars, *S.* Kisii and *S.* Bukavu, respectively. It should be noted that these were isolated through the official *Salmonella* control programme and not from diseased animals. These serovars were originally isolated and described from Bukavu in The Dem. Rep. Congo and Kisii in Kenya, and very few reports on these serotypes exist in the literature. Therefore, their virulence to humans and animals is grossly unknown. However, while the *S.* Bukavu isolate was susceptible to all tested compounds, the *S.* Kisii isolate was resistant to eight different compounds, including the critical antibiotics, fluoroquinolones and cephalosporins. It was susceptible to meropenem, and further tests showed that it was also susceptible to other carbapenems. It is unknown how the poultry flocks became contaminated with these isolates, but other studies have suggested that such exotic serovars are often feed contaminants.

Campylobacter

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

Of the 171 isolates, 63 (37%) were susceptible to the six tested antibiotics. There was no resistance recorded against erythromycin, gentamicin and tetracycline (Table 4.11). The level of quinolone resistance was comparable to previous years (Figure 4.4).

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

Occurrence of streptomycin resistance in *Campylobacter coli* is remarkably high (47%). Streptomycin resistance in *Campylobacter coli* from Swedish pigs is difficult to explain in the context of selection by use since streptomycin is rarely used in pigs in recent years. Neither is co-selection by use of other substances likely since 55% of the streptomycin resistant isolates were resistant only to this antimicrobial.

FIGURE 4.4. Ciprofloxacin, nalidixic acid and streptomycin resistance (%) in *Campylobacter coli* from pigs 1999-2019. In years 1999-2005 enrofloxacin was tested instead of ciprofloxacin. The number of isolates per year has varied (n=83-171).

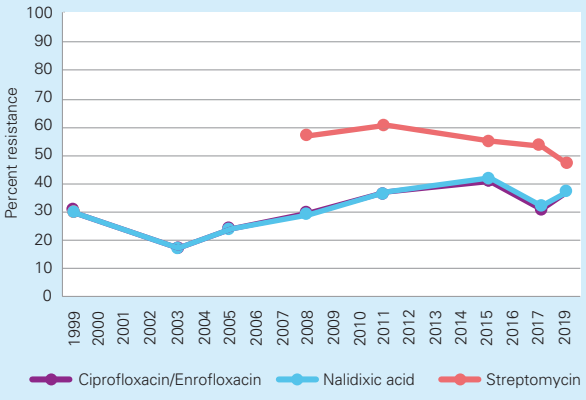


TABLE 4.11. Distribution of MICs and resistance (%) for *Campylobacter coli* from slaughter pigs, 2019.

Antibiotic	Resistance (%) n=171	Distribution (%) of MICs (mg/L)											
		≤0.12	0.25	0.5	1	2	4	8	16	32	64	128	>128
Ciprofloxacin	37	59.1	2.3	1.8			4.7	18.7	12.9	0.6			
Erythromycin	0				71.9	25.1	2.9						
Gentamicin	0		1.8	39.8	57.3	1.2							
Nalidixic acid	37						35.1	25.7	2.3	0.6	9.4	26.9	
Streptomycin	47				1.8	11.7	39.8	1.2		15.8	29.8		
Tetracycline	0			99.4	0.6								

Clinical isolates from animals

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

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

Pigs

Escherichia coli

Isolates of *E. coli* are from clinical submissions of faecal samples or samples taken post-mortem from the gastro-intestinal tract. Most 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 but the increase levelled off in 2015-2017 (Figure 4.5).

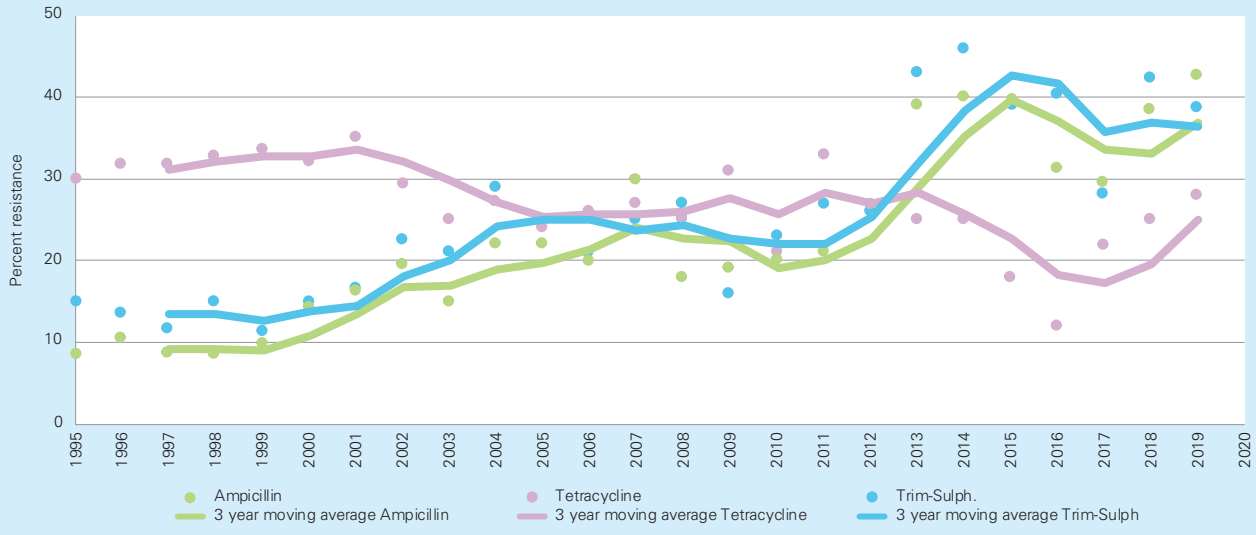
According to a national regulation from 2013 (SJVFS 2013:42), susceptibility testing is generally required before ordination of fluoroquinolones for animals. Due to this, sam-

TABLE 4.12. Distribution of MICs and resistance (%) in *Escherichia coli* from pigs 2019. Clinical isolates from faecal samples or from samples taken post-mortem from the gastro-intestinal tract.

Antibiotic	Resistance (%) 2019 n=75	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	43					57.3				42.7		
Cefotaxime	0		100									
Colistin	0				97.3	2.7						
Enrofloxacin	11	89.3	5.3	4.0	1.3							
Gentamicin	0					100						
Neomycin	9						90.7		1.3	2.7	5.3	
Nitrofurantoin	0							30.7	62.7	6.7		
Streptomycin	45							49.3	5.3	4.0	9.3	32.0
Tetracycline	28					72.0			4.0	24.0		
Trim-Sulph.[a]	39			61.3				38.7				

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

FIGURE 4.5. Resistance (%) in *Escherichia coli* from pigs 1995-2019 with a three-year moving average. Clinical isolates from faecal samples or from samples taken postmortem from the gastro-intestinal tract. The number of isolates each year varies (n=52-482, 2019 n=75).



pling 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 randomised (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 33% (25/75) of the isolates in 2019 and has varied over the years (31% in 2018, 20% in 2017, 25% in 2016 and 2015, 42% in 2014 and 38% in 2013). Resistance phenotypes are shown in Table 4.13. For comparison of resistance in *E. coli* from other animal species see Comparison of antibiotic resistance in *E. coli* and *Staphylococcus* spp, Table 4.34.

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

TABLE 4.13. Resistance phenotypes of isolates of *Escherichia coli* from pigs 2019. 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					6
R	R	R	R							4
R	R	R		R						1
R	R	R								10
R	R		R							1
R	R			R						2
R	R									1
R		R								2
R			R	R						1
R			R							2
R					R					1
R										1
	R	R								4
		R	R							2
		R		R						1
		R								4
			R							5
				R						3
										24
									Sum	**75**

TABLE 4.14. Resistance (%) in *Brachyspira hyodysenteriae* from pigs 2005-2019 and distribution of MICs for isolates from 2017-2019. Clinical isolates from faecal samples.

Antibiotic	Resistance (%)					Distribution (%) of MICs (mg/L)												
	2005-06	2007-08	2009-11	2012-16	2017-19	≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	>128
	n=54[a]	n=38[c]	n=40[e]	n=40[f]	n=27[g]														
Doxycycline	9	3	5	0	0			22.2	63.0	14.8									
Tiamulin	7	18	8	10	33[h]		33.3	3.7	29.6	14.8	11.1		3.7		3.7				
Tylosin	81	76	60	45	52							14.8	22.2	7.4	3.7				51.9
Tylvalosin	NA[b]	93[d]	55	48	67				3.7	11.1	18.5	14.8	7.4	11.1	29.6		3.7		
Valnemulin	0	18	3	13	41	37.0	22.2		7.4	11.1	11.1	3.7	3.7	3.7					

[a]29 isolates 2005, 25 isolates 2006; [b]Not analysed; [c]23 isolates 2007, 15 isolates 2008; [d]15 isolates; [e]24 isolates 2009, 9 isolates 2010, 7 isolates 2011; [f]7 isolates 2012, 8 isolates 2013, 7 isolates 2014, 7 isolates 2015, 11 isolates 2016; [g]15 isolates 2017, 5 isolates 2018, 7 isolates 2019 ; [h]All isolates with MICs above 2 mg/L are from a defined outbreak.

MICs above the clinical breakpoint (>2 mg/L) were detected for the first time from Swedish pigs. Therapeutic failure was also observed. Three isolates from 2016 and two from 2017 were classified as clinically resistant.

The cut-off value for tylosin (>16 mg/L) has not been changed compared to previous years. Tylosin resistance has decreased over the years but increased slightly in 2017-2019. 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.

Brachyspira pilosicoli

Isolates of *Brachyspira pilosicoli* are from clinical submissions of faecal samples. ECOFFs for *B. pilosicoli* are not defined for the antibiotics tested. As guide for the choice of antibiotic for treatment of spirochaetal diarrhoea, clinical breakpoints for tiamulin of >2 mg/L and for tylosin of >16 mg/L are used at SVA. With these breakpoints, 11% of the isolates were resistant to tiamulin and 53% to tylosin (Table 4.15). If the same wild type cut-off value as for *B. hyodysenteriae* is used, 26% of the isolates were resistant to tiamulin.

Actinobacillus pleuropneumoniae

Isolates of *Actinobacillus pleuropneumoniae* are from post-mortem investigations of lungs. The resistance situation is favourable and almost no resistance was detected (Table 4.16). 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 2005-2019, n=383. Clinical isolates from faecal samples. The number of isolates each year varies (n=7-67, 2019 n=27).

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			38.9	50.7	4.2	2.3	3.4	0.5						
Tiamulin		40.7	21.9	11.5	8.6	5.0	1.6	0.5	2.3	7.8				
Tylosin							7.6	17.8	17.8	3.9	5.0	3.7	6.0	38.4
Tylvalosin[a]				0.5	13.2	26.4	27.3	7.3	2.3	3.6	9.1	10.5		
Valnemulin	51.2	16.2	5.5	10.2	7.3	3.9	1.8	1.0	2.9					

[a]220 isolates tested.

TABLE 4.16. Distribution of MICs and resistance (%) in *Actinobacillus pleuropneumoniae* from pigs 2018-2019. Clinical isolates from post-mortem investigations of lungs.

Antibiotic	Resistance (%) 2018-2019	Distribution (%) of MICs (mg/L)												
	n=32	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	>128
Ampicillin	0		15.6	84.4										
Enrofloxacin	0	100												
Florfenicol	0			93.8	6.25									
Gentamicin	NR[b]								93.8	6.3				
Oxytetracycline	0				53.1	46.9								
Penicillin	0		3.1	6.3	90.6									
Trim-Sulph.[a]	0					100								

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

Cattle

Escherichia coli from faecal samples

Isolates of *E. coli* are from the gastro-intestinal tract of calves. Most of the isolates are from calves no more than a few weeks old, i.e. during a period when resistance in enteric bacteria often is high in cattle. Resistance was high to ampicillin, streptomycin and tetracycline (Table 4.17 and Figure 4.6), as in previous years. Multiresistance occurred in 41% (27/66) of the isolates from 2017-2019, compared to 32% in 2016, 56% in 2015, 76% in 2014 and 70% in 2013. For resistance phenotypes in isolates in 2017-2019, see Table 4.18. For comparison of resistance in *E. coli* from other animal species see Comparison of antibiotic resistance in *E. coli* and *Staphylococcus* spp, Table 4.34.

FIGURE 4.6. Resistance (%) in *Escherichia coli* from calves 2007-2019. 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, 2017-2019=66).

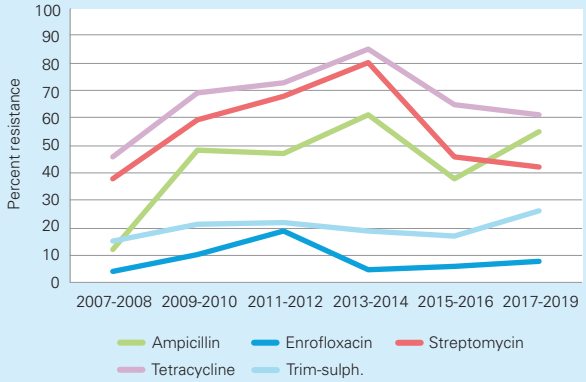


TABLE 4.17. Distributions of MICs and resistance (%) in *Escherichia coli* from calves 2017-19. Clinical isolates from faecal samples or from samples taken post-mortem from the gastro-intestinal tract.

Antibiotic	Resistance (%) 2017-2019 n=66	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	55					43.9	1.5			54.5		
Cefotaxime	2[b]		98.5	1.5								
Colistin	0				93.9	6.1						
Enrofloxacin	8	92.4	1.5	6.1								
Gentamicin	6					93.9	6.1					
Neomycin	21						75.8	3.0	3.0	9.1	9.1	
Nitrofurantoin	0							42.4	56.0	1.5		
Streptomycin	42							51.5	6.0		7.6	34.8
Tetracycline	61					37.9	1.5			60.6		
Trim-Sulph.[a]	26			74.2				25.8				

[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 4.18. Resistance phenotypes of isolates of *Escherichia coli* from calves 2017-19. Shaded areas with "R" indicate resistance.

Resistance phenotypes Amp	Tet	Str	Tsu	Neo	Enr	Gen	Ctx	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			R					1
R	R	R				R				1
R	R	R								5
R	R				R					2
R	R									2
R		R	R	R						1
R		R	R		R					1
R		R	R			R				2
R		R	R							4
R		R								4
R										4
	R			R		R				1
	R			R						8
	R									8
			R	R						1
				R						1
										11
									Sum	66

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. Therefore, the number of isolates of *E. coli* from milk samples that were susceptibility tested increased in 2013 and this number is constantly higher than prior to 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 2019, 32% (24/74) of the isolates were resistant to at least one antibiotic. Resistance to ampicillin, streptomycin, tetracycline or trimethoprim-sulphamethoxazole was the most common as in previous years (Table 4.19). Multiresistance occurred in 14% (10/74) of all isolates.

Klebsiella pneumoniae from milk samples

Isolates of *Klebsiella pneumoniae* are from clinical submissions of milk samples from dairy cows (Table 4.20). Resistance was uncommon and 76% (26/34) of isolates was susceptible to all tested antibiotics, excluding ampicillin. Multiresistance did not occur in isolates from 2019.

TABLE 4.19. Resistance (%) in *Escherichia coli* from dairy cows 2016-2019. Distribution of MICs from 2019. Clinical isolates from milk.

Antibiotic	Resistance (%)				Distribution (%) of MICs (mg/L)										
	2016 n=74	2017 n=79	2018 n=100	2019 n=74	≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	27	15	24	24					64.9	9.5	1.4		24.3		
Cefotaxime	1[b]	0	0	0		100									
Colistin	0	4[c]	0	0				85.1	14.9						
Enrofloxacin	4	3	1	3	97.3		2.7								
Gentamicin	1	0	1	3					97.3	2.7					
Neomycin	0	4	5	1						97.3	1.4			1.4	
Nitrofurantoin	0	0	0	1							16.2	71.6	8.1	2.7	1.4
Streptomycin	26	14	20	14							78.4	8.1	1.4	1.4	10.8
Tetracycline	16	9	8	18					81.1	1.4			17.6		
Trim-Sulph.[a]	22	9	14	11			89.2				10.8				

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphamethoxazole); [b]One isolate with MIC 1 mg/L was further tested and had an AmpC phenotype but no genes conferring transferable ESC resistance were detected with PCR; [c]Three isolates with MIC 4 mg/L were negative for *mcr-1, mcr-2, mcr-3, mcr-4* and *mcr-5* genes with PCR.

TABLE 4.20. Resistance (%) in *Klebsiella pneumoniae* from dairy cows 2016-2019. Distributions of MICs from 2019. Clinical isolates from milk.

Antibiotic	Resistance (%)				Distribution (%) of MICs (mg/L)										
	2016 n=36	2017 n=34	2018 n=52	2019 n=34	≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	NR[b]	NR[b]	NR[b]	NR[b]							5.9	5.9	88.2		
Cefotaxime	0	0	0	0		100									
Colistin	3[c]	9[d]	0	0				94.1	5.9						
Enrofloxacin	14	3	8	6	94.1	2.9		2.9							
Gentamicin	0	0	0	0					100						
Neomycin	0	0	0	0						100					
Nitrofurantoin	NR[b]	NR[b]	NR[b]	NR[b]								2.9	47.1	35.3	14.7
Streptomycin	3	3	13	18							79.4	2.9	8.8	8.8	
Tetracycline	6	12	8	3					91.2	5.9			2.9		
Trim-Sulph.[a]	6	0	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]One isolate with MIC 16 mg/L was negative for *mcr-1* and *mcr-2* genes with PCR; [d]Two isolates with MIC 16 mg/L were negative for *mcr-1, mcr-2, mcr-3, mcr-4* and *mcr-5* genes with PCR. One isolate with MIC 4 mg/L was not available for further investigations.

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 2013-2019 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 4.21.

Antibiotic resistance was generally rare among isolates of *Pasteurella* spp. (Table 4.21), but beta-lactamase producing *P. multocida* have been isolated every year since 2016. Penicillin is considered the first choice antibiotic for pneumonia in cattle in Sweden. Sampling and susceptibility testing are of importance for early detection of resistance, especially if therapeutic failure is seen.

TABLE 4.21. Resistance (%) in *Pasteurella* spp. from calves 2005-2019. Distribution of MICs from 2019. 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	2019 n=63	Distribution (%) of MICs (mg/L) ≤0.06	0.12	0.25	0.5	1	2	4	8	16	>16
Ampicillin	0	13	2	5	3				50.8	46.0			3.2		
Enrofloxacin	0[b]	0	0	0	0		100								
Florfenicol	0	0	0	0	2						95.2	3.2	1.6		
Penicillin	0	13	2	5	8		88.9	3.2		7.9					
Tetracycline	0	0	0	0	0					100					
Trim-Sulph.[a]	0[c]	0	1	0	0				96.8	3.2					

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphamethoxazole); [b]314 isolates tested; [c]31 isolates tested.

Farmed fish

Flavobacterium psycrophilum

Isolates of *Flavobacterium psycrophilum* are from clinical submissions of farmed fish. Data from 2015-2019 are compiled and presented as distributions of MICs in Table 4.22. Most isolates are from rainbow trout. Smith et al. (2016) have proposed epidemiological cut-offs for florfenicol, oxolinic acid and oxytetracycline for *F. psycrophilum*. These are used in the distributions in Table 4.22. Resistance to oxolinic acid and oxytetracycline was high in this material whereas no resistance to florfenicol was detected.

In Figure 4.7 resistance to tetracycline and quinolones (nalidixic acid or oxolinic acid) in *F. psycrophilum* 2005-2019 is shown. A three-year moving average is used. There is a marked increase in resistance to these antibiotics over the years, despite a limited use up until recently (Svarm 2011, Svarm 2019). 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 2005-2019 with a three-year moving average. The number of isolates each year varies (n=8-31, 2019 n=8).

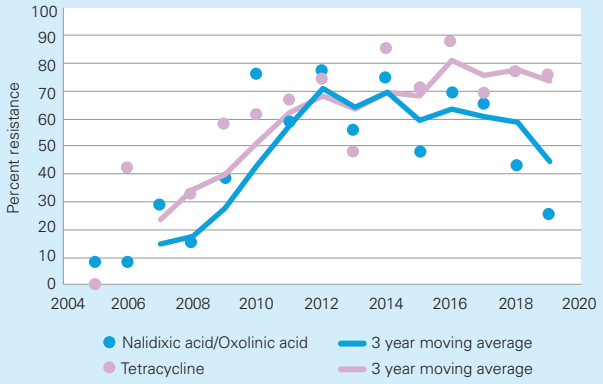


TABLE 4.22. Distributions of MICs and resistance (%) in *Flavobacterium psycrophilum* from farmed fish 2015-2019. The number of isolates each year varies (n=8-31, 2019 n=8).

Antibiotic	Resistance (%) 2015-2019 n=102	Distribution (%) of MICs (mg/L) ≤0.008	0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	>8
Florfenicol	0					4.9	11.8	46.1	32.4	4.9			
Oxolinic acid	53	1.0			4.9	33.3	7.8	1.0	2.0	50.0			
Oxytetracycline	76			1.0	21.6	2.0	2.0	2.0	12.8	24.5	30.4	3.9	

SvarmPat – monitoring of resistance in pathogens from farm animals

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

The purpose of SvarmPat is to reduce emergence and spread of antibiotic resistance in pathogenic bacteria from farm animals. This is achieved by monitoring and documenting antibiotic resistance, by activities that increase knowledge of antibiotic resistance and prudent use of antibiotics, and by communication of knowledge to practitioners and farmers.

Selected studies within SvarmPat in 2019

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

Milk samples from dairy cows

Screening for MRSA in milk samples from dairy cows started in 2010 and is still ongoing. Selected isolates of beta-lactamase producing *Staphylococcus aureus* from routine submissions to SVA are investigated for methicillin resistance. During 2010-2019, about 1300 isolates were tested and MRSA was confirmed in 9 isolates. In addition, about 500 isolates of *S. aureus* without beta-lactamase production was tested in 2013, but MRSA was not detected.

Continuous monitoring of bacterial findings in clinical mastitis in dairy cows started in 2013. Randomly collected milk samples from dairy cows with clinical mastitis are cultured and isolated bacteria are susceptibility tested. Most bacteria causing mastitis in dairy cows in Sweden are sensitive to penicillin and penicillin is the drug of choice if antibiotic treatment is needed. *Staphylococcus aureus* was the most common bacterial species followed by *Streptococcus dysgalactiae*, *Escherichia coli* and *Streptococcus uberis*. Penicillin resistance in *S. aureus* from cows with clinical mastitis in this monitoring is very uncommon.

Respiratory tract samples from calves

One of the most common infection in calves is pneumonia caused by *Pasteurella multocida*, for which penicillin is considered the first-choice antibiotic in Sweden. However, since beta-lactamase producing *P. multocida* isolates have been isolated every year since 2016, sampling and susceptibility testing is important, especially if therapeutic failure is seen in a herd. A project conducted within SvarmPat in 2019 showed that sampling from the nasal cavity of live calves is an adequate method for this purpose.

Respiratory tract samples from pigs

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

Enteric samples from pigs

Brachyspira hyodysenteriae

Swine dysentery is a severe disease in pigs, with a few cases each year in Sweden. The resistance situation in the causative agent *B. hyodysenteriae* is favourable compared to other countries, but clinical resistance to tiamulin in *B. hyodysenteriae* was detected for the first time 2016 in an outbreak in several herds. Within SvarmPat whole genome sequencing was used to confirm that the outbreak was caused by the same clone. In 2019 no tiamulin resistant isolates (MIC >2 mg/L) were detected.

Escherichia coli

Resistance to ampicillin and trimethoprim-sulphamethoxazole in *Escherichia coli* from pigs with diarrhoea has been increasing over the years and multiresistance has varied between 20 and 42%. This emphasises the importance of susceptibility testing in herds with diarrhoea problems.

A study with randomised sampling that was run in 2016-2017 showed no clear difference in resistance between the isolates from the project and from routine clinical submissions. This indicates that the rather high resistance in isolates from routine submissions is true and cannot be explained by sampling bias towards herds with therapeutic failure.

Antibiotics in farmed fish

Within SvarmPat, a questionnaire was distributed to prescribing veterinarians and to fish farmers that had carried out treatments during 2019. The results show that the main indication for treatment is infection with *Flavobacterium psychrophilum* and that treatment with florfenicol in these cases have resulted in reduced morbidity and mortality. Susceptibility testing of isolates from outbreaks have shown that all isolates are sensitive to florfenicol.

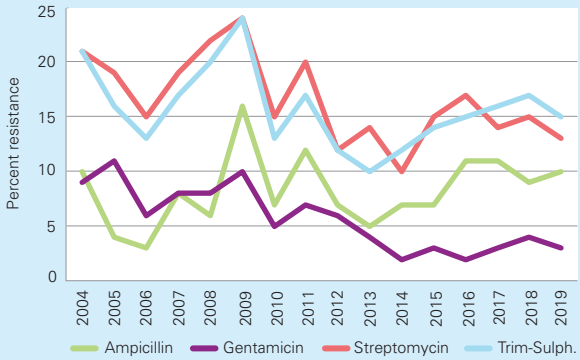
Horses

Escherichia coli

Isolates of *Escherichia coli* are from clinical submissions of samples from the genital tract of mares. As in previous years, resistance to trimethoprim-sulphamethoxazole and streptomycin were the most common traits in 2019 (Table 4.23 and Figure 4.8). The resistance to trimethoprim-sulphamethoxazole have gradually increased from 10 to 17% between 2013 and 2018, but in 2019 the figure was 15% (Table 4.23 and 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.

Eighty-two percent (199/244) of the isolates were susceptible to all the tested antibiotics. Multiresistance was detected in 9% (21/244) of the isolates, which is comparable to the figure from 2016 (10%) but more than in 2017-2018 (7 and 6% respectively) (see previous Swedres-Svarm reports). Eleven (52%) of the twenty-one multiresistant isolates were resistant to three antibiotics; four (19%) to four; five (24%) to five and one (5%) to six antibiotics. For comparison of resistance in *E. coli* from other animal species see Comparison of antibiotic resistance in *E. coli* and *Staphylococcus* spp, Table 4.34. The most common phenotype was resistance to ampicillin, streptomycin and trimethoprim-sulphamethoxazole, representing 52% (11/21) of all the multiresistant isolates. This phenotype was also the most common in *E. coli* isolated from dogs (81%). Three of the four isolates resistant to four antibiotics had the common phenotype and were in addition resistant to tetracycline (3/4) or gentamicin (1/4). The five isolates resistant to five antibiotics had the common phenotype but otherwise there was no specific type. The isolate resistant to six antibiotics had the common phenotype, and resistance to cefotaxime, enrofloxacin and tetracycline.

FIGURE 4.8. Resistance (%) in clinical isolates of *Escherichia coli* from horses 2004-2019. Isolates are from clinical sampling of the genital tract of mares. The number of isolates each year varies (n=124-324, 2019 n=244).



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

None of the isolates were resistant to colistin (MIC > 2mg/L).

Streptococcus equi ssp. *zooepidemicus*

Isolates of *Streptococcus equi* ssp. *zooepidemicus* are from clinical submissions, mainly from the respiratory tract (69%) and abcesses (15%). The material from 2019 included one isolate with high MIC to penicillin (>1). As the isolate was not available for further analyses, the result was 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 2015-2019 and for trimethoprim-sulphamethox-

TABLE 4.23. Distributions of MICs and resistance (%) in *Escherichia coli* from horses, 2019. Clinical isolates from the genital tract of mares.

Antibiotic	Resistance (%) 2019 n=244	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	10					75.0	14.3	0.8	0.4	9.4		
Cefotaxime	<1		99.2				0.8					
Colistin	0				91.8	8.2						
Enrofloxacin	<1	99.2		0.4	0.4							
Gentamicin	3					97.1	0.8	0.4	0.4	1.2		
Neomycin	2						98.4			1.6		
Nitrofurantoin	0							40.6	57.8	1.2	0.4	
Streptomycin	13							84.0	3.3	2.0	3.7	7.0
Tetracycline	7					92.2	1.2		0.4	6.1		
Trim-Sulph.[a]	15			84.8	0.4			14.8				

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

azole 5-18% in 2015-2019 (Table 4.24 and previous Swedres-Svarm reports).

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

Staphylococcus aureus

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

The proportions of resistance to gentamicin, penicillin, tetracycline and trimethoprim-sulphamethoxazole have differed somewhat over the years and therefore trends are difficult to estimate (Figure 4.9). Resistance to penicillin due to pencillinase production has been the most common trait, although the figures have declined from 36% in 2008-2009 to 24% in 2019 (Figure 4.9 and Table 4.25). For comparison of pencillinase production in staphylococci isolated from other animal species, see Comparison of antibiotic resistance in *E. coli* and *Staphylococcus* spp, Table 4.35.

Fifty-nine percent (61/104) of the isolates were susceptible to all the tested antibiotics. Multiresistance was detected in five (5%) of the isolates. Three of the multiresistant isolates were resistant to three antibiotics, one to four and one to five antibiotics. This is about the same figure as in previous years, except for 2018, when no multiresitance was detected among the tested isolates (see previous Swedres-Svarm reports). For comparison of resistance in staphylococci isolated from other animal species see Comparison of antibiotic resistance in *E. coli* and *Staphylococcus* spp., see Tables 4.34-35.

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

FIGURE 4.9. Resistance (%) in clinical isolates of *Staphylococcus aureus* 2008-2019 from skin of horses. The number of isolates each year varies (n=75-145, 2019 n=104).

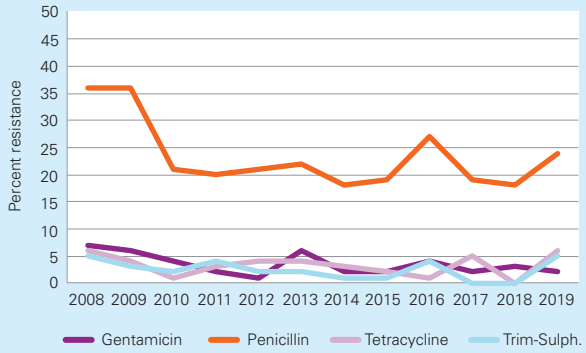


TABLE 4.24. Distribution of MICs and resistance (%) in *Streptococcus equi* ssp. *zooepidemicus* isolated from horses, 2019. Clinical isolates mainly from the respiratory tract.

Antibiotic	Resistance (%) 2019 n=52	Distribution (%) of MICs (mg/L) <0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Cephalotin	0						98.1	1.9						
Clindamycin	6					94.2	5.8							
Erythromycin	2					98.1	1.9							
Gentamicin	NR[b]							1.9	3.8	94.2				
Nitrofurantoin	0										100			
Penicillin	0	100												
Tetracycline	NR[b]					1.9	11.5	40.4	36.5	9.6				
Trim-Sulph.[a]	10				73.1	17.3	5.8	1.9		1.9				

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

TABLE 4.25. Distribution of MICs and resistance (%) in *Staphylococcus aureus* isolated from horses, 2019. Clinical isolates from the skin.

Antibiotic	Resistance (%) 2019 n=104	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Cefoxitin	0			1.0	1.0	22.1	76.0					
Cephalotin	6				94.2	4.8	1.0					
Clindamycin	4			96.2	2.9		1.0					
Enrofloxacin	5		81.7	13.5	2.9	1.9						
Erythromycin	3			86.5	10.6	1.0	1.9					
Fusidic acid	5			95.2	2.9		1.9					
Gentamicin	2				87.5	10.6		1.9				
Nitrofurantoin	3								92.3	4.8	2.9	
Penicillin[a]	24											
Tetracycline	6		66.3	27.9		3.8		1.9				
Trim-Sulph.[b]	5		82.7	12.5	1.0	3.8						

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

Dogs

Escherichia coli

Isolates of *Escherichia coli* are from clinical submissions of urine, submitted either as urine or cultures from dip-slides or other agar plates. As in previous years, resistance to ampicillin was the most common trait in 2019 (Table 4.26 and Figure 4.10). The proportion of resistance in the tested isolates has differed somewhat throughout the years and trends are difficult to estimate (Figure 4.10).

Seventy-seven percent (835/1082) of the isolates were susceptible to all the tested antibiotics. The proportion of multiresistance in the isolates was 8% (86/1082), and comparable to 2015-2018 (6-9%) (see previous Swedres-Svarm reports). Fifty percent (43/86) of the multiresistant isolates were resistant to three antibiotics; 36% (31/86) to four; 9% (8/86) to five and 5% (4/86) to six antibiotics. For comparison of resistance in *E. coli* from other animal species see Comparison of antibiotic resistance in *E. coli* and *Staphylococcus* spp, Table 4.34. The most common phenotype, resistance to ampicillin, streptomycin and trimethoprim-sulphamethoxazole, was detected in 81% (70/86) of the multiresistant isolates. The same phenotype was also the most common in *E. coli* isolated from horses (52%). Of the forty-three isolates resistant to four or more antibiotics, thirty-nine (91%) were of the common phenotype, and commonly also resistant to tetracycline (31/43, 72%) and/or enrofloxacin (12/43, 28%).

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

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

Staphylococcus pseudintermedius

In Swedres-Svarm before 2017 resistance from isolates of *Staphylococcus pseudintermedius* from clinical submissions of samples from skin lesions were reported (see previous Swedres-Svarm reports). From 2017 and onwards figures of resistance from three different sample collections (i.e. skin lesions (S1),

FIGURE 4.10. Resistance (%) in clinical isolates of *Escherichia coli* from dog urine 2005-2019. The number of isolates each year varies (n=304-1162, 2019 n=1082).

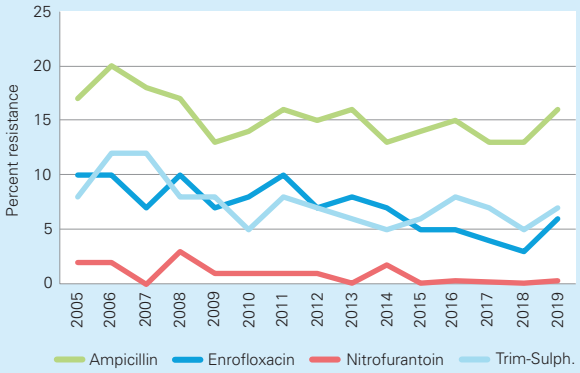


TABLE 4.26. Distribution of MICs and resistance (%) in *Escherichia coli* from dogs, 2019. Clinical isolates from urine.

Antibiotic	Resistance (%) 2019 n=1082	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	16					67.7	15.5	1.0	0.4	15.3		
Cefotaxime	<1		99.3	0.2		0.1	0.5					
Colistin	<1				90.6	9.3			0.1			
Enrofloxacin	6	94.2	1.2	2.7	0.8	0.1		1.0				
Gentamicin	2					98.3	0.9	0.4	0.1	0.3		
Neomycin	<1						99.2	0.4	0.1	0.2	0.2	
Nitrofurantoin	<1							28.1	69.2	1.8	0.6	0.3
Streptomycin	11							84.8	4.2	2.5	2.3	6.3
Tetracycline	5					93.3	1.4			5.4		
Trim-Sulph.[a]	7			91.9	1.0	0.1		7.0				

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

wounds (S2) and the external ear canal (S3)) have been compared (Table 4.27 and previous Swedres-Svarm reports).

Resistance to penicillin due to pencillinase production dominates for all sample collections (71-77%, Table 4.27), but has declined since 2009 (90%). For comparison of pencillinase production in staphylococci isolated from other animal species, see Comparison of antibiotic resistance in *E. coli* and *Staphylococcus* spp, Table 4.35. Resistance to clindamycin, fusidic acid and tetracycline has differed somewhat over the years but, compared to penicillin, remains at lower levels (Table 4.27 and Figure 4.11).

Seventeen percent (156/932) of the isolates in sample collection S1 (skin), 20% (102/507) in S2 (wounds) and 21% (172/827) in S3 (ear) were susceptible to all the tested antibiotics. The figures are low compared to other staphylococci isolated from animals. The proportion of multiresistance for the S1 isolates was 24% (121/507) in 2019. For both the sample collections S2 and S3, multiresistance was detected in 23% (213/932 and 191/827 respectively) of the isolates. For comparison of resistance in staphylococci isolated from other animal species see Comparison of antibiotic resistance in *E. coli* and *Staphylococcus* spp, Table 4.35.

Forty-eight percent (58/121) of the multiresistant S1-isolates were resistant to three antibiotics; 32% (39/121) to four; 16% (19/121) to five; 2% (3/121) to six; <1% (1/121) to seven and <1% (1/121) to eight antibiotics. Twenty percent (24/121) of the multiresistant S1-isolates were resistant to five or more antibiotics, which is comparable to figures in 2017 and 2018 (21% and 22% respectively) but less than in 2016 when one-third of the isolates were resistant to five or more antibiotics.

Resistance to penicillin, clindamycin and erythromycin was the most common phenotype in all sample collections, for the multiresistant S1-isolates, 47% (73/121), S2 62% (131/213) and S3 49% (93/191). Of the multiresistant S1-isolates resistant to four or more antibiotics, 83% (52/63) had the common phenotype combined with resistance to fusidic acid 41% (26/63), tetracycline 33% (21/63) and/or trimethoprim/sulphamethoxazole 32% (20/63).

Three of the S1 isolates, two of the S2 isolates and one of the S3 isolates were resistant to oxacillin (MIC >0.5 mg/L). All isolates were tested with PCR for detection of the *mecA* and *mecC* genes and all six were found to be MRSP. For more information on MRSP isolated from dogs in Sweden, see Notifiable diseases, Methicillin-resistant *Staphylococcus pseudintermedius* (MRSP).

FIGURE 4.11. Resistance (%) in *Staphylococcus pseudintermedius* from dogs, 2004-2019. Clinical isolates from skin (S1). The number of isolates each year varies (n=89-566, 2019 n=507).

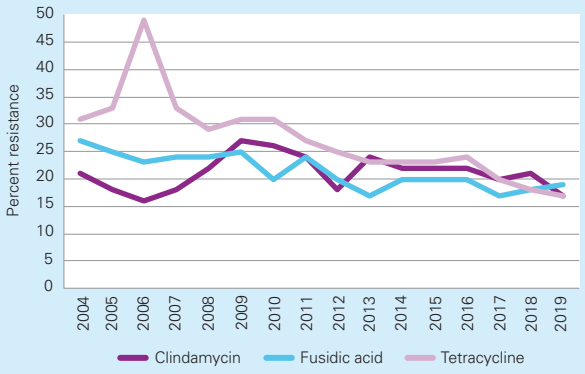


TABLE 4.27. Distribution of MICs and resistance (%) in *Staphylococcus pseudintermedius* from dogs 2019. Clinical isolates from skin (S1), wounds (S2) and external ear canals (S3).

Antibiotic	Resistance (%) 2019 n=827 S3	2019 n=932 S2	2019 n=507 S1	Distribution (%) of MICs (mg/L), isolates from skin (S1) ≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Cephalothin	2	3	3				97.4	2.4		0.2				
Cefoxitin[a]					70.6	27.0	1.2	1.0	0.2					
Clindamycin	13	16	17			83.0	2.0	0.6	14.4					
Enrofloxacin	1	1	2		91.5	6.9	0.8	0.8						
Erythromycin	16	19	19			80.9	1.6	0.2	17.4					
Fusidic acid	22	15	19			79.1	2.2	0.6	18.1					
Gentamicin	3	3	6				91.1	3.4	1.8	3.7				
Nitrofurantoin	<1	<1	<1								98.6	1.0	0.4	
Oxacillin	<1	<1	<1		97.6	1.8	0.2	0.4						
Penicillin[b]	71	77	72											
Tetracycline	20	18	17		78.7	3.7	0.6	0.2	0.2	16.6				
Trim-Sulph.[c]	14	14	15		50.9	33.9	10.6	1.8		2.8				

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

Staphylococcus schleiferi

Isolates of *Staphylococcus schleiferi* are from clinical submissions of samples from various locations, but mainly from the external ear canal (66%), skin (20%) or wounds (10%).

The proportion of resistance in isolates of *S. schleiferi* (Table 4.28) was lower for most antibiotics compared to isolates of the more common staphylococci isolated from dogs, *S. pseudintermedius* (Table 4.27). Three percent of the tested *S. schleiferi* isolates were penicillinase producing which is comparable to figures in 2014-2018 (<1-4%) (see previous Swedres-Svarm reports). The proportion of isolates with penicillinase production was low also compared to other staphylococci from animals, see Comparison of antibiotic resistance in *E. coli* and *Staphylococcus* spp, Table 4.35. Between 2016 and 2019 the proportion of resistance to enrofloxacin has declined from 20% to 3% and to fusidic acid from 14% to 8%, while for the other tested antibiotics there is no major difference (Table 4.28 and previous Swedres-Svarm reports).

Seventy-six percent (177/233) of the *S. schleiferi* isolates were susceptible to all the tested antibiotics. Multiresistance was detected in 1% (3/233), which is about the same as in 2017 and 2018 (2%). The three multiresistant *S. schleiferi* isolates were resistant to just three of the tested antibiotics. No specific phenotype was noticed. For comparison of resistance in staphylococci isolated from other animal species see Comparison of antibiotic resistance in *E. coli* and *Staphylococcus* spp.

Pseudomonas aeruginosa

Isolates of *Pseudomonas aeruginosa* are from clinical submissions of samples from the external ear canal. The bacterium is inherently resistant to trimethoprim-sulphonamides, tetracyclines and aminopenicillins (including combinations with clavulanic acid).

The isolates of *P. aeruginosa* were 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 2019, 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 2019 and the figures for gentamicin have stabilised to about 1-2% over the recent years (see Table 4.29 and previous Swedres-Svarm reports). One of the isolates was resistant to all three antibiotics, and one isolate was resistant to both gentamicin and enrofloxacin and one to colistin and enrofloxacin.

TABLE 4.28. Distribution of MICs and resistance (%) in *Staphylococcus schleiferi* from dogs, 2019. Clinical isolates from various locations.

Antibiotic	Resistance (%) 2019 n=233	Distribution (%) of MICs (mg/L)										
		≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Cephalothin	2				97.9	2.1						
Cefoxitin[a]			33.0	63.5	2.6	0.9						
Clindamycin	4			96.1	1.7	0.4	1.7					
Enrofloxacin	5		85.0	10.3	2.6	2.1						
Erythromycin	3			97.4	0.4	0.4	1.7					
Fusidic acid	8			82.0	10.3	5.6	2.1					
Gentamicin	<1				97.4	2.1	0.4					
Nitrofurantoin	<1								97.4	2.1	0.4	
Oxacillin	0		98.7	1.3								
Penicillin[b]	3											
Tetracycline	3		91.4	5.2	0.9	0.4	0.4	1.7				
Trim-Sulph.[c]	3		88.4	8.6	2.6			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 4.29. Distribution of MICs and resistance (%) in *Pseudomonas aeruginosa* from dogs, 2019. Clinical isolates from the external ear canal.

Antibiotic	Resistance (%) 2019 n=349	Distribution (%) of MICs (mg/L)								
		≤0.12	0.25	0.5	1	2	4	8	16	32
Enrofloxacin	8	2.9	5.7	19.8	45.3	18.3	2.6	5.4		
Colistin[a]	<1				76.8	14.6	7.7	0.6	0.3	
Gentamicin	<1					87.1	10.9	1.1	0.9	

[a]Colistin is equivalent to polymyxin B.

Pasteurella canis

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

The most commonly detected *Pasteurella* sp. in the material was *P. canis* (n=263).

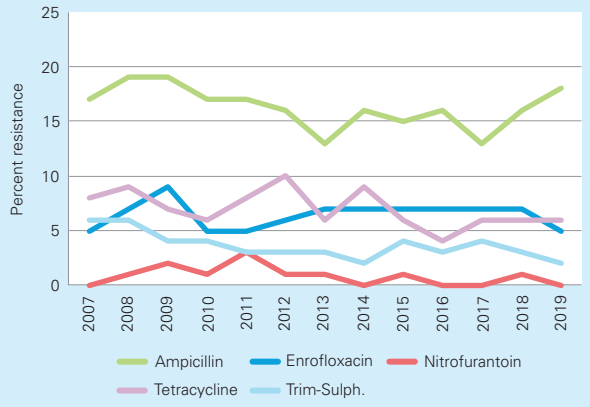
In 2019 the design of the test panel was changed and therefore only the isolates tested with one panel are presented (n=157). The *P. canis* isolates were susceptible to all the tested antibiotics, with the exception of three isolates resistant to enrofloxacin (Table 4.30).

TABLE 4.30. Distribution of MICs and resistance (%) in *Pasteurella canis* from dogs, 2019. Clinical isolates from various locations.

Antibiotic	Resistance (%) 2019 n=157	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	32
Ampicillin	0				100					
Enrofloxacin	2	98.1		1.3	0.6					
Gentamicin	0					100				
Penicillin	0	100								
Tetracycline	0				100					
Trim-Sulph.[a]	0			100						

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

FIGURE 4.12. Resistance (%) in clinical isolates of *Escherichia coli* from urine of cats, 2007-2019. The number of isolates each year varies (n=131-545, 2019 n=495).



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 4.26), resistance to ampicillin was the most common trait in 2019 (Table 4.31 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 4.23 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-five percent (369/495) of the *E. coli* isolates were susceptible to all the tested antibiotics. Multiresistance was detected in 3% (14/495) of the isolates, and comparable to figures between 2010 and 2018 (2-5%) (see previous Swedres-Svarm reports). Twelve of the isolates were resistant to three

TABLE 4.31. Distribution of MICs and resistance (%) in *Escherichia coli* isolated from cats, 2019. Clinical isolates from urine.

Antibiotic	Resistance (%) 2019 n=495	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	18					72.9	8.9	0.6	0.6	17.0		
Cefotaxime	<1		99.4	0.2			0.4					
Colistin	<1				92.9	6.9			0.2			
Enrofloxacin	5	94.9	1.8	2.8	0.4							
Gentamicin	1					98.8	0.4	0.4		0.4		
Neomycin	<1						99.4	0.4	0.2			
Nitrofurantoin	<1							31.1	66.1	1.4	1.0	0.4
Streptomycin	5							91.1	3.8	1.4	2.4	1.2
Tetracycline	6					92.5	1.0	0.4	0.8	5.3		
Trim-Sulph.[a]	2			97.0	1.4	0.4	0.2	1.0				

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

antibiotics and two to four. For comparison of resistance in *E. coli* from other animal species see Comparison of antibiotic resistance in *E. coli* and *Staphylococcus* spp, Table 4.34.

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

One isolate was resistant to colistin (MIC >2mg/L). The isolate was available for PCR detection of the *mcr-1* to *mcr-5* genes and was negative.

Staphylococcus felis

Isolates of *Staphylococcus felis* are from clinical submissions of samples from various locations, but mainly the external ear canal (39%), abscesses and wounds (28%), and urine (20%).

The proportion of resistance to the tested antibiotics in isolates of *S. felis* (Table 4.32) are less compared to *S. pseudintermedius* in dogs (Table 4.27). For example, resistance to penicillin due to penicillinase production was 19% in *S. felis*, but 70-77% in *S. pseudintermedius*. Seventy-one percent (221/312) of the *S. felis* isolates were susceptible to all the tested antibiotics. Multiresistance was detected in 4% (12/312) of the isolates. This figure is slightly lower than in 2018 (7%), but about the same as in 2015-2017 (4-5%). For comparison of resistance in staphylococci isolated from other animal species, see Comparison of antibiotic resistance in *E. coli* and *Staphylococcus* spp, Table 4.35.

Pasteurella multocida

Isolates of *Pasteurella* spp. are from clinical submissions of samples from various locations, but mainly from wounds or skin lesions (37%), abscesses (24%) and the external ear canal (21%).

Pasteurella multocida was the most common *Pasteurella* sp. isolated in samples from cats. In 2019 the design of the test panel was changed and therefore only the isolates tested with one panel are presented. The total number of isolated *P. multocida* was 356.

The proportion of resistance to antibiotics was low in the tested isolates (Table 4.33).

TABLE 4.32. Distribution of MICs and resistance (%) in *Staphylococcus felis* from cats, 2019. Clinical isolates from various locations.

Antibiotic	Resistance (%) 2019 n=312	Distribution (%) of MICs (mg/L)										
		≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Cephalothin	3				97.4	2.6						
Cefoxitin[a]			91.0	5.4		2.2	1.3					
Clindamycin	4			95.8	2.2	0.3	1.6					
Enrofloxacin	1		93.6	5.4		1.0						
Erythromycin	11			89.4	6.1		4.5					
Fusidic acid	2			95.8	2.2	0.6	1.3					
Gentamicin	<1				95.8	3.5	0.6					
Nitrofurantoin	0								96.8	3.2		
Oxacillin	0		98.4	1.6								
Penicillin[b]	19											
Tetracycline	3		91.3	5.4	0.6	1.0		1.6				
Trim-Sulph.[c]	<1		92.6	6.7	0.3	0.3						

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

TABLE 4.33. Distribution of MICs and resistance (%) in *Pasteurella multocida* from cats 2019. Clinical isolates from various locations.

Antibiotic	Resistance (%) 2019 n=216	Distribution (%) of MICs (mg/L)								
		≤0.12	0.25	0.5	1	2	4	8	16	32
Ampicillin	0				100					
Enrofloxacin	0	99.5	0.5							
Gentamicin	<1					54.2	40.7	4.2		0.9
Penicillin	0	91.2	6.9	1.9						
Tetracycline	0				100					
Trim-Sulph.[a]	4			93.5	1.4	0.9	0.5	3.7		

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

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

In order to describe the situation regarding antibiotic resistance in different animal species the occurrence of resistance in *E. coli* and different *Staphylococcus* spp. was compared. The occurrence of resistance was assessed as proportion of tested isolates that are susceptible to all tested substances and resistant to one or several substances respectively (Table 4.34 and 4.35). For *Staphylococcus* spp. occurrence of penicillinase production was also compared. All the tested isolates are from clinical submission. For details, see individual reports of animal and bacterial species in earlier sections.

TABLE 4.34. Resistance (%) and multiresistance (%) in *Escherichia coli* isolated from different animal species tested with a fixed panel of 10 antibiotics (see tables 4.12, 4.17, 4.23, 4.26 and 4.31). Isolates from clinical submissions, 2019.

Origin	Multiresistance (%)	Resistance (%) to 0-6 antibiotics							
		0	1	2	3	4	5	6	>6
Cats (urine)	3	75	16	7	2	<1			
Calves (faeces)	41	17	20	23	18	20	3		
Dogs (urine)	8	77	11	4	4	3	<1	<1	
Horses (genital tract)	9	82	5	5	5	2	2	<1	
Pigs (faeces)	33	32	17	17	19	7	8		

TABLE 4.35. Resistance (%), multiresistance (%) and penicillinase production (%) in different *Staphyloccus* spp. isolated from different animal species tested with a fixed panel of 11 antibiotics (see tables 4.25, 4.27, 4.28 and 4.32). Isolates from clinical submissions, 2019.

Staphyloccus spp. and origin	Multiresistance (%)	pcas[a] (%)	Resistance (%) to 0-8 antibiotics									
			0	1	2	3	4	5	6	7	8	>8
S. aureus – horses (skin)	5	24	59	29	8	3	1	1				
S. felis – cats (various)	4	19	71	21	5	3	<1	<1				
S. pseudintermedius - dogs (skin)	24	74	20	34	22	11	8	4	<1	<1	<1	
S. schleiferi – dogs (various)	1	3	76	18	4	1						

[a]Pencillinase production.

Indicator bacteria from animals

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

In 2019, indicator bacteria from fattening pigs were studied. Samples of intestinal contents were collected at slaughter and cultured for *E. coli*. The samples were also screened for *E. coli* resistant to ESCs by selective culture on media supplemented with cefotaxime. For details on methodology see Material and methods, resistance in bacteria from animals.

Escherichia coli

Pigs

Escherichia coli was isolated from 174 (99%) of 176 cultured caecal samples from fattening pigs. The majority of the isolates (71%) was susceptible to all antibiotics tested (Table 4.36). Resistance to ampicillin (19%), sulphonamides (18%), trimethoprim (15%) and tetracycline (13%) 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 of these had resistance to sulphonamides in their phenotype. Furthermore, all but one had resistance to ampicillin and all but three had resistance to trimethoprim in their phenotype.

Levels of resistance in *E. coli* from fattening pigs are low in an international perspective. The proportion of isolates susceptible to all antibiotics tested has been stable in the latest years (68% in 2015, 71% in 2017 and 71% in 2019). Looking at specific antibiotics, the proportion of resistance to some substances have been stable over the years studied whereas resistance to others have increased during the last years (Figure 4.13). More precisely, resistance to ampicillin, sulphonamides and trimethoprim in *E. coli* from fattening pigs increased considerably from 2008 to 2015. Since then, the proportion of isolates resistant to these substances has leveled off or even decreased somewhat. The differences are however not statistically significant. The reason(s) for these changes is not known.

None of the isolates were resistant to cefotaxime or ceftazidime. However, using selective culture, ESC resistant *E. coli* was isolated from 39 (13%) of 300 samples. In eight isolates (3%), transferable genes for resistance to ESC were found. Four had $bla_{\text{CTX-M-14}}$, three $bla_{\text{CTX-M-15}}$, and one $bla_{\text{CTX-M-55}}$. The remaining thirtyone isolates had an AmpC phenotype and genome sequencing of these isolates revealed mutations causing hyperproduction of AmpC beta-lactamases. For more details and comments see section Antibiotic resistance in animals, Notifiable disease.

FIGURE 4.13. Resistance (%) in *Escherichia coli* from fattening pigs 2000-2019. The number of isolates each year varies (n=140-390, 2019 n=174).

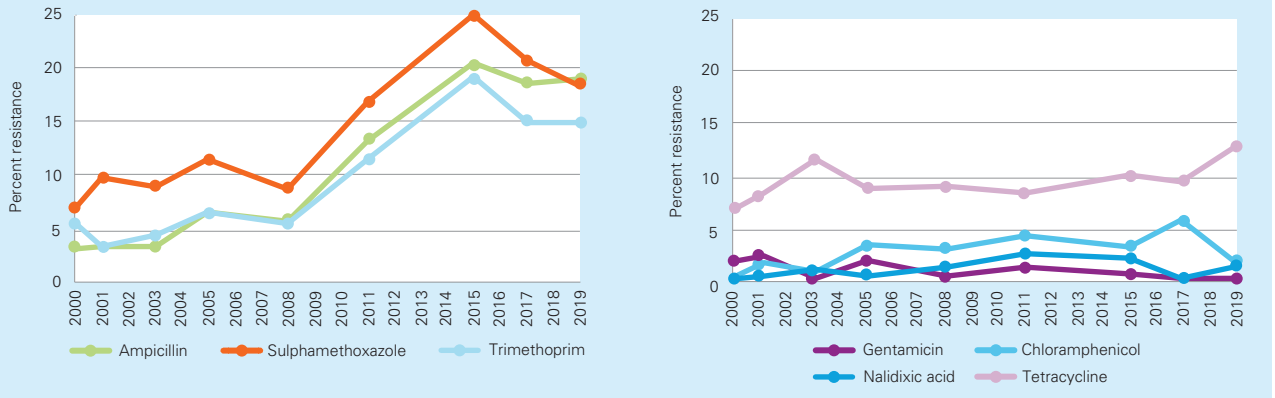


TABLE 4.36. Resistance (%) and multiresistance (%) in indicator *Escherichia coli* from fattening pigs, 2019. Data on indicator *E. coli* from previous Svarm-reports are given for comparison.

Antibiotic	ECOFF (mg/L)	Resistance (%)									
		Broilers	Broiler meat	Cattle	Laying hens	Pigs	Pig meat	Sheep	Turkeys	Dogs	Horses
		2018	2012	2015	2012	2019	2011	2006-09	2018	2012	2010-11
		n=178	n=92	n=101	n=61	n=174	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	2	0	0	2	0	<1
Ciprofloxacin	>0.06	7	4	0	5	1	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	>8	7	4	0	5	2	0	<1	3	0	<1
Sulphamethoxazole	>64	15	16	2	8	18	10	7	2	4	15
Tetracycline	>8	13	14	1	13	13	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	6	10	8	18	8	2
Resistant to 2		6	7	2	7	12	5	3	2	7	12
Resistant to 3		7	3		7	6	15	<1			2
Resistant to >3		4	5			5				<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 fattening pigs (n=174), 2019.

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	19							11.5	39.7	29.3	0.6				19.0				
Azithromycin	0								5.2	28.2	60.3	6.3							
Cefotaxime	0					100													
Ceftazidime	0						100												
Chloramphenicol	2										97.1	1.1	1.7						
Ciprofloxacin	1	93.7	4.6	0.6		1.1													
Colistin	0							100											
Gentamicin	0						87.9	11.5	0.6										
Meropenem	0		100																
Nalidixic acid	2									97.7	0.6	0.6		0.6	0.6				
Sulphamethoxazole	18										25.9	43.1	12.1	0.6					18.4
Tetracycline	13								85.6	1.1	0.6			6.3	6.3				
Tigecycline	0					100													
Trimethoprim	15					38.5	39.7	5.7	1.1					14.9					

Svarm – 20 years of monitoring of resistance in bacteria from animals

It is now 20 years since the Swedish veterinary antibiotic resistance monitoring programme (Svarm) was started at the National Veterinary Institute (SVA) following a Governmental assignment. This marks the start of the formal monitoring of sales of antibiotics and resistance in bacteria from animals in Sweden. The remit was to follow and analyse the development of antibiotic resistance in bacteria from animals and later including also bacteria from food. When the program was designed, the objectives set were to detect trends that might require interventions and to provide a basis for recommendations on therapy of animals as well as for evaluation of zoonotic risks related to AMR.

Results from Svarm are presented in yearly reports together with data on sales of antibiotics for animals. The latter provides important information for interpretation of results, but in the following the focus will be entirely on resistance. To give the most complete picture of the national situation, relevant data from other studies on antibiotic resistance at SVA are also included in the reports. From 2002, data from Svarm were presented together with the corresponding data from the human sector, and from 2012 in the fully integrated Swedres-Svarm report.

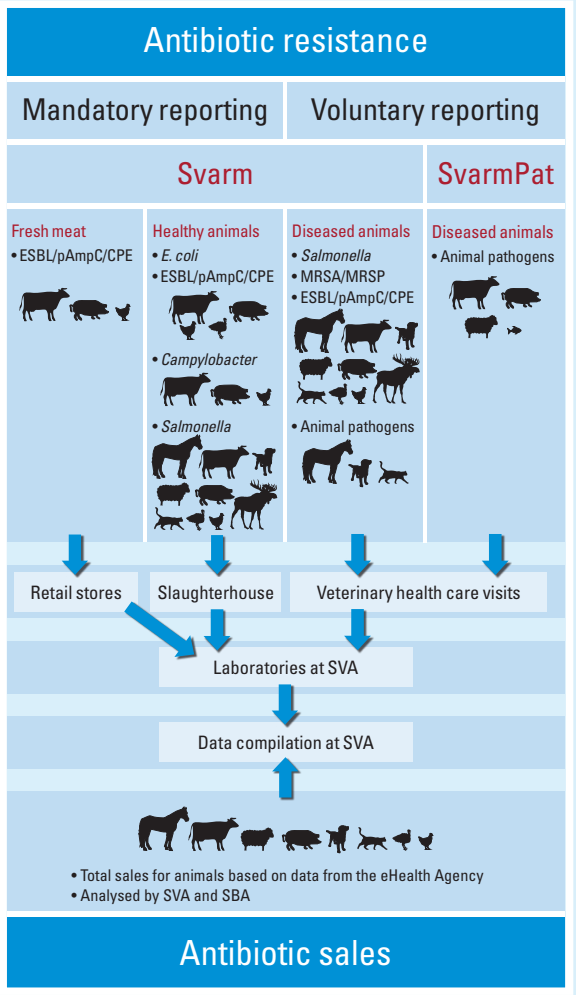
Scope and methodology – a moving target

The current scope of Svarm (figure) is basically the same as in 2000 when the programme was launched. Then, three types of bacteria were monitored: zoonotic bacteria (*Salmonella* and *Campylobacter*), animal pathogens, and indicator bacteria (*Escherichia coli* and *Enterococcus* spp.) from intestinal content of healthy pigs, cattle and broilers.

Data on zoonotic bacteria and indicators from Svarm have been reported to EFSA for inclusion in the EU summary report on antimicrobial resistance since this monitoring started in 2003. EU-monitoring was made mandatory in 2008 (2003/99/EC) and was gradually refined and harmonised with respect to scope, matrices, laboratory methodology and interpretative criteria by subsequent decisions in the following years (2007/407/EC, 2007/516/EC, and 2013/652/EC). Svarm has successively been adapted to these new provisions. The EU-monitoring is currently under revision and further adaptation of Svarm can be expected by 2021.

The programme has also been gradually extended to include data on isolates with resistance types that are notifiable in Sweden, i.e. methicillin resistant coagulase positive staphylococci (e.g. MRSA and MRSP) and $ESBL_{CARBA}$ (carbapenemase producing Enterobacteriaceae; not yet found in animals in Sweden), and on other isolates with resistance of specific importance. i.e. $ESBL_A$ or $ESBL_M$ (ESBL and plasmid mediated AmpC producing Enterobacteriacease). Several studies outside the basic scope of Svarm have also been performed within the framework of the programme. For example, screening of healthy animals for MRSA, MRSP, VRE (vancomycin resistant enterococci) and *E. coli* with $ESBL_A$ or $ESBL_M$. Other examples are studies on resistance in indicator bacteria from dogs, horses, sheep and wildlife and of *Salmonella* in reptiles.

To broaden the basis for data on antibiotic resistance in pathogenic bacteria from the major food producing animals, Svarm was complemented by the SvarmPat programme in 2005. For more information on this programme see In Focus SvarmPat - monitoring of resistance in pathogens from farm animals.



Matrices and isolates

Since the start of Svarm, data on susceptibility of about 70,000 bacterial isolates have been presented in the yearly reports. For an overview see Materials and methods, resistance in bacteria from animals, Tables 6.13-18. Isolates emanate from different sources including randomly selected healthy animals sampled at slaughter, clinical submissions and various research projects. The majority have been isolated and all have been confirmed at SVA.

Zoonotic bacteria

Any finding of *Salmonella* in animals is notifiable in Sweden and isolates from each incident is confirmed at SVA. *Campylobacter* from pigs and cattle are isolated from samples collected at slaughter and isolates from broilers are obtained from the Swedish Campylobacter programme.

Indicator bacteria

Indicator bacteria, *E. coli* and *Enterococcus* spp., are isolated from intestinal content of healthy animals sampled at slaughter within the framework of Svarm, or from faeces collected from live animals in other projects.

Pathogenic bacteria

Isolates of animal pathogens mostly emanate from routine bacteriological examinations at SVA but also from specific field studies. Extraction of historic data from the database at SVA made it possible to present data back to 1992 already at the start of Svarm in 2000.

Screening for specific resistance

Already from the start of Svarm, and at regular intervals thereafter, intestinal contents of healthy animal were screened for VRE. A screen for *E. coli* with $ESBL_A$ or $ESBL_M$ on the same matrices, and on fresh meat from retail, was introduced in 2008, seven years before it became mandatory in the EU-monitoring. As from 2015, screening for $ESBL_{CARBA}$ in the same matrices was introduced in accordance with recommendations for the EU-monitoring.

Susceptibility testing and interpretative criteria

In Svarm, antibiotic susceptibility has throughout been defined by determination of MICs using microdilution, in essence following the standards of CLSI (CLSI, 2018). The antibiotics and range of concentrations tested has changed over the years, and the mandatory part of the monitoring has successively been adapted to the provisions for the EU-monitoring. To further characterise resistance, molecular methods, such as PCR and genome sequencing, have increasingly been used in Svarm.

Interpretative criteria for susceptibility tests are continuously being revised in the light of new knowledge. This complicates the analysis of data over time, for example detection of trends which is an important aspect of resistance monitoring. From the start of Svarm, the principle of 'microbiological resistance' has been used to classify isolates with and without acquired resistance as sensitive and resistant, respectively. Initially interpretation of data in Svarm was partly based on distributions of MICs obtained in the programme, and partly also on clinical break-points available from CLSI. As from 2005, ECOFFs issued by EUCAST are normally used when available. Historical data from Svarm presented in the yearly reports are updated to account for revised ECOFFs.

More information on current methodology and interpretive criteria can be found in Material and methods, resistance in bacteria from animals.

Outcomes of Svarm

In the twenty years since Svarm started, levels of resistance in most bacteria have been stable at low or moderate levels, or even declined. There are however exceptions, for example, resistance to ampicillin and the combination trimethoprim-sulphamethoxazole has increased notably in *E. coli* from pigs. See Clinical isolates from animals for more information.

Several types of resistance, previously not observed in bacteria from animals in Sweden, have however been detected. In the early 2000s, VRE emerged among broilers due to spread of a single clone of *Enterococcus faecium*. Levels peaked in 2005 when VRE were found in about 40 percent of broilers at slaughter but thereafter declined to about 10 percent in 2015.

In 2006, MRSA was found in a dog and later in several other animal species. The same year MRSP was found in a dog and later in cats and horses. In the following years MRSP emerged as a problematic pathogen in dogs and 130 cases were confirmed in 2009. The number of notified cases has thereafter declined and stabilised at about 50 each year. For more information on MRSA and MRSP see Notifiable diseases.

One year later, 2007, *E. coli* with $ESBL_M$ was found in healthy broilers. Bacteria with $ESBL_A$ and $ESBL_M$ resistance have since then been isolated from several other animal species and on fresh meat. Occurrence in broilers is the most prominent, reaching a peak in 2011 when *E. coli* with $ESBL_A$ or $ESBL_M$ resistance was found in more than half of broilers at slaughter. Since then the occurrence has decreased significantly and in 2019 *E. coli* with $ESBL_A$ or $ESBL_M$ resistance was detected in only 3 out of 101 samples. ESBL resistance has become problematic in veterinary practice, although $ESBL_{CARBA}$ has hitherto not

been found in bacteria from animals. For more information on ESBL-resistance see Notifiable diseases.

Beta-lactamase producing *Pasteurella multocida* from cattle was first documented in 2003 and beta-lactamase producing *Mannheimia haemolytica* in 2010. From 2016 a small number of beta-lactamase producing *P. multocida* have been isolated every year.

Tiamulin resistance in *Brachyspira hyodysenteriae*, causing Swine dysentery, was detected 2016 in an outbreak in several pig herds. The outbreak was caused by a single clone. The outbreak was successfully contained and in 2019 no tiamulin resistant isolates were detected in the monitoring. For more information see In Focus SvarmPat – monitoring of resistance in pathogens from farm animals

In Svarm, isolates of *E. coli* phenotypically resistant to colistin are investigated for *mcr*-genes with molecular methods, and hitherto no genes conferring transmissible colistin resistance have been detected in such isolates. In 2018 multiresistant Enterobacteriacease carrying the *mcr-9* gene, that may confer reduced susceptibility to colistin, was detected in clinical isolates from horses, see Multiresistant ESBL-producing Enterobacteriaceae from horses for more information.

Impact of Svarm

To contain antibiotic resistance, monitoring is essential as data are needed to guide treatment, as a basis for actions and to assess the effectiveness of actions taken (WHO 2015). The information gathered in Svarm has been used in line with these statements. Data on susceptibility of pathogenic bacteria have formed a basis for the guidelines on antibiotic therapy of animals issued by the Swedish Veterinary Association and the Medical Products Agency in Sweden. Knowledge on antibiotic resistance gathered in Svarm has also been communicated to veterinarians, farmers, companion animal owners and other stakeholders in various ways and by different actors. Increased awareness of antibiotic resistance has likely improved compliance to prudent use of antibiotics. Especially the findings of MRSA, MRSP and ESBL were likely important for the stricter infection prevention and control (IPC) routines implemented in veterinary practice in recent years. Also, the findings of VRE and *E. coli* with ESBL resistance in broilers led to actions by the Swedish Poultry Meat Association to contain the spread.

Knowledge gathered in Svarm were also important to initiate the legislative measures on antibiotic resistance taken by the Swedish Board of Agriculture (SBA) in the last decade. Thus, findings of MRSA, MRSP or $ESBL_{CARBA}$ in animals were made notifiable and specific procedures for handling cases in companion animals and horses were made mandatory. Also, use of some antibiotic classes in animals were forbidden or restricted and IPC plans in veterinary practices made mandatory.

The activities in Svarm, and the actions taken to contain antibiotic resistance in Sweden, relies on cooperation between several stakeholders (SBA, PHAS, SVA, 2020). National authorities, veterinarians, animal health care providers, farmers and their organisations, companion animal owners and other players have all contributed in various ways. Containment of ESBL in broilers and of tiamulin resistant *B. hyodysenteriae* in pigs as well as the comparatively favourable situation regarding MRSA and MRSP in companion animals are examples of specific actions that have been successful. The comparatively favourable situation regarding antibiotic resistance, and the low usage of antibiotics in the veterinary sector in Sweden, corroborate that the stakeholder cooperation has been fruitful.

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Comparative analysis

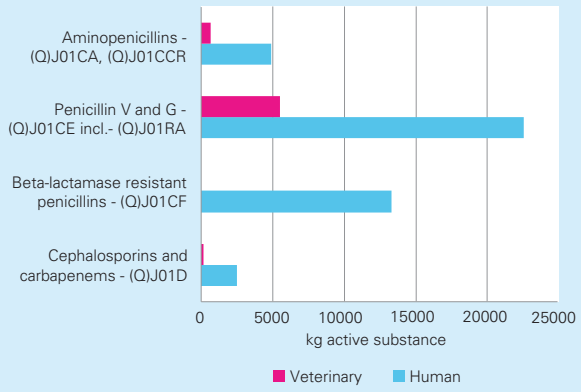
Comparison of antibiotic sales in human and veterinary medicine

Data included and calculations

The numbers 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 and QA07AA) are those presented in Sales of antibiotics for animals except products for intramammary and intrauterine use (QG01 and QJ51). Sales for aquaculture were not included, nor were sales of drugs authorised for human use but sold for animals. The contribution of such sales to the total volumes is minor.

To estimate the biomass of the human population, data on population numbers by age were multiplied with the corresponding average body weights from studies made by Statistics Sweden in 2016. For animal body mass, the data on population correction unit for 2017 was used as a proxy for 2019 (EMA, 2019b). This unit roughly corresponds to the total biomass of major animal populations, excluding dogs and cats.

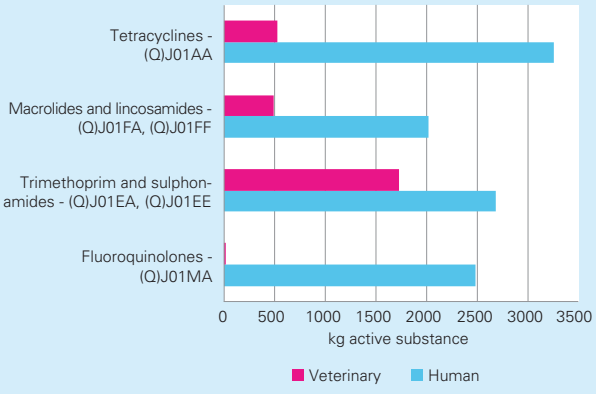
FIGURE 5.1. Sales of beta-lactam antibiotics for human and veterinary medicine, kg active substance, 2019. Please note the difference in indexation of the x-axis between Figures 5.1 and 5.2.



Comparison of sales in tonnes active substance

In 2019, a total of 61.0 and 9.5 tonnes of antibiotics in included ATC classes were consumed in human and veterinary medicine, respectively. Figure 5.1 displays the sales of beta-lactam antibiotics. Substances in that class 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; 67 and 58%, respectively. In the subclass cephalosporins and carbapenems, there were no sales of carbapenems for animals as no products are authorised for such use. The subclasses 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 2019 are included.

FIGURE 5.2. Sales of fluoroquinolones, macrolides, lincosamides, trimethoprim and sulphonamides, and tetracyclines for human and veterinary medicine, kg active substance, 2019. Please note the difference in indexation of the x-axis between Figures 5.1 and 5.2.

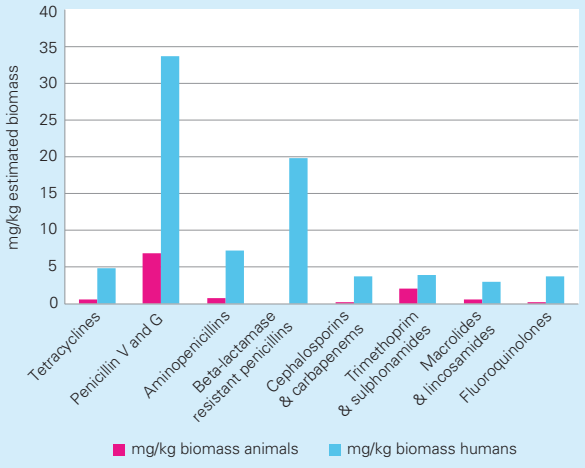


Comparison of sales expressed as mg per kg estimated biomass

In 2019, the sales were 90.8 and 12.0 mg active substance per kg estimated biomass in human and veterinary medicine, respectively. In Figure 5.3, a comparison of sales of antibiotics for use in humans and animals is shown expressed as mg per estimated kg biomass. Data on the total sales do not take the heterogeneity of the likelihood of exposure within the population into account. This is especially true for data on sales for use in animals, as certain substances may only or mainly be sold for use in one particular animal species. This means that the selective pressure in a particular subset of the population (i.e. a particular animal species) can be far larger than in the total population. Nevertheless, in Figure 5.3 the largest differences are noted for beta-lactamase resistant penicillins where the sales for animals are negligible (only sold on license as products for intramammary use), and for the fluoroquinolones where sales for humans are 148 times higher than for animals.

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

FIGURE 5.3. Sales of antibiotics for humans and animals expressed as mg active substance per estimated kg biomass in 2019.



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. Previously the occurrence in intestinal samples from broilers was high but it has decreased in recent years. Moreover, when the proportion of $ESBL_A$- or $ESBL_M$-producing *E. coli* has been quantified such bacteria only constitute a small part of all the *E. coli* in the intestinal flora in a majority of the broiler samples. Finally, it has been previously shown that most isolates from humans in Sweden is not of the same types of $ESBL_A$ or $ESBL_M$ as in broilers. Due to an increased relative occurrence of $bla_{CTX\text{-}M\text{-}1}$ among *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.

MRSA

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

Livestock-associated MRSA

During more than ten years, the zoonotic aspects on MRSA in farm animals has widened in many countries. 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 still commonly detected. In 2019 three of five cases of MRSA in horses were of this type.

In humans, cases of MRSA CC398 acquired in Sweden is uncommon. Among all MRSA cases with available typing results in 2019, there were 14 cases with isolates belonging to CC398, and their *spa*-types were t011 (n=3), t034 (n=8), t1451 (n=1) and t10890 (n=2). 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).

Throughout 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 and 2019, as part of an ongoing research project there were fourteen cases of MRSA with *mecC* from hedgehogs.

In humans, cases of MRSA acquired in Sweden with *mecC* are also uncommon. In 2019, there were 11 reported cases with *spa*-types t373 (n=3), t843 (n=6), t3391 (n=1) and t9111 (n=1). The epidemiological information concerning possible animal contacts is scarce but some of the *spa*-types in cases from humans have also been found in cases from animals. However, even if there would be zoonotic transfer it is currently not considered a public health problem as the number of cases of MRSA with *mecC* in humans in Sweden is low.

MRSA-types typically associated with humans

MRSA isolated from dogs and cats often belong to *spa*-types seen in MRSA from humans. This supports the view that humans often are the source of MRSA in companion animals (EFSA 2009, CVMP, 2009). 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 anonymised origin from 2014 and 2017, respectively. Because also these *spa*-types are common among human MRSA-cases, transmission from humans to cows can be suspected. There is, however, no epidemiological information available about these cases.

Conclusions

The MRSA situation in Sweden is still favourable both in humans and in animals. If this situation is preserved in animals, a reservoir of MRSA in animals with risk of spread from animals to humans can be prevented. Biosecurity, with caution in trade of live animals and measures to prevent introduction by indirect routes, is important for preventing introduction and spread of MRSA in animal populations. Furthermore, 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. Resistance to fluoroquinolones (e.g. ciprofloxacin) is rare and in 2019 a strain with ESBL resistance was for the first time detected, this in an environmental sample from a farm. Thus, the overall situation in the veterinary sector is favourable which is largely due to the strategies in the Swedish salmonella control programme initiated in the 1950-ies. In 2019, a number of isolates from animals had MIC of 4 mg/L for colistin and therefore should be considered resistant. This 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 (20%) in comparison to the very rare occurrence of such resistance in isolates from Swedish food-producing animals also suggests that most of these isolates from human infections do not have a domestic origin.

Campylobacter

Resistance to fluoroquinolones, tetracycline and erythromycin among faecal isolates of *Campylobacter jejuni* from humans was 61%, 33% and <1% respectively. From animals, 171 *C. coli* from pigs were tested. The resistance to fluoroquinolones was 37% and no resistance to tetracycline or erythromycin was found.

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.

Clinical resistance in *Escherichia coli* from humans and animals

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

For the purpose of this comparison, some data sets for *E. coli* from animals presented in Swedres-Svarm have been interpretated using clinical breakpoints for humans (Table 5.1).

Resistance was generally more common in *E. coli* from humans than in isolates from animals (Table 5.1). Notably, clinical resistance to fluoroquinolones or 3rd generation cephalosporins is considerably more common in *E. coli* from humans

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. 9.0 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	2019	1 082	15.7	1.0[a]	0.5	1.7		0.3	7.0[b]
Cat (UTI)	Urinary	2019	495	17.6	0[a]	0.4	0.4		0.4	1.0[b]
Horse (e.g. endometritis)	Genital tract	2019	244	9.8	0.8[a]	0.8	2.0		0	14.8[b]
Dairy cow (mastitis)	Milk	2019	74	24.3	0[a]	0	0		1.4	10.8[b]
Calf (enteritis)	Faeces/Post-mortem	2017-19	66	54.5	0[a]	0	0		0	25.8[b]
Calf (healthy)	Faeces	2017	85	23.6	0	0	0			4.7
Pig (enteritis)	Faeces/Post-mortem	2019	75	42.7	0[a]	0	0		0	38.7[b]
Pig (healthy)	Intestinal content	2019	174	19.0	0	0	0	0		14.9
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	2019	204 386	30.6	10.9	4.0			1.2	20.4
Humans (bloodstream inf.)	Blood	2019	9 414		14.3	7.6	6.0[c]	0		21.1[b]

[a]Enrofloxacin tested, BP >2mg/L except for horses (>0.25) and laying hens (>1) (CLSI 2018b); [b]Trimetoprim-sulphamethoxazole tested, BP >4 mg/L, NordicAST v. 9.0.

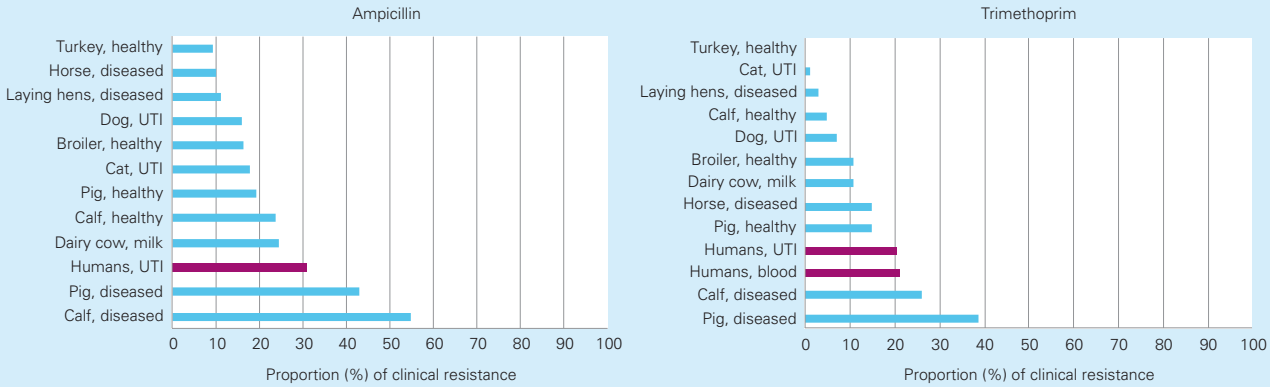
than in isolates from animals with the highest occurrence in blood stream isolates from humans (Table 5.1). This agrees with a low use of these antibiotic classes in animals (see Sales of antibiotics for animals). However, although few isolates of *E. coli* from animals show clinical resistance to fluoroquinolones, reduced susceptibility (i.e. non wild-type) is common in some categories of diseased and healthy animals (See Antibiotic resistance in animals in this and previous reports). Possibly, the selection pressure from fluoroquinolone use in animal populations is not sufficient to select for further mutations to clinical resistance in isolates with reduced susceptibility.

For the antibiotics commonly used in both animals and humans, e.g. ampicillin and trimethoprim, resistance is more frequent. In particular, the occurrence of resistance is high among clinical isolates from calves, pigs and humans (Table 5.1, Figure 5.4). When comparing resistance to trimethoprim, it should be kept in mind that for some categories (i.e. clinical isolates from animals and blood isolates from humans) trimethoprim-sulphonamide was tested. This could possibly result in a lower occurrence of resistance than if susceptibility to only trimethoprim had been tested. The comparatively high level of trimethoprim resistance in *E. coli* from the genital tract of mares most likely reflects the relatively common use of trimethoprim-sulphonamide combinations in horses.

Occurrence of resistance to ampicillin or trimethoprim could also be due to co-selection by use of other antibiotics or to other factors selecting for resistance. For example, although exact data 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.

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

FIGURE 5.4. Proportion of resistance (%) to ampicillin and trimethoprim in *Escherichia coli* from humans and animals interpreted with clinical breakpoints. For details see Table 5.1.



Background data, material, methods and references

Demographics and denominator data

Humans

TABLE 6.1. Inhabitants in Sweden per region, per age group, 2019.

	<1 years	1-4 years	5-19 years	20-44 years	45-64 years	65-84 years	85 years and older	All age groups
Blekinge	1 640	6 937	27 451	46 265	39 840	32 581	4 970	159 684
Dalarna	3 057	12 920	48 411	80 670	72 460	60 823	8 850	287 191
Gotland	515	2 352	9 418	16 145	15 815	13 214	1 790	59 249
Gävleborg	3 127	12 323	47 963	81 218	73 629	59 978	8 309	286 547
Halland	3 546	15 381	59 818	95 957	83 202	62 181	9 267	329 352
Jämtland	1 404	5 881	21 714	38 214	32 746	26 504	3 817	130 280
Jönköping	4 236	17 594	65 182	111 184	88 036	64 066	10 527	360 825
Kalmar	2 560	10 704	40 478	68 359	62 231	52 488	7 850	244 670
Kronoberg	2 282	9 697	35 858	62 624	47 230	36 183	6 012	199 886
Norrbotten	2 368	10 256	39 610	73 053	65 187	52 751	7 272	250 497
Skåne	15 960	66 994	239 235	446 171	327 847	231 316	34 641	1 362 164
Stockholm	28 798	119 096	415 907	836 886	571 183	326 837	45 417	2 344 124
Sörmland	3 290	14 331	53 259	84 488	73 122	58 140	8 065	294 695
Uppsala	4 311	18 241	65 208	130 924	87 855	61 404	8 411	376 354
Värmland	2 932	12 404	45 437	81 695	72 185	57 607	9 222	281 482
Västerbotten	2 927	12 196	44 917	89 130	64 045	49 746	7 193	270 154
Västernorrland	2 563	10 558	41 499	68 946	62 971	51 607	7 309	245 453
Västmanland	3 067	12 825	47 700	82 747	68 190	51 586	7 814	273 929
Västra Götaland	19 754	81 276	293 600	565 381	418 202	288 139	43 462	1 709 814
Örebro	3 481	14 092	52 529	95 171	72 898	56 103	7 978	302 252
Östergötland	5 021	21 601	79 550	149 783	111 347	81 851	12 430	461 583
Sweden	116 839	487 659	1 774 744	3 305 011	2 510 221	1 775 105	260 606	10 230 185

TABLE 6.2. Population in Sweden, per year, 2000-2019.

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

TABLE 6.3. Number of admissions and patient-days in somatic medical care in Sweden, 2015-2018. Data represent production by acute care hospitals in all regions except Dalarna.

Year	Admissions	Patient-days
2015	1 406 941	6 376 593
2016	1 360 540	6 140 745
2017	1 325 969	5 926 402
2018	1 317 455	5 785 393

TABLE 6.4. Number of admissions and patient-days in somatic medical care in the regions, 2018. Data represent production by acute care hospitals in all regions except Dalarna.

Region	Admissions	Patient-days
Blekinge	22 875	100 199
Gotland	10 473	45 749
Gävleborg	37 510	150 337
Halland	40 192	156 112
Jämtland	18 431	79 735
Jönköping	49 370	179 734
Kalmar	39 240	138 720
Kronoberg	24 041	102 124
Norrbotten	33 432	155 565
Skåne	170 160	780 967
Stockholm	306 591	1 377 811
Sörmland	36 870	165 575
Uppsala	50 072	252 218
Värmland	40 142	177 351
Västerbotten	44 973	204 604
Västernorrland	34 465	141 719
Västmanland	37 277	169 237
Västra Götaland	217 433	986 329
Örebro	42 251	180 712
Östergötland	61 657	240 595
Sweden	**1 317 455**	**5 785 393**

TABLE 6.5. Denominator data from the microbiological laboratories 2018. No data was collected 2019.

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 *Clostridioides difficile* (toxin)	Blood (pair of bottles)	*Staphylococcus aureus*	*Streptococcus pneumoniae*	*Streptococcus pyogenes*	*Escherichia coli*	*Clostridioides 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	4 565[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**	**68 386**	**81 093**	**185 841**	**15 361**	**23 282**	**300 072**	**8 602**

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

Animals

Official statistics on agriculture in Sweden is provided by the Board of Agriculture. The Board of Agriculture maintains a statistical database accessible online (www.jordbruksverket.se). The statistics are also as Statistical Messages (SM). Annual figures on number of animals are given in Table 6.6, on 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) 1980-2019. From the statistical database of the Board of Agriculture.

Animal Species	1980[a]	1985[a]	1990	1995	2000	2005	2010	2015	2017	2018	2019
Cattle											
Dairy cows	656	646	576	482	428	393	348	338	322	319	305
Beef cows	71	59	75	157	167	177	197	184	208	214	210
Other cattle >1 year	614	570	544	596	589	527	513	487	500	498	500
Calves <1 year	595	563	524	542	500	509	479	466	472	475	451
Total, cattle	1 935	1 837	1 718	1 777	1 684	1 605	1 537	1 475	1 502	1 507	1 466
Sheep											
Ewes and rams	161	173	162	195	198	222	273	289	301	296	280
Lambs	231	252	244	266	234	249	292	306	304	291	269
Total, sheep	392	425	406	462	432	471	565	595	605	587	549
Pigs											
Boars & sows	290	260	230	245	206	188	156	142	141	132	130
Fattening pigs >20 kg[a]	1 254	1 127	1 025	1 300	1 146	1 085	937	830	836	901	943
Piglets <20kg[b]	1 170	1 113	1 009	769	566	539	427	384	385	361	383
Total, pigs	2 714	2 500	2 264	2 313	1 918	1 811	1 520	1 356	1 362	1 393	1 456
Laying hens											
Hens	5 937	6 548	6 392	6 100	5 670	5 065	6 061	7 571	7 294	7 699	8 909
Chickens reared for laying	2 636	2 159	2 176	1 812	1 654	1 697	1 647	1 842	1 994	1 927	2 067
Total, hens	8 573	8 708	8 568	7 912	7 324	6 762	7 707	9 413	9 288	9 626	10 976
Horses											
Total, horses						283[c]	363		356[d]		

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

TABLE 6.7. Number of animals slaughtered (in thousands) at slaughterhouses, 1980-2019. From the statistical database of the Board of Agriculture.

Animal species	1980	1985	1990	1995	2000	2005	2010	2015	2017	2018	2019
Cattle											
Cattle >1 year	574	584	523	502	490	433	425	406	392	410	418
Calves < 1 year	130	152	70	30	39	33	27	22	14	15	15
Total, cattle	704	736	593	532	529	466	453	428	406	426	433
Sheep	302	328	280	189	202	206	255	256	261	280	252
Pigs	4 153	4 283	3 653	3 743	3 251	3 160	2 936	2 560	2 576	2 646	2 573
Broilers	40 466[a]	36 410[a]	38 577[a]	61 313	68 617	73 458	78 507	95 974	101 876	100 535	106 121
Turkeys							495	475	526	526	508

[a]Data supplied by the National Food Administration.

TABLE 6.8. Quantity of livestock slaughtered (in 1 000 tonnes) at slaughterhouses, 1990-2019. From the statistical database of the Board of Agriculture.

Animal Species	1990	1995	2000	2005	2010	2015	2017	2018	2019
Cattle									
Cattle >1 year	139.5	140.1	145.4	131.4	133.5	129.7	129.7	134.3	137.2
Calves < 1 year	6.8	3.2	4.4	4.5	4.3	3.5	2.4	2.5	24.4
Total, cattle	146.3	143.3	149.8	135.9	137.8	133.1	132.1	136.9	161.6
Sheep	5.0	3.5	3.9	4.1	5.0	4.2	5.3	5.6	5.1
Pigs	293.1	308.8	277.0	275.1	263.5	233.5	240.7	249.8	240.3
Broilers	44.0[a]	73.6[a]	89.9	96.2	112.0	137.7	148.6	149.3	159.2
Turkeys					3.2	3.8	4.3	4.4	4.6

[a]Data supplied by the National Food Administration.

TABLE 6.9. Average number of animals per holding 1995-2019. From the statistical message JO 20 SM 1901.

Animal Species	1995	2000	2005	2010[a]	2015[a, b]	2016[a]	2017[a, b]	2018[a, b]	2019[a, b]
Cattle									
Dairy cows	27.2	33.7	46	61.9	81.5	85.4	89.1	91.8	93.9
Beef cows	9.2	12.0	13.8	16.2	17.7	18.7	19.8	20.6	20.5
Sheep	19.5	24.8	29.2	31.7	31.8	32.5	32.7	32.4	33.1
Boars and sows	31	63	156	156	186	182	165	158	193
Fattening pigs	157	294	471	664	845	820	825	852	1 053
Laying hens	640	995	471	1 638	2 587	2 822	2 506	2 413	3 700

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

TABLE 6.10. Number of holdings with animals of different types, 1980-2019. From the statistical database of the Board of Agriculture.

Animal Species	1980	1985	1990	1995	2000	2005	2010	2015	2017	2018	2019
Cattle											
Dairy cows	44 143	35 063	25 921	17 743	12 676	8 548	5 619	4 161	3 614	3 477	3 253
Beef cows	12 436	10 310	10 883	17 069	13 861	12 821	12 190	10 405	10 471	10 418	10 266
Other cattle >1 year	63 179	52 652	42 696	39 160	30 457	24 808	20 295	16 432	15 722	15 343	14 925
Calves <1 year	62 314	52 001	41 986	36 542	27 733	22 888	18 494	15 186	14 517	14 139	13 630
Total holdings with cattle	70 503	58 872	47 292	41 990	32 063	26 179	21 586	17 466	16 674	16 317	15 851
Sheep	10 238	10 595	9 749	10 037	8 089	7 653	8 657	9 110	9 219	9 120	8 463
Pigs	26 122	19 937	14 301	10 753	4 809	2 794	1 695	1 228	1 272	1 346	1 089
Laying hens	23 603	17 531	12 900	9 593	5 678	4 916	3 703	2 927	2 911	3 197	2 408

Materials and methods, sales of antibiotics

Legal framework and distribution of drugs

Marketing of drugs in Sweden is regulated by the Medicinal products Act, which applies both to human and veterinary medicinal products. According to this Act, a medicinal product may not be sold until it has been granted marketing authorisation by the Medical Products Agency (MPA). In case there are no authorised medicinal products for a certain condition, the MPA can permit special licence prescription for a medicinal product for a specified pharmacy, prescriber or clinic.

Medicinal products in which an antibiotic is the active substance are only dispensed through pharmacies, which are supplied by drug wholesalers or manufacturers. In outpatient care, antibiotic drugs (including premixes for feed for veterinary use) may only be sold on prescriptions, ApoDos (individually packed doses of drugs often dispensed to the elderly) or requisitions. Prescribers (veterinarians or medical doctors) are not permitted to own a pharmacy or to otherwise sell medicinal products for profit. In hospital care, both for humans and animals, 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. These data are protected by the Public Access to Information and Secrecy Ordinance and publication of data needs to be carefully reviewed to avoid risk of disclosure of sensitive information. For this publication, consent has been obtained from the legal entities concerned and measures for protection of information have been taken.

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 (eHälsomyndigheten) 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 per 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 2019 version of the ATC/DDD index, available at https://www.whocc.no/atc_ddd_index/.

Antibiotic sales in humans

Swedish national statistics on drug utilisation

Sales statistics on 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. Outpatient 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 per 1000 inhabitants per day or number of prescriptions per 1000 inhabitants.

Hospital care data include drugs delivered by all hospital pharmacies to the hospital departments (see the section "Completeness of data" below). The sales are expressed as cash value, number of packages and number of defined daily doses.

Following the de-monopolisation of the pharmacy market in Sweden in July 2009, the responsibility for collection of 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.

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 2019

TABLE 6.11. DDD for all antibiotic substances (J01) sold in Sweden in 2019.

	DDD (g)		DDD (g)
J01AA02 - doxycycline	0.1	J01EA01 - trimethoprim	0.4
J01AA04 - lymecycline	0.6	J01EC02 - sulfadiazin	0.6
J01AA07 - tetracycline	1	J01EE01 - sulfamethoxazol and trimethoprim	1.92
J01AA08 - minocycline		J01FA01 - erythromycin	1
J01AA12 - tigecycline	0.1	J01FA01- erythromycin erythylsuccinat tablets	2
J01BA01 - chloramphenicol	3	J01FA06 - roxithromycin	0.3
J01CA01 - ampicillin - parenteral	6	J01FA09 - clarithromycin - oral	0.5
J01CA01 - ampicillin - oral	2	J01FA10 - azithromycin - parenteral	0.5
J01CA04 - amoxicillin	1.5	J01FA10 - azithromycin - oral	0.3
J01CA08 - pivmecillinam	0.6	J01FA15 - telithromycin	0.8
J01CA12 - piperacillin	14	J01FF01 - clindamycin - parenteral	1.8
J01CA17 - temocillin	4	J01FF01 - clindamycin - oral	1.2
J01CE01 - benzylpenicillin	3.6	J01FG01 - pristinamycin	2
J01CE02 - fenoximethylpenicillin	2	J01GB01 - tobramycin - parenteral	0.24
J01CE08 - benzathine benzylpenicillin	3.6	J01GB01 - tobramycin - oral inhalation solution	0.3
J01CF01 - dicloxacillin	2	J01GB01 - tobramycin - oral inhalation powder	0.112
J01CF02 - cloxacillin	2	J01GB03 - gentamicin	0.24
J01CF05 - flucloxacillin	2	J01GB06 - amikacin	1
J01CR02 - amoxicillin and enzyme inhibitor	1.5	J01MA01 - ofloxacin	0.4
J01CR05 - piperacillin and enzyme inhibitor	14	J01MA02 - ciprofloxacin - parenteral	0.8
J01DB01 - cefalexin	2	J01MA02 - ciprofloxacin - oral	1
J01DB04 - cefazolin	3	J01MA06 - norfloxacin	0.8
J01DB05 - cefadroxil	2	J01MA12 - levofloxacin	0.5
J01DC01 - cefoxitin	6	J01MA14 - moxifloxacin	0.4
J01DC02 - cefuroxime - parenteral	3	J01XA01 - vancomycin	2
J01DC02 - cefuroxime - oral	0.5	J01XA02 - teicoplanin	0.4
J01DC04 - cefaclor	1	J01XA04 - dalbavancin	1.5
J01DD01 - cefotaxime	4	J01XB01 - colistin - parenteral	9 MU
J01DD02 - ceftazidime	4	J01XB01 - colistin - oral	3 MU
J01DD04 - ceftriaxon	2	J01XB02 - polymyxin B	0.15
J01DD08 - cefixime	0.4	J01XC01 - fusidic acid	1.5
J01DD14 - ceftibuten	0.4	J01XD01 - metronidazole	1.5
J01DD52 - ceftazidim and enzyme inhibitor	6	J01XE01 - nitrofurantoin	0.2
J01DE01 - cefepime	4	J01XX01 - fosfomycin - parenteral	8
J01DF01 - aztreonam - parenteral	4	J01XX01 - fosfomycin - oral	3
J01DF01 - aztreonam - inhalation	0.225	J01XX04 - spectinomycin	3
J01DH02 - meropenem	3	J01XX05 - methenamine - hippurate	2
J01DH03 - ertapenem	1	J01XX05 - methenamine - mandelate	3
J01DH51 - imipenem and enzyme inhibitor	2	J01XX08 - linezolide	1.2
J01DI01 - ceftobiprolmedocaril	1.5	J01XX09 - daptomycin	0.28
J01DI02 - ceftarolinfosamil	1.2	J01XX11 - tedizolid	0.2
J01DI54 - ceftolozan and enzyme inhibitor	3		

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 organise their own drug supplies organisation for hospitals.

Therefore, no national database with complete sales statistic is available at this time. Efforts have been made to complement the data from the Swedish eHealth Agency with data from regions. In 2019, two regions did not report data to the Swedish eHealth Agency. In this year's report, Region Dalarna is not included in the statistics showing total sales or the statistics showing hospital care, due to failure to report data for sales of antibiotics to hospitals and other care facilities since 2017.

Data sources and inclusion criteria

Data on sales of antibiotics in outpatient and hospital care as well as population data for the calculations are obtained from the Swedish eHealth Agency through their database Concise. For the overall statistics, the data include all antimicrobial products marketed in Sweden in the ATC class J01. The data include all sales of these products, even if the antimicrobial

(J01) is prescribed by a veterinarian. Throughout this report, methenamine is excluded in all displays of J01 as a group. Measures used are defined daily 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 were obtained from Statistics Sweden, a Swedish authority responsible for official Swedish statistics.

Antibiotic sales to hospital care are measured in DDD per 1000 inhabitants per day and DDD per 100 admissions or patient-days. The number of DDDs is obtained from the Swedish eHealth Agency and from local medicines statistics systems in the regions. The Swedish National Board of Health and Welfare has provided data on admissions and patient-days to hospitals. Admission is calculated as number of discharges (one patient can be discharged and admitted multiple times if transferred between wards during one hospital stay). Patient-days is defined as each additional day during one hospital stay. The number of admissions and patient-days includes data on somatic medical care by each region.

Trend analysis

In the report, some general regression models were executed in the section "Sales of antibiotics". Time was used as explanatory variable and the outcome was the sales of antibiotics, adjusted for population size in Sweden. The analyses were executed on a basis of a negative binomial distribution. The analyses were executed on the sales of antibiotics in outpatient care commonly used to treat respiratory tract infections between 2000 and 2019 and on the sales of antibiotics in outpatient care commonly used to treat UTI in men 65 years and older between 2000 and 2019.

The Swedish Prescribed Drug Register

Since July 2005, the National Board of Health and Welfare supplies an individually based register on all drugs prescribed and dispensed in outpatient care. Among other things, these 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 2019 is not available until the end of 2020, and therefore denominator data from 2018 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) 2015-2018 is shown in Table 6.3.

Sales of antibiotics for animals

Data sources, inclusion criteria and analysis

For the overall statistics, the data include all products with antibiotics as active substance marketed in Sweden and sold for use in terrestrial animals in the ATCvet classes QA07, QJ01, QG01A and QJ51. Medicinal products authorised for human use but prescribed for use in animals are not included in the overall statistics.

Data are retrieved as number of packages sold per product. Calculation to kg active substance is done based on information on strength and package size obtained from the national product register of the MPA, or for products sold on special license from other sources, e.g. pharmacies.

For the reporting years 2017 and 2018, it was not possible for SVA to obtain raw data per product for calculation to kg active substance and subsequent analyses from the eHealth Agency. These data have now been obtained and recalculated. Some errors in previous aggregated data were discovered, resulting in updates of the figures presented for these years in the chapter on Sales of antibiotics for animals.

Products sold with special licence

Antibiotic products sold with special licence (products prescribed and sold on exemption from general Swedish market authorisation) are included in the dataset. However, in 2011 it was noticed that the information on sales of products with special licence was less complete than in previous years. Figures for 2011 are therefore likely to be a slight underestimate. Between 2012 and 2014, efforts were made to 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 eHealth Agency on sales of products with special licence is no less complete than for products with general marketing authorisation.

Calculation of defined course doses for pigs

For In focus Sales of antibiotics for pigs, two types of defined course doses (DCD) were used to adjust for differences in dosing: DCDvet as assigned by the European surveillance of veterinary antimicrobial consumption (EMA), and a national DCD, called DCDse. To assign DCDse, the highest authorised daily dose and the longest treatment period given in the Summary of product characteristics was used. As for DCDvet, the DCDse was defined for injectables, premixes and for other products for oral use for each active substance or substance combination (i.e. not on a product basis).

Materials and methods, resistance in bacteria from animals

Sampling strategy

Antibiotic resistance as notifiable diseases

ESBL

Screening for $ESBL_A$, $ESBL_M$ and $ESBL_{CARBA}$-producing *Escherichia coli* was performed on caecal samples from healthy pigs as well as on samples of fresh pork and beef meat. Samples from 301 pigs were collected at slaughter under the supervision of the National Food Agency (SLV) at six abattoirs which together processed more than 85% of the total number of pigs slaughtered in Sweden 2019. At each abattoir, a proportional number of samples in relation to slaughter volume were collected throughout the year. Samples were sent to SVA for culture within one week after collection and in the meantime kept refrigerated. The number of samples collected at each abattoir was proportional to the annual volume of pigs slaughtered at an abattoir and each sample represented a unique herd. By these measures, bacterial isolates included were from randomly selected healthy pigs of Swedish herds.

Samples from broilers were collected at slaughter within the Swedish Campylobacter programme in which whole caeca are collected from each batch of broilers slaughtered. From these samples, 50 were selected in May-June and 50 in September-October. Each sample was from a unique flock but not always from a unique production site. Samples cultured were collected at seven abattoirs that in 2019 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.

Meat samples of fresh pork (293) and beef (294) were collected throughout the year at retail stores by municipal environmental departments in ten different cities in Sweden. The number of samples from each municipal was roughly proportional to the human population.

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

MRSA and MRSP

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

Findings of MRSA and MRSP in animals are notifiable in Sweden and hitherto 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

Screening for *Campylobacter coli* in caecum from pigs were performed on the same samples as for ESBL (see above). Samples from 232 pigs were cultured to isolate 171 *C. coli* and these samples were evenly distributed over the year.

Clinical isolates from animals

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

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

In cattle, isolates of *E. coli* are from samples from the gastro-intestinal tract from calves or from milk samples. Isolates of *Klebsiella pneumoniae* are from milk samples. Isolates of *Pasteurella* spp. are from the respiratory tract from calves.

In farmed fish, isolates of *Flavobacterium psychrophilum* 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.

In dogs, isolates of *E. coli* are from urine, *Staphylococcus pseudintermedius* is isolated from three sampling collections and compared; 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

Culturing for indicator *E. coli* in caecum from pigs was performed on the same samples as for ESBL (see above). Samples from 176 pigs were cultured to isolate 174 indicator *E. coli* and these samples were evenly distributed over the year.

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 homogenised in 225 ml BPW and incubated at 37°C overnight. From the BPW homogenisate 10 µl per agar plate was spread on MacConkey agar with cefotaxime (1 mg/L), CC agar and CO agar and incubated overnight at 44°C (MacConkey agar) or 37°C (CC, CO agar). From MacConkey agar with cefotaxime one lactose positive colony with morphology typical for *E. coli* was sub-cultured on MacConkey agar with cefotaxime and then subcultured again on horse-blood agar (5% v/v), after which the isolate was tested for production of tryptophanase (indole). Only lactose and indole positive isolates with typical morphology were selected for susceptibility tests and further tested for ESBL production. From MacConkey agar with cefotaxime up to three lactose positive colonies with morphology typical for *E. coli* was sub-cultured on MacConkey agar with cefotaxime and then subcultured again. *Escherichia coli* like colonies on CC agar and CO agar were sub-cultured on MacConkeyagar, and if they were lactose positive, they were sub-cultured on horse-blood agar. Lactose positive isolates were species identified by MALDI-TOF MS and if positive for any Enterobacteriaceae species the isolate would be further tested for ESBL production.

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

MRSA and MRSP

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

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

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 coli from pigs were isolated and identifed at the Dept. of Animal Health and Antimicrobial Strategies, SVA. Briefly, samples were cultured direct on Preston selective agar at 42°C for 48 h in a microaerophilic environment. Isolates were selected based on colony morphology and microscopic appearance including motility. All isolates were species identified by MALDI-TOF MS.

Clinical isolates from animals

Clinical isolates were isolated and identified with accredited methodology, following standard procedures at SVA.

Indicator bacteria

Escherichia coli

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

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

Susceptibility testing

Microdilution

At SVA, fast growing aerobic bacteria, *Campylobacter* and bacteria from fish are tested for antibiotic susceptibility with accredited methodology using dilution methods in cation adjusted Mueller-Hinton broth (CAMHB) (Difco). Tests are performed following the standards for microdilution of the Clinical and Laboratory Standards Institute (CLSI, 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 CO_2, 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. *S. equi* subsp. *zooepidemicus* was tested using CAMHB supplemented with 5-10% horse serum followed by incubation at 37°C in CO_2 for 16-18 hours.

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

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

Bacteria from fish are tested for antibiotic susceptibility by broth microdilution adapted for aquatic bacteria according to CLSI (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 subjected to genome sequence analyses (see below). Isolates suspected of being $ESBL_M$ based on phenotype was first subjected to PCR detecting genes encoding $ESBL_M$ (Perez-Perez and Hanson, 2002) and $ESBL_A$ (Woodford et al., 2006 and Fang et al., 2008). After confirmation of suspected transferable genes these isolates were subjected to genome sequencing.

DNA from confirmed ESBL-producing 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. For a subset of ESBL-producing Enterobacteriaceae was DNA extracted by using IndiMag® Pathogen Kit (Indical Bioscience) in a Maelstrom 9600 (TANBead). DNA-concentrations were determined using Qubit HS DNA-kit (Life technologies). DNA was then sent to 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 and genome assembly was performed with SPAdes with the careful parameter, followed by Pilon with default settings to correct assemblies (Bankevich et al., 2012; Bolger et al., 2014; Walker et al., 2014). Using the assembled contigs the isolates were assigned an MLST, when available, using Ridom SeqSphere+ software (Ridom GmbH, Germany).

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 such as source of cultured sample, identification results, antibiotic susceptibility etc. were registered in a laboratory information management (LIM) system at SVA.

Cut-off values for resistance

For interpretation of MICs from susceptibility testing of zoonotic bacteria (*Salmonella* and *Campylobacter*) and indicator bacteria (*Escherichia coli* and enterococci) epidemiological cut-off values (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, 2015) 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 20) 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	>0.25				>8	>8			>1		>8			
Azithromycin					>16									
Cefepime					>0.12									
Cefotaxime					>0.25	>0.25		>0.25			>0.5			
Cefoxitin													>4	
Ceftazidime					>0.5									
Cephalothin												>1	>1	>2
Chloramphenicol					>16	>16			>2		>16		>16	
Ciprofloxacin			>0.5	>0.5	>0.06				>0.06		>0.06		>1	
Clindamycin												>0.5	>0.5[c]	>0.5
Colistin					>2	>2		>2		>4	>2			
Doxycycline		>0.5												
Enrofloxacin	>0.12				>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	>0.5						>2		>4		>16			
Fusidic acid												>1	>0.5	
Gentamicin			>2	>2	>2	>2		>2	>8	>8	>2	>2	>2	
Imipenem					>0.5									
Linezolid													>4	
Meropenem					>0.12									
Nalidixic acid			>16	>16	>8						>16			
Neomycin						>8		>8			>4			
Nitrofurantoin						>64						>32 (UTI)	>32 (UTI)	
Oxacillin												>0.5		
Oxolinic acid							>0.25							
Oxitetracycline	>1													
Penicillin	>0.5								>0.5			[b]	[b]	>0.06
Streptomycin			>4	>4		>16		>16			>16			
Sulphamethoxazole					>64						>256			
Temocillin					>16									
Tetracycline			>1	>2	>8	>8	>0.12	>8	>2		>8	>1	>1	
Tiamulin		>0.25												
Tigecycline					>0.5									
Trimethoprim					>2						>2		>2	
Trim & sulpha[a]	>1					>1		>0.5	>4			>0.5	>0.5	>0.5
Tylosin		>16												
Tylvalosin		>1												
Valnemulin		>0.12												

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

Svarm 2000–2019

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 2000-2019.

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

TABLE 6.14. *Campylobacter* spp., number of isolates 2000-2019.

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

TABLE 6.15. Indicator *Escherichia coli,* number of isolates 2000-2019.

Source	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Cattle	293						314			223				197		101		85		
Pigs	260	308		303		390			349			167				200		140		174
Pig meat									19			20								
Broilers	274	296	306		300			296			181		194		197		175		178	
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 2000-2019 *(E. faecalis/E. faecium).*

Source	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
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 2000-2019.

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

TABLE 6.18. Clinical isolates from companion animals and horses, number of isolates 2000-2019.

Animal species & bacterial species	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Horses																				
Actinobacillus spp.		40																		
Escherichia coli (genital)	323	103	166	188	188	161	124	273	174	210	236	174	196	140	229	188	324	240	309	244
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	52
Staphylococcus aureus										308	131	135	145	139	132	116	75	127	118	104
Fusobacterium spp.																			40	
Dogs																				
Escherichia coli (urinary)	185	183	204	234	247	304	366	425	503	599	803	661	407	840	943	1 112	1 162	1 038	1 082	1 082
Pasteurella canis															207	194	253	152	232	157
Pasteurella multocida					231										29	46	23			
Pseudomonas aeruginosa				234						261	313	353	178	309	389	355	349	306	366	349
Staphylococcus pseudintermedius (skin)	145	156	133	102	159	126	89	220	258	381	444	388	229	566	513	393	376	417	515	507
Staphylococcus pseudintermedius (external ear)																		648	784	827
Staphylococcus pseudintermedius (wound)																		844	1005	932
Staphylococcus schleiferi															297	201	163	175	240	233
Cats																				
Escherichia coli (urinary)			46	52	55	74	95	131	170	245	236	274	310	404	461	455	537	539	545	495
Betahemolytic streptococci												184								
Pasteurella dagmatis															20	22	19			
Pasteurella multocida															244	340	349	301	392	216
Staphylococcus felis															244	227	277	287	310	312

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SWEDRES|SVARM 2019

This annual report describes the monitoring of antibiotic resistance and antibiotic sales in human and veterinary medicine in Sweden in 2019.

From an international perspective the situation in Sweden regarding antibiotic resistance in bacteria from humans and animals is favourable. In spite of this, there are still problems with cross infection and increasing resistance. Thus, the preventive efforts must continue, and in some instances be intensified.

The total sales of antibiotics for both humans and animals have 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. 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 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 Sweden's strategies to promote prudent use of antibiotics and for infection prevention and control are effective.

Focus areas:
- Clinical trial – Duration of treatment for tonsillitis
- Success factors in antibiotic stewardship activities in Sweden
- The national and international reference and development laboratory for phenotypic antimicrobial susceptibility testing
- Shorter time to antimicrobial susceptibility testing results in sepsis with new EUCAST methodology
- Multiresistant ESBL-producing Enterobacteriaceae from horses
- Sales of antibiotics for pigs in Sweden
- Svarm – 20 years of monitoring resistance in bacteria from animals
- SvarmPat – monitoring of resistance in pathogens from farm animals

New features:
- Data on antibiotic sales in telemedicine for humans
- Combined resistance in bacteria from 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.