2017

SWEDRES | SVARM

Consumption of antibiotics and occurrence of antibiotic resistance in Sweden

Folkhälsomyndigheten
PUBLIC HEALTH AGENCY OF SWEDEN

SVA NATIONAL VETERINARY INSTITUTE

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

Published by:

Public Health Agency of Sweden and National Veterinary Institute

Editors:

Erika Olsson and Olov Aspevall,
Public Health Agency of Sweden
Oskar Nilsson and Märit Pringle,
National Veterinary Institute

Addresses:

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

National Veterinary Institute
SE-751 89 Uppsala, Sweden
Phone: +46 (0) 18 67 40 00
Fax: +46 (0) 18 30 91 62
E-mail: sva@sva.se
www.sva.se

Suggested citation:

Swedres-Svarm 2017. Consumption of antibiotics and occurrence of resistance in Sweden. Solna/Uppsala ISSN1650-6332

ISSN 1650-6332
Article no. 18003

This title and previous Swedres and Svarm reports are available for downloading at www.folkhalsomyndigheten.se/publicerat-material/ or at www.sva.se

Layout: Dsign Grafisk Form, Helen Eriksson AB

Print: Taberg Media Group, Taberg 2018

Cover by Ingvar Westerdahl/Thomas Isaksson

Scan the QR code to open Swedres-Svarm 2017 as a pdf in your mobile device, for reading and sharing.

Download a free QR code reader in the App Store for Apple devices or in Google Play for Android, for example Quick Scan QR Code Reader (iPhone) or QR Droid Code Scanner (Android).

Preface

Since the mid-1940s, antibiotics have been a highly valuable in effectively treating serious infections in humans and animals. However, the effectiveness of antibiotics is threatened by increasing levels of resistance to more and more antibiotics. The spread of resistance is fuelled by high selective pressure from imprudent use in humans and animals, from environmental pollution with antibiotics, e.g. from production facilities, and from use for growth promotion purposes in animal husbandry. In addition, healthcare-associated infections promote the spread of resistant bacteria in hospitals. All of these issues must be addressed globally in order to improve the current situation.

Fortunately, the urgency to stop the development of antibiotic resistance has been recognised internationally, and several initiatives are being taken. These include recent action plans and strategies from the United Nations, the World Health Organization, the World Organization of Animal Health, and the EU Commission as well as the on-going implementation of the Global AMR Surveillance system.

Sweden has put into place national, inter-sectorial strategies and action plans for addressing antibiotic resistance. The Swedish action plan to counteract antibiotic resistance was revised in 2017, and follow-ups and revisions will be made annually.

In the autumn of 2017, the European commission (DG SANTE F) undertook a fact-finding mission to gather information from competent authorities and other stakeholders in Sweden on the implementation of measures for tackling the issues of antibiotic resistance relating to use of veterinary medicines, and to identify good practices or difficulties experienced. The report from the mission, published on the web of the European Commission, concludes that a number of aspects of the measures put in place in Sweden could serve as an illustration of potential good practices to other Member States.

Surveillance of antibiotic resistance and antibiotic use and cooperation between sectors in a One Health perspective are crucial in the work to counteract the spread of antibiotic resistance. This report is the result of collaboration between the National Veterinary Institute and the Public Health Agency of Sweden to present and analyse Swedish data on antibiotic resistance and the use of antibiotics in animals and humans.

Last year the Public Health Agency of Sweden focused on improving surveillance through cooperation with regional clinical microbiological laboratories and healthcare – connecting laboratories and automatically collecting data on resistance and issuing warnings when serious resistance is discovered. Related to this is an initiative led by the National Veterinary Institute to develop a network of Swedish veterinary laboratories to increase the quality of diagnostic susceptibility testing. Another aim of this initiative is to include data from more laboratories in the surveillance.

While the situation in Sweden regarding antibiotic resistance is favourable compared to other countries, resistance in bacteria from humans have gradually increased since surveillance started. In addition, several regional and a few national hospital outbreaks are reported every year. This emphasises the need for continued efforts in all preventive areas and for collaboration among all sectors in society. The situation in the veterinary sector is also generally favourable, with low occurrence of most types of resistances, and bacteria causing clinical disease in animals are mostly susceptible to the antibiotics that are relevant for treatment.

Solna and Uppsala 2018-05-22

Johan Carlson

Director General
The Public Health Agency of Sweden

Jens Mattsson

Director General
National Veterinary Institute

Contributors and participants

Editors

Olov Aspevall and Erika Olsson,
Public Health Agency of Sweden
Oskar Nilsson and Märit Pringle,
National Veterinary Institute, Sweden

Project Manager

Hanna Billström, Public Health Agency of Sweden

Authors Swedres

Public Health Agency of Sweden
Olov Aspevall, Hanna Billström, Alma Brolund, Petra Edquist, Nasanin Hashemi, Sara Hæggman, Jenny Hellman, Jerker Jonsson, Eva Morfeldt, Barbro Mäkitalo, Erika Olsson, Karin Sjöström, Anders Ternhag, Tomas Söderblom, Vendela Wiener and Thomas Åkerlund

Medical Products Agency
Sahra Barzi

Department of Clinical Microbiology, Karolinska University Hospital, Solna
Christian Giske

National Reference laboratory for Antibiotic Resistance, Växjö Hospital
Gunnar Kahlmeter

National Reference Laboratory for Pathogenic Neisseria, Örebro University Hospital
Hans Fredlund, Susanne Jacobsson and Magnus Unemo

Authors Svarm

National Veterinary Institute
Björn Bengtsson, Karin Bergström, Stefan Börjesson, Anna Duse, Helle Ericsson Unnerstad, Christina Greko, Annica Landén, Oskar Nilsson and Märit Pringle

Other contributors in Svarm

National Veterinary Institute
Boel Harbom, Mattias Myrenås and Eva Säker

Farm & Animal Health
Maria Lindberg

Acknowledgements

The analysis of data was made in collaboration with: Ingrid Brännström, Charlotta Edlund, Christer Norman, Mats Erntell, Annika Hahlin, Mikael Hoffmann, Gunnar Kahlmeter, Johan Struwe and Christina Åhrén.

Data on antibiotic use in relation to number of admissions and number of patient days in somatic hospital care during 2013-2017 were kindly provided by pharmacists in local Strama-groups.

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

Complementary epidemiological information on clinical notifications has been performed by the local County Departments for Communicable Disease Control.

Thank you to Kerstin Ortman and Hanna Arosenius at Animalycen, Skara for kindly providing SVA with clinical isolates and susceptibility results from clinical submissions from animals.

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

Content

Sammanfattning/Summary

Sammanfattning

När det gäller antibiotikaresistens hos bakterier från människor och djur har Sverige fortfarande en gynnsam situation, ur ett internationellt perspektiv. Detta stöder att vi har effektiva strategier för att främja rationell användning av antibiotika och begränsa spridningen av antibiotikaresistens. Antibiotikaanvändningen i Sverige har under de senaste årtiondena minskat inom både humanmedicin och veterinärmedicin. Trots det ökar de flesta typer av resistens som övervakas hos människor och i några fall ses ökningar också hos djur. Den trenden har pågått sedan den nationella övervakningen startade i slutet av 90-talet.

De viktigaste resultaten i årets rapport är en minskning av antalet fall av MRSA och ESBL, att fallen av $ESBL_{CARBA}$ bland Enterobacteriaceae hos människor kvarstår vid den tidigare nivån (ca 120 fall/år), flera utbrott av VRE på sjukhus, i likhet med de föregående åren och en fortsatt minskande förekomst av Clostridum difficile infektion. Föregående års ökande förekomst av MRSA och ESBL i samband med det stora antalet asylsökande, visar på den stora betydelsen av resande och vistelse i högendemiska områden för spridning av dessa. Ingen ökad smittspridning av MRSA på sjukhus har setts i samband med detta och den risken bedöms som liten även i framtiden, eftersom förebyggande arbete under lång tid har hållit smittspridning av MRSA inom sjukvården på en låg nivå.

De extremt resistenta bakterierna $ESBL_{CARBA}$ är hittills ovanliga i Sverige men det är mycket viktigt att upptäcka dem tidigt och förebygga spridningen inom vården, eftersom det finns få eller inga behandlingsalternativ vid en eventuell infektion.

MRSA är ovanliga hos både lantbrukets djur och sällskapsdjur i Sverige. Även ESBL är ovanligt hos djur, med undantag för slaktkycklingar, och $ESBL_{CARBA}$ har inte påvisats hos några djur i Sverige.

Årets rapport visar även att försäljningen av antibiotika fortsätter att minska inom humanmedicinen. Även inom veterinärmedicinen har försäljningen minskat över tid.

Förbrukning av antibiotika

Antibiotikaförbrukning inom humanmedicin

Den totala antibiotikaförsäljningen (öppenvård och slutenvård) minskade med 1,9 procent (från 12,5 till 12,3 DDD per tusen invånare och dag) under 2017 jämfört med 2016.

Öppenvård

I öppenvården (all antibiotika försåld på recept) minskade försäljningen med 2,8 procent, från 318 till 309 recept per tusen invånare och år. Försäljningen minskade i alla åldersgrupper och störst minskning sågs bland barn 0-6 år. Försäljningen i denna åldersgrupp minskade med 7,2 procent jämfört med 2016 och innefattar de flesta antibiotikagrupper med undantag av kombinationer av penicilliner, trimetoprim med sulfonamider, makrolider samt nitrofurantoin. Dessa grupper var undantaget mot en generell minskning även bland övriga åldersgrupper. Försäljningen till kvinnor är större än den till män i majoriteten av alla åldersgrupper.

Betalaktamaskänsliga penicilliner var tillsammans med tetracykliner och betalaktamasresistenta penicilliner de antibiotika som såldes mest på recept under 2017. Antibiotika som ofta används mot luftvägsinfektioner försäljs mest på recept och det är även inom denna grupp som den största minskningen över tid skett. Under 2017 fortsatte denna minskning med 4,1 procent. Försäljningen av cefalosporiner minskade med 41 procent jämfört med 2016.

Behandlingen av nedre urinvägsinfektioner (UVI) hos kvinnor ser ut att fortsätta följa de nationella behandlingsrekommendationerna. Under 2017 minskade den totala försäljningen av UVI-antibiotika till kvinnor 18–79 år något (1,1 procent) jämfört med 2016. Under året fortsatte också den trend som setts under de senaste åren med en ökad försäljning av förstahandspreparatet nitrofurantoin, och en minskad försäljning av de breda och mer resistansdrivande preparaten trimetoprim och fluorokinoloner.

Den totala försäljningen av antibiotika som ofta används mot UVI till män 65 år och äldre var oförändrad under 2017 jämfört med 2016. Försäljningen av fluorokinoloner till denna grupp fortsatte att minska (4,3 procent) jämfört med året innan, medan försäljningen av pivmecillinam och nitrofurantoin ökade (4,1 respektive 10,3 procent).

Antibiotikaförsäljningen minskade i 19 av 21 län. Skillnaderna mellan länen är fortfarande stora; från 353 recept per tusen invånare och år i region Gotland till 246 i Västerbottens län.

Försäljningen av antibiotika förskriven av tandläkare står för cirka 6 procent av den totala antibiotikaförsäljningen på recept. Under 2017 fortsatte försäljningen att minska, från 22 till 21 recept per tusen invånare och år (J01 inklusive metronidazol P01AB01).

Slutenvård

Den totala mängden antibiotika som sålts på rekvisition till slutenvården har legat på ungefär samma nivå sedan 2007. Under 2017 minskade försäljningen från 1,58 DDD per 1 000 invånare och dag till 1,53 DDD per 1000 invånare och dag. Under de senaste åren har försäljningen av betalaktamasresistenta penicilliner, betalaktamaskänsliga penicilliner samt kombinationer av penicilliner inom sjukhusvården ökat. Karbapenemer minskade något under 2017, vilket kan indikera en förändring av den tidigare stadigt ökande trenden. Kombinationer av penicilliner, i vilken grupp Piperacillin med tazobactam utgör den största delen, minskade efter många års ökning under 2017. Detta tros förklaras av restnoteringar av dessa preparat. Sett över en längre period, har

försäljningen av betalaktamasresistenta penicilliner och betalaktamaskänsliga penicilliner ökat till att bli de antibiotikagrupper som försäljs mest på slutenvårdsrekvisition i Sverige.

Antibiotikaförbrukning inom veterinärmedicin

Den rapporterade försäljningen av antibiotika för djur uppgick 2017 till 10 310 kilogram varav 57 procent var bensylpenicillin. Siffran inkluderar produkter för lokalbehandling i juvret. Motsvarande värden för 2008 var 16 364 kilogram och 47 procent bensylpenicillin.

Den totala försäljningen av antibiotika för djur har minskat med cirka två tredjedelar sedan 1986 då användningen av tillväxtbefrämjande antibiotika upphörde, korrigerat för att antalet av vissa djurarter har minskat över tid. Under 90-talet minskade användningen av antibiotika som läkemedel till hela djurgrupper, och under det senaste decenniet ses också en minskad användning av antibiotika för behandling av enstaka djur.

Jämförelse av försäljning inom human- och veterinärmedicin

Under 2017 såldes 60,8 respektive 10,2 ton antibiotika för allmänbehandling inom human- och veterinärmedicin. Mätt som milligram aktiv substans per skattad kilogram biomassa var förbrukningen 90,5 respektive 12,8 milligram per kilogram. Försäljning inom humanmedicin dominerade för alla antibiotikaklasser utom trimetoprim-sulfa och aminoglykosider.

Anmälningspliktig resistens

ESBL-producerande Enterobacteriaceae

År 2017 rapporterades totalt 10 084 fall av Enterobacteriaceae med betalaktamaser med utvidgat spektrum (ESBL) hos människa, vilket var en minskning med fem procent jämfört med året innan. Färre fall rapporterades från 11 av 21 län och regioner, och som tidigare år var Escherichia coli den vanligaste arten och förekom i 86 procent av fallen. Klebsiella pneumoniae var näst vanligast med 10 procent. De flesta fynden av ESBL gjordes i urinprov. År 2017 anmäldes 594 fall av invasiva infektioner med ESBL-producerande bakterier, jämfört med 609 året innan.

ESBL-typen $ESBL_{CARBA}$ innebär även resistens mot karbapenemer, och Enterobacteriaceae med denna resistens blev under 2012 anmälningspliktiga för både den behandlande läkaren och laboratoriet som gör fyndet. Totalt 116 nya fall upptäcktes 2017 (127 fall 2016), och de två vanligaste enzymtyperna var OXA-48 och NDM. Ett utbrott med OXA-48 producerande E. coli sågs under året med fem fall. Dessa extremt resistenta bakterier är hittills ovanliga i Sverige men det är mycket viktigt att upptäcka dem tidigt och förebygga spridningen inom vården, eftersom det finns få eller inga behandlingsalternativ vid en eventuell infektion.

Bakterier som bildar ESBL är ovanliga hos djur i Sverige, med undantag för slaktkycklingar. Under 2017 undersöktes förekomsten av ESBL-bildande E. coli i tarm- och köttprov från gris, köttprov från nöt samt i tarmprov från slaktkyckling med selektiva metoder. Sådana bakterier hittades i 4 procent av tarmproven från gris och i 0 respektive <1 procent av proven från gris- respektive nötkött av svenskt ursprung. Vidare hittades sådana bakterier i 34 procent av tarmproven från slaktkyckling. Förekomsten i tarmprov är jämförbar med föregående år. Det är dock svårt att göra direkta jämförelser längre bak i tiden på grund av förändringar i odlingsmetoderna.

MRSA

Totalt anmäldes 3 375 nya fall av meticillinresistenta Staphylococcus aureus (MRSA) hos människa 2017, vilket är en minskning med 15 procent från året innan. Efter den snabba ökningen av fall 2015–2016 ses en återgång till tidigare mer långsam ökningstakt. Den kraftiga ökningen 2015–2016 berodde på det stora antalet asylsökande som togs emot, varav många kom från länder med en högre förekomst av MRSA än genomsnittet i Sverige. Provtagningen i den gruppen är också större än i den övriga befolkningen eftersom de har fler kontakter med sjukvården.

Nästan lika många fall var smittade i Sverige som utomlands. Samhällsförvärvad smitta var vanligare bland de inhemskt smittade fallen (72 procent) än bland de som smittats utomlands (53 procent), medan sjukhusförvärvad smitta var vanligare bland importerade fall (22 procent) än bland inhemska (7 procent). Invasiva infektioner med MRSA rapporterades hos 55 personer under 2017.

MRSA är anmälningspliktig hos djur i Sverige. Förekomsten är fortfarande låg, vilket begränsar risken för spridning till människor. Under året isolerades MRSA från djurslagen häst, hund, katt, kanin, nötkreatur, get och får. MRSA med mecC påvisades hos ett flertal djur i en getbesättning. 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, men andra typer förekommer. Vid två tillfällen under 2017 misstänktes smittspridning mellan hästar i djursjukvårdsverksamhet.

MRSP

Under 2017 var antalet anmälda fall av meticillinresistenta Staphylococcus pseudintermedius (MRSP) hos djur på samma nivå som 2016. Totalt anmäldes 47 fall av MRSP, vilket kan jämföras med 55 fall 2016 och 60 fall 2015. Tidigare år har klonen ST71 dominerat bland de svenska fallen, men läget har blivit mer varierande. Klonerna ST71 och ST258 är vanligast men ett flertal andra typer har också påvisats 2017. MRSP är inte anmälningspliktig vid förekomst hos människa.

PNSP

År 2017 anmäldes 61 fall, varav 5 fall var invasiva, jämfört med 2016 då 67 fall av Streptococcus pneumoniae med nedsatt känslighet för penicillin (PNSP) anmäldes. Antalet fall per år är betydligt lägre efter 2012, då definitionen för vilka fall som ska rapporteras ändrades.

VRE

År 2017 anmäldes 244 nya fall av vankomycinresistenta enterokocker (VRE) hos människa, och 2016 anmäldes 165 fall. Enterococcus faecium med vanA (161 fall) var vanligare än vanB (68 fall). Fyra stora smittspridningar på sjukhus förekom under 2017. Under tidigare år med stora smittspridningar på sjukhus har vanB dominerat. Två invasiva isolat av VRE rapporterades 2017.

Resistens hos zoonotiska smittämnen

Salmonella är ovanligt hos djur i Sverige och isolerade stammar är oftast känsliga för antibiotika. Överförbar resistens mot tredje generationens cefalosporiner har aldrig påvisats hos isolat från djur i Sverige, och resistens mot antibiotikagruppen fluorokinoloner är mycket ovanlig. Människor som diagnosticeras med Salmonella i Sverige har oftast smittats utomlands eller via importerade livsmedel. Detta är sannolikt förklaringen till att resistens, exempelvis mot fluorokinoloner, är mycket vanligare hos isolat från människor än hos isolat från svenska djur.

Campylobacter-stammar från djur i Sverige är oftast känsliga för relevanta antibiotika och exempelvis är resistens mot erytromycin mycket ovanligt.

Vanligtvis behandlas inte infektioner som orsakas av Salmonella eller Campylobacter med antibiotika, varken hos människor eller hos djur. Se vidare avsnittet ”Comparative analysis” för respektive bakterie.

Resistens hos kliniska isolat från människor

I årets Swedres-Svarm sammanställs nästan all data från kliniska odlingar från Svebar. Det är ett system som automatiskt samlar in alla odlingsresultat från de 19 laboratorier som deltar. Till skillnad från tidigare års data kommer nu upprepade resultat från samma individ att räknas med. Det förväntas medföra vissa skillnader i resistensnivå, särskilt för bakteriearter med litet antal isolat och för ovanliga resistenstyper.

Hos E. coli och Klebsiella pneumoniae har andelen cefalosporinresistenta (till största delen orsakad av ESBL-produktion) isolat funna i blod ökat gradvis och uppgick till ca 7,3 respektive 5,4 procent 2017. Andelen MRSA av ca 47 000 fynd av S. aureus i hud- och mjukdelsinfektioner var 1,8 procent, vilket är lågt ur ett europeiskt perspektiv. Andelen PNSP av de cirka 2 500 testade isolaten av S. pneumoniae från nasofarynx var ca 12 procent. För invasiva Enterococcus faecalis var andelen resistenta mot vankomycin 0,5 procent medan ingen vankomycinresistens hittades bland invasiva Enterococcus faecium.

För vissa bakteriearter finns speciella övervakningsprogram och/eller speciallaboratorier som kan utföra analyserna. Det gäller dels Clostridium difficile, dels bakteriearterna Neisseria gonorrhoeae, Neisseria meningitidis och Mycobacterium tuberculosis.

Under 2017 rapporterades 6 466 nya fall av Clostridium difficile infektion, vilket motsvarar en incidens av 64 fall per 100 000 invånare och år. Det är något färre fall än 2016.

Inga isolat med resistens mot metronidazol eller vankomycin hittades 2017.

Under 2017 anmäldes 2 531 fall av gonorré. Andelen med resistens mot cefixim var 0,6 procent och ingen resistens mot ceftriaxon påvisades. Det är mycket positivt eftersom ceftriaxon är det sista tillgängliga medlet för empirisk behandling av gonorré.

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 Staphylococcus felis från katter. Resistens hos E. coli från olika djurslag förekommer också men är vanligast hos isolat från träckprover från unga kalvar. Resistensundersökning är motiverat för val av lämpligt antibiotikum vid behandling, särskilt för stafylokocker, E. coli och Brachyspira spp.

Indikatorbakterier från friska djur

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

Summary

The situation in Sweden regarding antibiotic resistance in bacteria 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. In the last decades the consumption of antibiotics in Sweden has decreased in both humans and in veterinary medicine. Despite this, most of the monitored types of antibiotic resistance in bacteria from humans have continued to increase since national surveillance began in the late 1990s. This is, in some cases, also true for bacteria from animals.

The key findings in this year's report are a lower number of cases of methicillin-resistant *Staphylococcus aureus* (MRSA) and ESBL, that the cases of carbapenemase-producing Enterobacteriaceae ($ESBL_{CARBA}$) in humans remains at around 120 cases per year, several outbreaks of VRE in hospitals, as in previous years, and a continuing decrease in the occurrence of *Clostridium difficile* infections. Previous years increased number of cases of MRSA and ESBL associated with the high number of refugees seeking asylum highlights the importance of travelling for the spread of these resistant bacteria. This increase in MRSA has not led to an increased spread in hospitals, and future risk of such spread is considered small, as preventive measures during several years has succeeded in maintaining the spread of MRSA in health care at a low level.

The extremely resistant bacteria $ESBL_{CARBA}$ are so far uncommon in Sweden, and it is important to detect them early and prevent dissemination in health care.

In the veterinary sector, MRSA is rare in both farm and companion animals in Sweden. ESBL-producing Enterobacteriaceae are, with the exception of broilers, rare among animals in Sweden and $ESBL_{CARBA}$ has not been reported.

This year's report also show that the consumption of antibiotics has continued to decrease in human medicine. Within veterinary medicine has the consumption of antibiotics also decreased over time.

Consumption of antibiotics

Antibiotic consumption in humans

The total antibiotic sale (including outpatient care and hospital care) decreased by 1.9% in 2017 compared with 2016 (from 12.5 to 12.3 DDD per 1 000 inhabitants and day).

Outpatient care

In outpatient care (including prescription sales), antibiotic sales decreased by 2.8% from 318 to 309 prescriptions per 1 000 inhabitants. The sales decreased in all age groups with the greatest decrease seen among children 0-6 years. The sales in this age group decrease by 7.2% compared with 2016. The decrease encompasses most antibiotic groups with the exception of combinations of penicillins, trimethoprim with sulphonamides, macrolides and nitrofurantoin. Overall, women are prescribed more antibiotics than men.

Beta-lactamase sensitive penicillins, along with tetracyclines and beta-lactamase resistant penicillins, were the most commonly used antibiotics in outpatient care in 2017. Antibiotics commonly used to treat respiratory tract infections were the most frequently sold antibiotics. These substances have decreased most over time out of all types of antibiotics. In 2017 the trend continued with a decrease in sales of these drugs of 4.1% compared with 2016. Cephalosporins decreased by 41% between 2016 and 2017.

Treatment of lower urinary tract infections (UTIs) in women appears to be following national treatment recommendations. In 2017, the total sale of antibiotics commonly used to treat UTIs in women aged 18–79 years decreased by 1.1% compared with 2016. Sales increased for the recommended drug, nitrofurantoin, and decreased for trimethoprim and fluoroquinolones. These trends are also seen when it comes to UTI antibiotics to men with decreasing sales over time.

In 2017, the total sales of antibiotics commonly used to treat UTIs in men 65 years and older remained the same as in 2016. However, the sales of fluoroquinolones decreased by 4.3% compared with 2016, while the sales of pivmecillinam and nitrofurantoin both increased, by 4.1% and 10.3% respectively (measured as prescriptions per 1 000 men per year).

The sales of antibiotics decreased in 19 of Sweden's 21 counties. There are still major regional differences within Sweden and the number of prescriptions per 1 000 inhabitants ranges from 353 in Gotland County to 246 in Västerbotten County.

Dentists account for approximately 6% of all antibiotics prescribed in outpatient care in Sweden. In 2017 the sales of J01 and metronidazole (P01AB01) prescribed by dentists continued to decrease, from 22 to 21 prescriptions per 1 000 inhabitants.

Hospital care

The total antibiotic sale to hospital care in Sweden has been relatively stable since 2007. During 2017 the sales decreased slightly compared with 2016, from 1.58 DDD per 1 000 inhabitants and day to 1.53 DDD per 1 000 inhabitants and day. In acute care hospitals, there has been a significant increase in sales of beta-lactamase resistant penicillins, beta-lactamase sensitive penicillins and combinations of penicillins the last years. Carbapenems decreased slightly in 2017, which might indicate a change of the former increasing trend of this substance. After many years of increase, sales of Combinations of penicillins (in which Piperacillin with tazobactam (J01CR05) represents the biggest proportion) decreased for the first time in several years (7%). This can be explained by shortages of these substances. In general, the sales of narrow spectrum antibiotics have increased in the last years and are the groups that are used the most in hospital care in Sweden.

Sales of antibiotics for animals

In 2017, reported sales of antibiotics for animals were 10 310 kg, of which 57% were for benzylpenicillin. The corresponding figures for 2008 were 16 364 kg and 47%, respectively. These figures include products for intramammary treatment.

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

Comparing consumption of antibiotics in human and veterinary medicine

In 2017, a total of 60.8 tonnes of antibiotics were sold for human use and 10.2 tonnes were sold for animal use. Measured as milligrams of active substance per kilogram biomass, the consumption was 90.5 and 12.8 milligrams per kilogram, respectively. Consumption by humans still dominates for all classes of antibiotics except for trimethoprim-sulphonamides and aminoglycosides.

Notifiable resistance

ESBL

A total of 10 084 human cases of extended spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae were reported in 2017, a decrease with 5% compared to 2017, and 11 of Sweden's 21 counties reported less cases. The most commonly reported species was *Escherichia coli* with 86% of all cases followed by *Klebsiella pneumoniae* with 10%. Most ESBL-producing bacteria were found in urine samples. Invasive infections with ESBL-producing bacteria were reported in 594 cases in 2017 compared to 609 cases in 2016.

A special type of ESBLs, so-called $ESBL_{CARBA}$, confers resistance to carbapenems as well as other classes of beta-lactam antibiotics. Bacteria with this extended resistance mechanism are notifiable for both clinicians and laboratories since 2012. A total of 116 new cases were detected in 2017 compared to 127 cases 2016, and the two most common types of enzymes were OXA-48 and NDM. An hospital-related outbreak with an OXA-48 producing *E. coli* was detected during the year with five cases. As the treatment alternatives for these infections are few if any, it is necessary to undertake active surveillance of these new and extremely resistant bacteria in order to detect them at an early stage and thereby prevent their spread within the health care system.

ESBL-producing Enterobacteriaceae are, with the exception of broilers, rare among animals in Sweden. In 2017, the occurrence of ESBL-producing *E. coli* in intestinal samples from pigs, samples of pork and beef, and in intestinal samples from broilers was investigated with screening methods. Such bacteria were isolated from 4% of the intestinal samples from pigs, 0 and <1% of the pork and beef samples of Swedish origin, and 34% of the intestinal samples from broilers. The occurrence in intestinal samples from broilers was comparable with previous years. Changes in the screening methodology prevent any direct comparisons with the figures from previous years.

MRSA

The total number of human cases of MRSA was 3 375 in 2017, a decrease with 15% compared to 2016. After the sharp increase of cases seen in 2015–2016 the rate of increase seems to decline to the slower rate seen in previous years. The increase during 2015–2016 was mainly comprised of cases among persons seeking asylum and was likely due to higher prevalence, increased need for medical care, and increased sampling in this group. No increased spread of MRSA in hospitals has been reported in connection with this increase among persons seeking asylum, nor has there been a progressive increase in domestic cases of MRSA in the general population.

A nearly equal number of MRSA infections were acquired in Sweden and abroad. Community-acquired infections dominated among domestic cases (72%) and were less frequent among imported cases (53%). Hospital-acquired infections were comparatively more common in imported cases (22%) than among domestic cases (7%). Fifty-five invasive isolates of MRSA were reported in 2017.

MRSA is notifiable in animals in Sweden. The occurrence is still low, which limits the spread from animals to humans. In 2017, MRSA was isolated from the animal species horse, dog, cat, rabbit, cattle, goat and sheep. MRSA with *mecC* was isolated from several animals in a goat herd. 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 CC398 is the most common type but other types occur. At two occasions in 2017, spread of MRSA was suspected between horses in equine clinic facilities.

MRSP

In 2017, the number of notified cases of methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) was on the same level as 2016. In total, 47 cases were notified in 2017, which can be compared to 55 cases in 2016 and 60 cases in 2015. All cases in 2017 were dogs. In previous years, the clone ST71 has dominated among Swedish cases, but now the picture is becoming more diverse. The clones ST71 and ST258 are most common but several other types were also detected in 2017. MRSP in humans is not notifiable.

PNSP

Sixty-one cases of pneumococci with reduced susceptibility to penicillin (PNSP, defined as MIC > 1 mg/L) were reported in 2017, and in 2016 there were 67 reported cases. Five invasive cases were reported.

VRE

In 2017, a total of 244 new cases of vancomycin-resistant enterococci (VRE) were reported compared to 165 cases in 2016. *Enterococcus faecium* carrying the resistance gene *vanA* (161 cases) was more common than those carrying *vanB* (68 cases). In 2017 there were four large hospital outbreaks reported. During earlier years with large hospital outbreaks, *vanB* has been the most common resistance gene. Two invasive VRE infection were reported in 2017.

Zoonotic pathogens

Salmonella is rare in animals in Sweden, and few incidents involve antibiotic-resistant strains. Strains with ESBL resistance have never been found in isolates from animals in Sweden, and resistance to fluoroquinolones is rare. Usually humans diagnosed with Salmonella in Sweden has contracted the infection abroad or through imported foodstuffs. This is most likely the explanation to the higher levels of resistance, e.g. to fluoroquinolones, in isolates from humans than in isolates from Swedish animals.

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

Infections, either in humans or in animals, caused by *Salmonella* and *Campylobacter* are usually not treated with antibiotics. See the "Comparative analysis" section of each bacterium.

Human clinical isolates

In this Swedres-Svarm report almost all data on clinical isolates from humans have been collected through Svebar. This is an automated system that collects all culture results from participating laboratories. Currently 19 laboratories deliver data to Svebar. In contrast to previous years, the data for this year will contain all culture results from different individuals, e.g. duplicate findings from blood cultures. This is expected to cause some differences in resistance levels, especially for species isolated less frequently and for unusual resistance types.

In *E. coli* and *K. pneumoniae* from blood, the levels of resistance to third-generation cephalosporins has increased continually, and is now approximately 6% and 5.4%, respectively. MRSA isolates accounted for 1.8% of *S. aureus* from skin and soft tissue infection, which is low from a European perspective. The rate of non-susceptibility to penicillins in *Streptococcus pneumoniae* from nasopharynx (referred to as PNSP) was 12% in 2017. For invasive *E. faecalis* the rate of vancomycin resistance was 0.5 % and no vancomycin resistance was found among invasive *E. faecium*.

Other bacterial species are included in special surveillance programmes and are often referred to special laboratories, including *C. difficile*, *Mycobacterium tuberculosis*, *Neisseria gonorrhoeae*, and *N. meningitidis*.

In 2017, 6 466 new CDI cases were reported corresponding to an incidence of 64 cases per 100 000 inhabitants, a little less cases than in 2016. No isolates resistant against metronidazole or vancomycin were found in 2017.

In 2017, 2 531 cases of gonorrhea were reported. Resistance to cefixime was 0.6%, and no resistance to ceftriaxone was detected. This is a very positive result because ceftriaxone is the last available agent for the empirical treatment of gonorrhoea.

Animal clinical isolates

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

Indicator bacteria from healthy animals

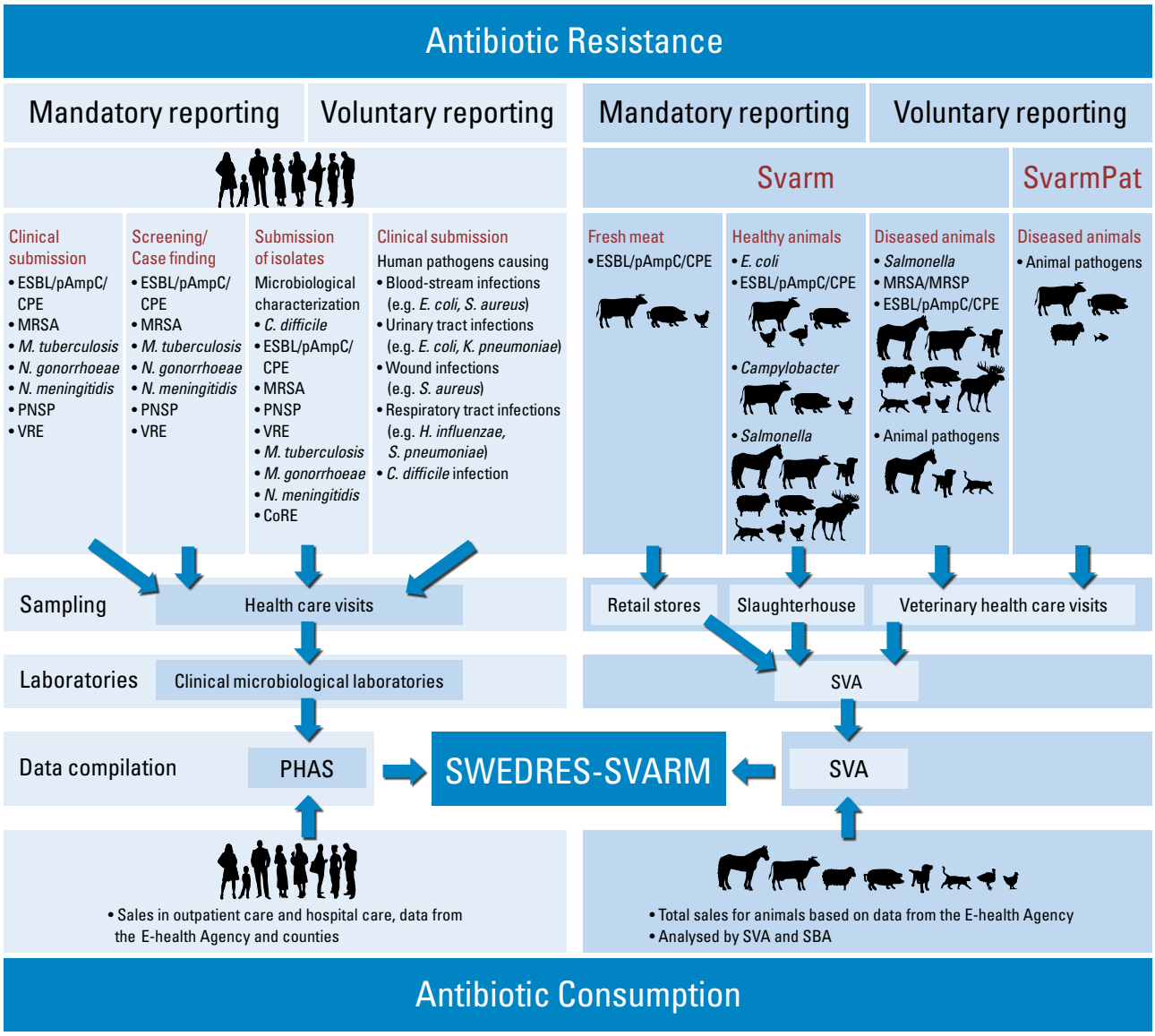
Antibiotic resistance in *E. coli* from the intestinal flora of healthy animals serves as an indicator for the presence of resistance in an animal population. The prevalence of acquired resistance in such commensal bacteria also indirectly indicates the magnitude of the selective pressure from the use of antibiotics in an animal population. The prevalence of resistance in indicator bacteria from animals in Sweden is 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 (FOHM) and the National Veterinary Institute (SVA) with the aim to present data relating to both humans and animals on the use of antibiotics and on antibiotic resistance in a joint report.

Data on occurrence of notifiable diseases caused by resistant bacteria as well as data on resistance in zoonotic bacteria and in bacteria from clinical submissions are presented. In addition, data on resistance in so called indicator bacteria from healthy animals and from food of animal origin are presented. The report also describe the sales of antibiotics in humans and animals.

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 organized 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. Data on sales of antibiotics among humans are achieved from the eHealth Agency and counties. Data on sales of antibiotics among animals are achieved from the eHealth Agency. For details on data sources see Background data, material, methods and references.



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 any version of Adobe Acrobat Reader.

Antibiotic consumption

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

Comparison of antibiotic sales in different counties 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, and data on these sales are included in outpatient care data. However, there are also nursing homes where medicines are bought by the institution and then dispensed to the residents. Such sales are included in hospital care data. Since routines differ between counties 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 18-79 years, inhabitants in a county), the denominator is the number of individuals in the same group, provided in the eHealth Agency Database Concise.

In this report the term outpatient care includes all antibiotic sales on prescriptions. Hospital care includes antibiotic sales on hospital requisition (including hospitals, parts of nursing homes and other care units). Since national data on sales of antibiotics to hospitals in Sweden are aggregated with sales to some nursing homes, this is not suitable for evaluation of antibiotic use in hospital care. Therefore, data on sales exclusively to acute care hospitals have been provided by pharmacists in local Strama groups in all counties.

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

Antibiotic resistance

Swedres - Humans

Most of the data on resistance in Swedres are derived from routine diagnostic samples sent for testing at clinical laboratories. The results are mostly presented as proportion resistance in tables or graphs. The methods used for antibiotic susceptibility testing, whether MIC determination or disk diffusion inhibition zones, are standardized by European Committee on Antimicrobial Susceptibility Testing (EUCAST) and available online at www.eucast.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 *Clostridium 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, 2013). Results for isolates of zoonotic and indicator bacteria are interpreted by ECOFFs from EUCAST (www.eucast.org) and also, 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
Bac	Bacitracin	Flf	Florfenicol	Oxa	Oxacillin
Caz	Ceftazidime	Fox	Cefoxitin	Pen	Penicillin G
Cdr	Cefadroxil	Fus	Fusidic acid	Ptz	Piperacillin-Tazobactam
Cer	Ceftiofur	Gen	Gentamicin	Rif	Rifampicin
Cet	Cephalothin	Imp	Imipenem	Str	Streptomycin
Chl	Chloramphenicol	Kan	Kanamycin	Sul	Sulphonamide
Cip	Ciprofloxacin	Lin	Linezolid	Tet	Tetracycline
Cli	Clindamycin	Mec	Mecillinam	Tmp	Trimethoprim
Col	Colistin	Mer	Meropenem	Tsu	Trimethoprim-sulfonamide
Ctx	Cefotaxime	Nal	Nalidixic acid	Tob	Tobramycin
Enr	Enrofloxacin	Nar	Narasin	Van	Vancomycin

Abbreviations

AST	Antimicrobial Susceptibility Testing
ATC	Anatomical therapeutic chemical classification system
BLNAR	Beta-lactamase negative ampicillin resistant (in *Haemophilus influenzae*)
CC	Clonal complex used in the context of epidemiological typing
CDI	*Clostridium difficile* infection
CMO	County medical officer
CPE	Carbapenemase producing Enterobacteriaceae
CoRE	Colistin resistant Enterobacteriaceae
DDD	Defined daily dose
ECDC	European Centre for Disease Prevention and Control
ECOFF	Epidemiological cut-off value for non-susceptibility
EARSS/EARS-Net	European antimicrobial resistance surveillance system/network
ESC	Extended spectrum cephalosporin
ESBL	Extended spectrum beta-lactamase
$ESBL_A$	Extended spectrum beta-lactamase, plasmid-mediated, inhibited by clavulanic acid (A = classical)
$ESBL_M$	Extended spectrum beta-lactamase inhibited by cloxacillin, also called plasmid-mediated AmpC (M = miscellaneous)
$ESBL_{CARBA}$	Extended spectrum beta-lactamase with activity against carbapenems
EUCAST	European Committee on Antimicrobial Susceptibility Testing
GAS	Group A streptococci or *Streptococcus pyogenes*
GBS	Group B streptococci or *Streptococcus agalactiae*
HLAR	High-level aminoglycoside resistance (e.g. in *Enterococcus*)
MALDI-TOF MS	Matrix-assisted-laser-desorption/ionization time-of-flight mass spectrometry
MDR	Multidrug resistance, i.e. phenotypic resistance to three or more antibiotic classes
MIC	Minimal inhibitory concentration
MLST	Multilocus sequence typing
MRB	Multi-resistant bacteria
MRSA	Methicillin-resistant *Staphylococcus aureus*
MRSP	Methicillin-resistant *Staphylococcus pseudintermedius*
NordicAST	Nordic Committee on Antimicrobial Susceptibility Testing
PHAS	PHAS the Public Health Agency of Sweden
PNSP	Penicillin non-susceptible pneumococci
PVL	Panton-Valentine leukocidin
ResNet	Webb application for resistance surveillance and quality control programme
RTI	Respiratory tract infection
spa	*Staphylococcus aureus* protein A gene
SSTI	Skin and soft tissue infection
ST	Sequence type
Strama	Swedish strategic programme against antibiotic resistance
TB	Tuberculosis
RSV	Respiratory syncytial virus
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

In 2017, the total sales of antibiotics (J01 excl. methenamine) in Sweden (outpatient care and hospital care) decreased by 1.9% compared with 2016 (12.5 to 12.3 DDD per 1 000 inhabitants and day). The overall sales of antibiotics in Sweden has decreased by 15.4% since 2000. The total sales differs within the country, from 14.1 DDD per 1 000 inhabitants and day in Gotland County to 9.9 in Jämtland County, Figure 1.1.

Just under eighty-nine (88.6) percent of all the total sales of antibiotics in Sweden 2017 were sold on prescriptions in outpatient care and the proportion is similar among the different counties.

Beta-lactamase sensitive penicillins and tetracyclines were the two most sold antibiotic groups in Sweden during 2017. Overall, the use of tetracyclines has decreased and nitrofurantoin, a recommended first-line treatment for urinary tract infections, has increased. The use of fluoroquinolones has decreased in recent years, Figure 1.2.

FIGURE 1.1. Sales of antibiotics (J01 excl. methenamine) in outpatient care (sales on prescriptions) and in hospital care (sales on requisition including hospitals and parts of nursing homes) in Sweden and per county, 2002-2017, DDD/1 000 inhabitants and day. The data are sorted according to the consumption in 2017. The figure shows every third year.

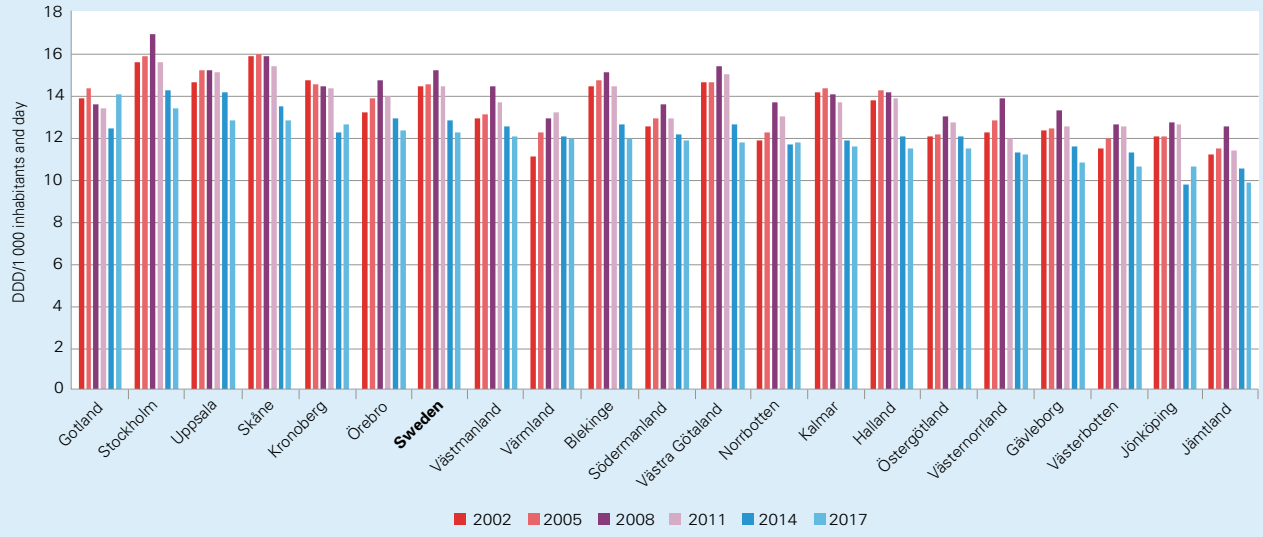
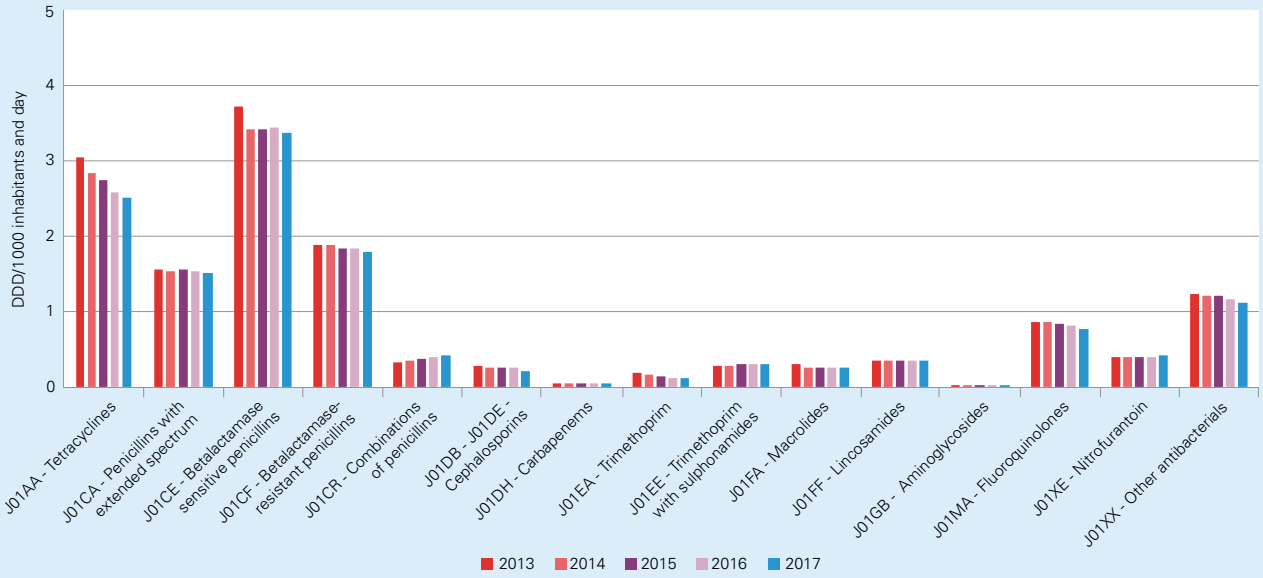


FIGURE 1.2. Sales of antibiotics (ATC-5) in outpatient care (sales on prescriptions) and hospital care (sales on requisition including hospitals and parts of nursing homes) in 2013-2017, DDD/1 000 inhabitants and day. The data are sorted according to ATC codes.



Antibiotics in outpatient care

The statistics for outpatient care reported in Swedres-Svarm includes all sales of antibiotics on prescription, both from healthcare centres and from hospital care.

Since 1992, the total sales of antibiotics on prescriptions has decreased by 44.9%, Figure 1.3. The greatest decrease during these years has been in the 0-4 years age group, where sales decreased by 74.5%, from 1 328 prescriptions per 1 000 inhabitants and year in 1992 to 338 in 2017, Figure 1.3. In addition, less seasonal variation in sales of antibiotics is seen over the years. This indicates a more rational consumption and less misuse of antibiotics for colds or the flu.

The total sales of antibiotics in outpatient care has decreased by 2.8% during 2017 compared with 2016, from 318 to 309 prescriptions per 1 000 inhabitants and year. The antibiotic sales decreased in all age groups during the last year, Figure 1.4, with the greatest decreases in the age groups 0-6 years (7.2%) and 7-19 years (3.5%), followed by the age group 20-64 years, in which the sales decreased by 2.4%. In the age groups 65-79 and among 80 years and older the sales decreased slightly, by 0.2% and 0.1% respectively.

A trend analysis was executed on the changes between 2000 and 2017, Figure 1.4. Since 2000 there has been a significant decrease of antibiotic sales in all age groups ($p < 0.001$). The decrease rate differs between the groups, but focusing on the group. All age groups the decrease rate is accelerating.

The decrease in sales in outpatient care during 2017 encompasses a majority of all antibiotic groups, except combinations of penicillins (J01CR), trimethoprim with sulphonamides (J01EE), macrolides (J01FA) and nitrofurantoin (J01XE), Figure 1.5.

FIGURE 1.3. The sales of antibiotics for systemic use in outpatient care (sales on prescriptions) 1987- 2017, prescriptions/1 000 inhabitants and year, both sexes, different age groups.

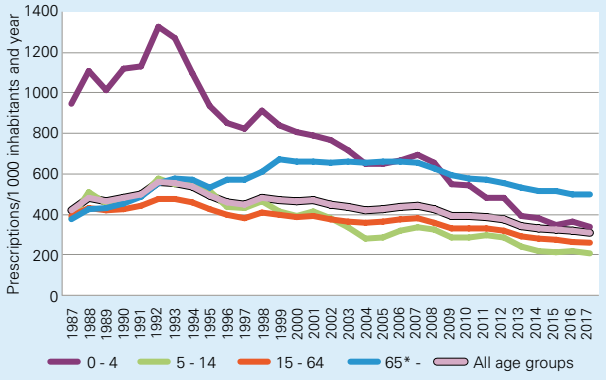


FIGURE 1.4. The sales of antibiotics for systemic use in outpatient care (sales on prescriptions) 2000-2017, prescriptions/1 000 inhabitants and year, both sexes, different age groups.

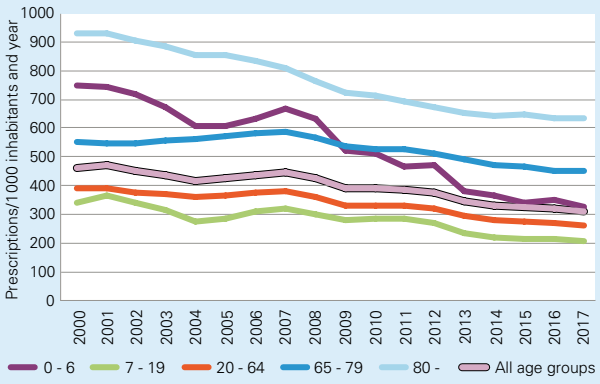
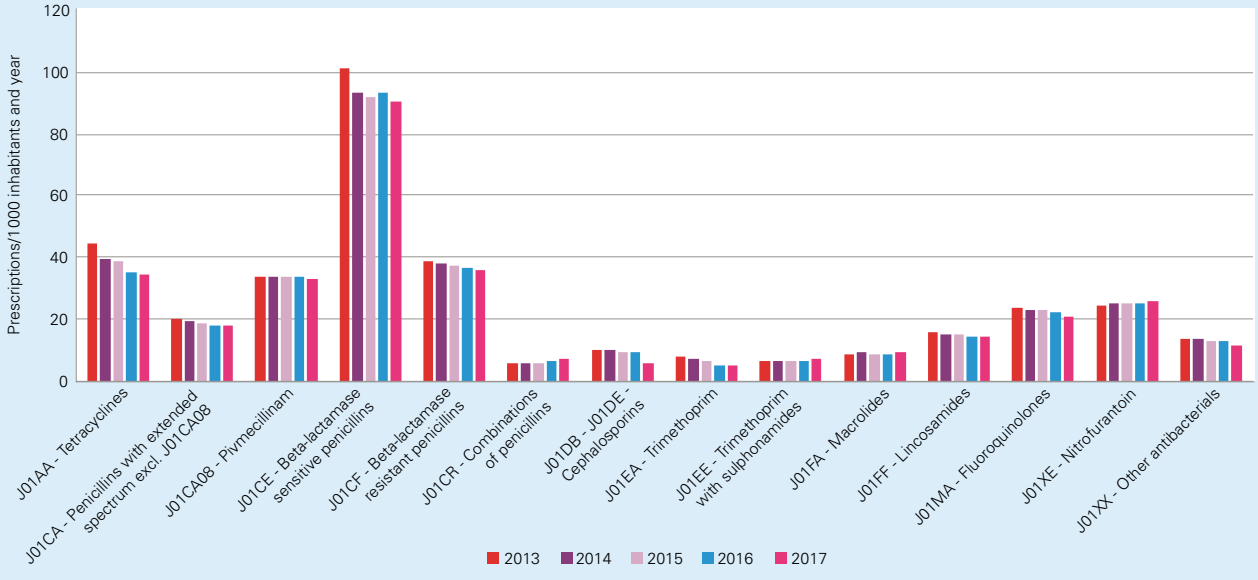


FIGURE 1.5. Sales of antibiotics in outpatient care (includes sales on prescriptions) 2013-2017, prescriptions/1 000 inhabitants and year, both sexes, all ages. The data are sorted according to ATC codes.



Beta-lactamase sensitive penicillins (J01CE) and tetracyclines (J01AA) were the most commonly sold antibiotics in 2017 measured in DDD per 1000 and day. Measured in prescriptions per 1000 inhabitants and year, beta-lactamase sensitive penicillins (J01CE) and beta-lactamase resistant penicillins (J01CF) were the most commonly sold antibiotics, Figure 1.5 and Table 1.1. Doxycycline (J01AA02) is the most frequently sold tetracycline and represents 73.0% of the sales in this group, measured in prescriptions per 1 000 inhabitants and year.

Gender differences

Of all antibiotics prescribed in Sweden during 2017, 60.2% were prescribed to women. This proportion has been stable over time and the decrease in antibiotic sales during the last years has been seen among both sexes equally. During 2017, women were prescribed 367 antibiotic prescriptions per 1 000 inhabitants and year while men were prescribed 243. The antibiotic sales decreased by 2.5% to men and 2.0% to women compared with 2016. The greatest differences in prescriptions between men and women occurred in the age groups 20-39 years (20-24, 25-29 and 30-39). In these age groups, 67-70% of the total antibiotic sales were to women, Figure 1.6. In these age groups, the main differences are seen among antibiotics commonly used to treat urinary tract infections (UTI), which are predominantly sold to women.

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

Antibiotic sales in different ages groups

The antibiotic use is greatest in the age group 80 years and older, 634 prescriptions per 1 000 inhabitants and year (data measured in DDD per 1 000 inhabitants and day are available in the embedded excel file), Figure 1.7. As mentioned in the chapter "Guidance for readers", some parts of the antibiotic use among elderly people are not included in the statistics for outpatient care and a possible underestimation in the age group 80 years and older cannot be ruled out.

In the age group 0-4 years, antibiotics commonly used to treat respiratory tract infections (RTI) are the most frequently prescribed antibiotics, among both women and men, and represent 85% of the total antibiotic sales in this age group for both sexes. RTI antibiotics are prescribed more to women than to men, Figure 1.8 and Figure 1.9. In the older age groups (from 70-79 years for women and 80 years and older for men) there is a shift, where antibiotics commonly used to treat UTI are the most frequently prescribed

FIGURE 1.6. The sales of antibiotics for systemic use in outpatient care (sales on prescriptions) in 2017, prescriptions/1 000 inhabitants and year, gender and different age groups.

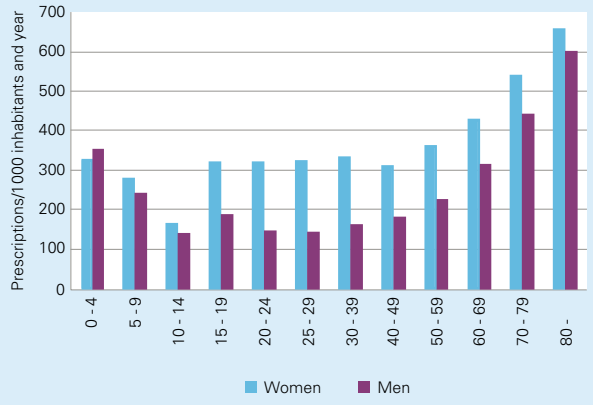


FIGURE 1.7. Sales of antibiotics (J01 excl. methenamine) in outpatient care, prescriptions/1 000 inhabitants and year, different age groups.

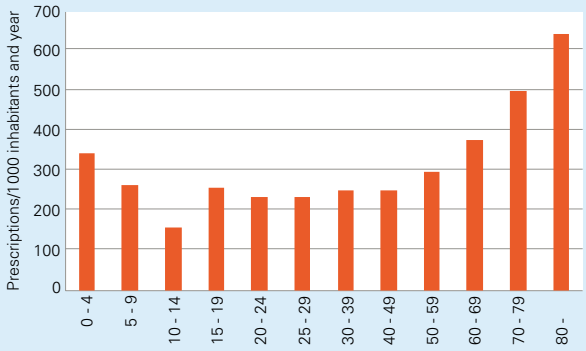
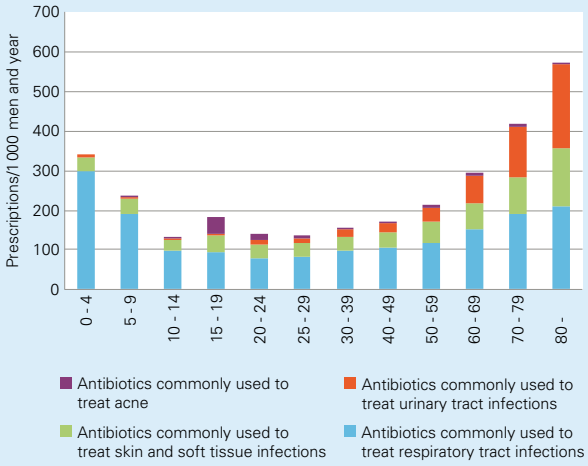


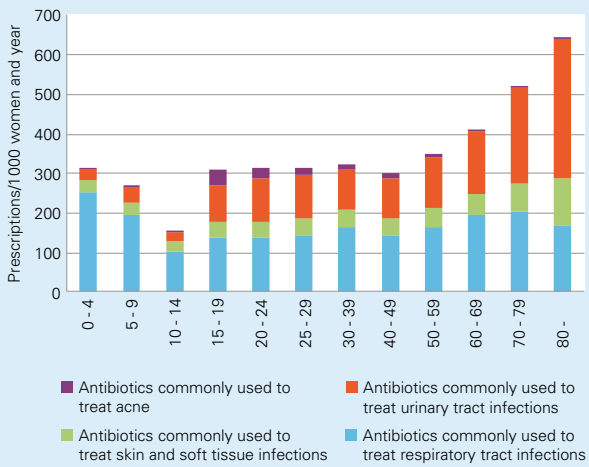
FIGURE 1.8. Antibiotics commonly used to treat RTI, UTI, SSTI and Acne, different age groups, men, prescriptions/1 000 men in 2017.



Antibiotics commonly used to treat RTI=J01AA02[a], J01CE02, J01CA04, J01CR02, J01DB-DE and J01FA. Antibiotics commonly used to treat UTI=J01CA08, J01EA01, J01MA02, J01MA06 and J01XE01. Antibiotics commonly used to treat SSTI=J01FF01 and J01CF05. Antibiotics commonly used to treat acne=J01AA02[b], J01AA04, J01AA06 and J01AA07.

[a] Excluding packages containing more than 50 tablets.
[b] Including packages containing more than 50 tablets.

FIGURE 1.9. Antibiotics commonly used to treat RTI, UTI, SSTI and Acne, different age groups, women, prescriptions/1 000 women in 2017.



Antibiotics commonly used to treat RTI=J01AA02[a], J01CE02, J01CA04, J01CR02, J01DB-DE and J01FA. Antibiotics commonly used to treat UTI=J01CA08, J01EA01, J01MA02, J01MA06 and J01XE01. Antibiotics commonly used to treat SSTI=J01FF01 and J01CF05. Antibiotics commonly used to treat acne=J01AA02[b], J01AA04, J01AA06 and J01AA07.

[a] Excluding packages containing more than 50 tablets.
[b] Including packages containing more than 50 tablets.

antibiotics, Figure 1.8 and Figure 1.9. In contrast, in the age group 15-19 years, antibiotics commonly used to treat acne represent a larger proportion for both sexes. Women in all age groups are prescribed more antibiotics than men (except in the age group 0-4 years), and it applies to all groups of antibiotics.

Antibiotics commonly used to treat respiratory tract infections

Antibiotics commonly used to treat respiratory tract infections (RTI) are overall the most frequently prescribed antibiotics in Sweden. Among these substances, we also find the greatest decrease over time in terms of number of prescriptions per 1 000 inhabitants and year, from 294 in 2000 to 155 in 2017. In 2017, the sales decreased by 4.1% compared with 2016. However, in 2017 the sales did increase for macrolides (J01FA) by 3.1% and amoxicillin with clavulanic acid (J01CR02) by 8.6%. All antibiotics commonly used to treat respiratory tract infections have decreased significantly since 2004 ($p < 0.001$). The decrease rate differs between the substances and among many of them the decrease rate accelerates over time.

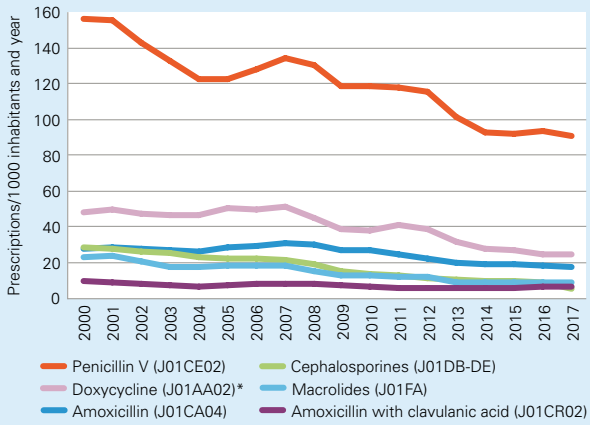
Narrow spectrum penicillin, (J01CE), is the recommended first line antibiotic for treatment of community acquired RTI in Sweden (Medical Products Agency & Strama, 2008) and the most frequently prescribed antibiotic in outpatient care, measured both in DDD per 1 000 inhabitants and day and in prescriptions per 1 000 inhabitants and year, Figure 1.10 and Table 1.1.

Measured in DDD per 1 000 inhabitants and day, tetracyclines are the second most frequently prescribed antibiotics in outpatient care. The sales of tetracyclines commonly used to treat respiratory tract infections (packages containing less than 50 tablets) continued to decrease in 2017 compared to 2016 (2.0%). As doxycycline is used to treat acute bronchitis (including Mycoplasma pneumoniae), the decrease in sales seen during the last five years may indicate an improved compliance to the national treatment recommendations. These state that acute bronchitis generally should not be treated with antibiotics (Medical Products Agency & Strama, 2008).

Beta-lactamase resistant penicillins (J01CF) were the second most frequently prescribed antibiotics in outpatient care measured in prescriptions per 1 000 inhabitants. The sales of this group decreased by 1.9% in 2017 compared with 2016 and represent 11.7% of the total sales of antibiotics in outpatient care in 2017, Table 1.1.

The increased sales of amoxicillin with clavulanic acid seen during the last four years might be a consequence of an increased number of urinary tract infections caused by

FIGURE 1.10. Sales of antibiotics commonly used to treat respiratory tract infections in outpatient care (sales on prescriptions), 2000-2017, prescriptions/1 000 inhabitants and year, both sexes, all ages.



*Excludes packages with more than 50 tablets

ESBL producing bacteria, where amoxicillin with clavulanic acid could possibly be an oral treatment alternative (Public Health Agency of Sweden, 2014). In addition, amoxicillin with clavulanic acid has since 2013 been part of initial sensitivity testing against Enterobacteriaceae for patients with uncomplicated UTI. This might have affected the prescription rate of this substance for this indication (RAF, 2014).

A new national recommendation for treatment of pharyngotonsillitis was published in 2012 (Medical Products Agency & Swedish Institute for Communicable Disease Control, 2012). Successful communication about treatment recommendations may be one contributed explanation for the decreased sales over time of antibiotics commonly used to treat RTI.

Antibiotics commonly used to treat urinary tract infections in women

National treatment recommendations for lower urinary tract infections in women over 18 years (Medical Products Agency, 2017), recommends pivmecillinam and nitrofurantoin before trimethoprim, and prescribers are also encouraged to minimise the use of fluoroquinolones because of the resistance situation. In 2017, the total sales of antibiotics commonly used to treat UTI in women aged 18-79 years decreased by 1.1% compared with 2016. The same positive trend as previous years, with increased use of the first-line drugs pivmecillinam and nitrofurantoin and reduced sales of trimethoprim (10.1%) and fluoroquinolones (3.2%), was also seen, Figure 1.11.

The total sales of these antibiotics have decreased slowly over the years; by 7.7% since 2000, measured in prescriptions per 1 000 women aged 18-79 years and year. However, if measured in DDD per 1 000 women and day, the sales have decreased by 17.5% since 2000. This suggests shorter treatment durations for this condition with time, which is also according to recommendations.

Antibiotics commonly used to treat UTI are mostly prescribed to the age group 80 years and older, Figure 1.8 and Figure 1.9. In this age group the total sales have decreased by 32.8% since 2000, measured in prescriptions per 1 000 women and year. As mentioned earlier, some of the antibiotic use among the elderly is not included in the statistics. Nevertheless, the great decrease in the age group 80 years and older indicates increased compliance to recommendations. Many elderly have asymptomatic bacteriuria (ABU) and should not normally be treated with antibiotics (Medical Products Agency, 2017). Information and education on local and national level regarding treatment recommendations and ABU might be one explanation for the great decrease in sales over time in this age group. The same trend is seen in men, see below.

Antibiotics commonly used to treat urinary tract infections in men

The total sales of antibiotics commonly used to treat UTI in men 65 years and older has decreased by 27.7% since 2000. In 2017, the sales remained the same as in 2016 with 149 prescriptions per 1000 men and year.

Because of increasing resistance in gram-negative bacteria, the use of fluoroquinolones has been questioned and nitrofurantoin and pivmecillinam are now recommended as first line antibiotics for treatment of symptomatic UTI without fever in men (Public Health Agency of Sweden, 2013, Medical Products Agency, 2017).

The sales of fluoroquinolones to men aged 65 years and older has decreased significantly ($p < 0.001$) since 2000 (43.1%), measured in prescriptions per 1 000 men and year. The sales decreased further in 2017, by 4.3% compared with 2016. During the last years, sales of pivmecillinam and nitrofurantoin have increased. In 2017, the sales of these two antibiotics increased by 4.1% and 10.3% respectively, measured in prescriptions per 1 000 men and year, compared with 2016, Figure 1.12. The changes are significant ($p < 0.001$) for both antibiotics and nitrofurantoin is estimated to increase by 8% per year if the increasing trend continues.

FIGURE 1.11. Sales of antibiotics commonly used to treat lower urinary tract infections in women (sales on prescriptions), 18-79 years, 2000-2017, prescriptions/1 000 women and year.

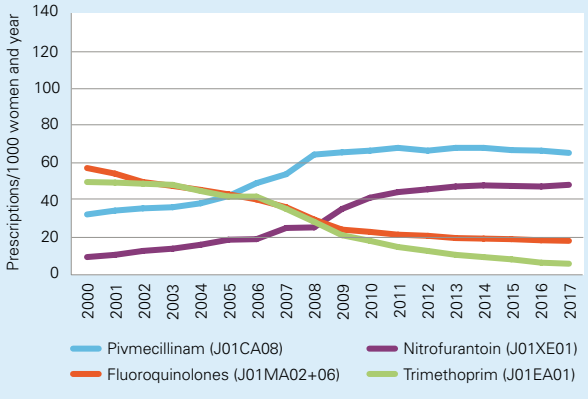


FIGURE 1.12. Sales of antibiotics commonly used to treat UTI in men 65 years and older 2000-2017, prescriptions/1 000 men and year.

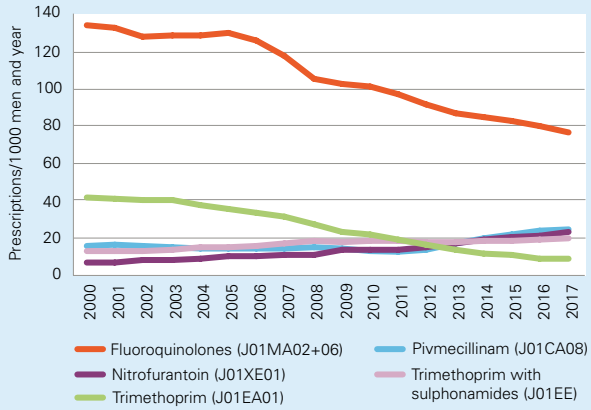


TABLE 1.1. Antibiotics in outpatient care, classes of antibiotics and age groups. DDD/1 000 inhabitants and day, prescriptions/1 000 inhabitants and year and user/1 000 inhabitants and year.

Age groups (years)	DDD/1 000 and day					Prescriptions/1 000 and year					User/1 000 and year				
	2013	2014	2015	2016	2017	2013	2014	2015	2016	2017	2013	2014	2015	2016	2017
Tetracyclines (J01AA)															
0-6	0.00	0.00	0.00	0.00	0.01	0.03	0.05	0.05	0.07	0.28	0.0	0.0	0.0	0.1	0.2
7-19	3.06	2.82	2.59	2.67	2.65	27.6	25.1	23.3	23.2	22.8	16.8	15.5	14.6	14.8	15.0
20-64	3.10	2.92	2.78	2.55	2.47	47.7	43.1	41.4	37.5	35.7	36.4	32.9	31.6	29.1	27.8
65-79	3.36	3.06	3.02	2.78	2.82	68.9	60.4	59.9	54.3	54.9	52.5	46.2	44.9	41.6	42.3
80-	2.15	1.97	2.06	1.90	2.05	52.5	45.7	48.0	43.8	46.9	41.9	36.3	38.4	35.2	37.4
All age groups	2.85	2.66	2.55	2.40	2.35	44.4	39.8	38.7	35.6	34.6	33.1	29.8	28.8	26.8	26.3
Penicillins with extended spectrum (J01CA) excl. Pivmecillinam (J01CA08)															
0-6	1.07	1.08	1.00	1.01	0.95	43.8	43.7	40.2	40.1	37.6	33.6	33.5	30.3	30.2	28.3
7-19	0.32	0.31	0.31	0.32	0.31	8.5	8.2	8.2	8.1	7.8	6.9	6.7	6.4	6.4	6.1
20-64	0.59	0.56	0.55	0.53	0.51	13.9	13.2	13.1	12.2	11.8	11.2	10.5	10.2	9.6	9.3
65-79	1.50	1.44	1.45	1.42	1.44	34.3	32.4	32.6	31.1	31.0	26.8	25.2	24.6	23.9	24.1
80-	1.73	1.71	1.81	1.75	1.86	37.7	36.8	38.1	36.2	37.6	30.4	29.4	30.1	28.7	30.0
All age groups	0.79	0.76	0.76	0.74	0.73	20.1	19.3	19.0	18.2	17.7	15.6	15.0	14.5	13.9	13.6
Pivmecillinam (J01CA08)															
0-6	0.01	0.01	0.01	0.02	0.02	1.0	1.0	1.1	1.2	1.4	0.9	1.0	1.0	1.1	1.3
7-19	0.20	0.20	0.19	0.19	0.19	13.8	13.4	12.7	12.7	12.9	12.0	11.7	10.9	11.1	11.2
20-64	0.46	0.48	0.47	0.47	0.47	29.5	29.8	29.4	29.5	29.1	24.3	24.6	24.1	24.3	24.0
65-79	0.98	1.00	1.01	1.02	1.00	59.3	59.5	59.4	59.1	58.3	44.0	44.2	43.1	43.7	43.3
80-	1.83	1.92	1.91	1.94	1.92	112.3	114.7	114.1	114.2	113.0	80.5	82.1	81.4	81.6	81.0
All age groups	0.53	0.55	0.55	0.56	0.55	33.7	34.0	33.7	33.8	33.3	26.3	26.5	26.0	26.2	26.0
Beta-lactamase sensitive penicillins (J01CE)															
0-6	3.07	2.82	2.60	2.89	2.68	226.3	211.5	195.5	209.3	196.1	169.8	159.2	146.4	155.7	147.1
7-19	2.92	2.66	2.61	2.72	2.63	103.6	94.0	92.9	96.9	92.5	83.9	75.7	73.3	77.0	73.4
20-64	3.55	3.24	3.22	3.19	3.17	84.8	77.6	77.2	76.5	75.8	72.7	66.2	65.3	65.2	64.7
65-79	3.86	3.58	3.62	3.51	3.61	89.9	83.4	84.4	81.4	84.0	76.4	70.4	69.5	68.1	70.5
80-	3.24	3.07	3.17	3.05	3.10	78.3	73.9	76.7	73.4	74.3	67.4	63.3	65.1	62.3	63.5
All age groups	3.49	3.21	3.19	3.20	3.15	101.1	93.1	92.1	93.2	90.8	82.7	75.8	73.9	74.8	73.7
Beta-lactamase resistant penicillins (J01CF)															
0-6	0.26	0.26	0.24	0.24	0.27	26.1	26.2	24.8	23.9	27.3	20.4	20.6	19.5	19.0	21.6
7-19	0.78	0.77	0.74	0.74	0.72	27.8	27.4	26.3	25.4	25.2	22.6	22.2	20.9	20.4	20.0
20-64	1.31	1.30	1.26	1.25	1.21	32.2	32.1	30.8	30.3	29.6	25.6	25.5	24.3	24.1	23.4
65-79	2.77	2.74	2.69	2.64	2.54	57.1	56.2	54.9	53.4	51.9	38.1	37.3	35.4	35.4	34.4
80-	5.11	5.18	5.22	5.26	5.23	103.2	102.6	101.6	100.4	99.1	63.4	62.8	61.2	61.2	59.9
All age groups	1.56	1.56	1.54	1.53	1.48	38.7	38.5	37.4	36.7	36.0	28.5	28.2	26.9	26.7	26.2
Combinations of penicillins (J01CR)															
0-6	0.21	0.21	0.18	0.18	0.20	13.9	13.5	11.6	11.5	12.8	8.8	8.3	7.2	6.9	7.7
7-19	0.14	0.14	0.15	0.15	0.17	3.9	4.0	4.1	4.2	4.8	2.8	2.7	2.7	2.7	2.8
20-64	0.22	0.24	0.25	0.25	0.27	4.7	5.0	5.1	5.3	5.6	3.9	4.0	4.1	4.3	4.4
65-79	0.34	0.37	0.40	0.44	0.50	6.8	7.5	8.2	8.8	9.9	5.2	5.6	6.0	6.4	7.1
80-	0.32	0.35	0.39	0.44	0.52	6.2	6.7	7.6	8.8	10.1	4.6	5.0	5.8	6.5	7.5
All age groups	0.23	0.25	0.26	0.27	0.30	5.8	6.1	6.2	6.5	7.0	4.4	4.5	4.5	4.7	5.0
Cephalosporins (J01DB-DE)															
0-6	0.27	0.27	0.25	0.24	0.03	25.7	26.9	25.0	24.3	2.9	21.2	22.2	20.7	20.0	2.6
7-19	0.15	0.13	0.13	0.13	0.05	10.4	9.3	9.0	8.9	3.7	8.5	7.6	7.2	7.1	3.1
20-64	0.12	0.11	0.11	0.11	0.08	7.3	6.7	6.6	6.4	5.1	6.0	5.5	5.3	5.1	4.1
65-79	0.19	0.17	0.18	0.17	0.12	10.4	9.4	9.7	9.4	7.5	7.8	7.0	6.9	6.9	5.6
80-	0.31	0.29	0.29	0.30	0.21	17.6	17.0	17.4	17.6	13.6	13.4	13.1	13.2	13.2	10.4
All age groups	0.16	0.14	0.14	0.14	0.08	10.4	9.8	9.6	9.4	5.5	8.3	7.8	7.5	7.3	4.4

Age groups (years)	DDD/1 000 and day					Prescriptions/1 000 and year					User/1 000 and year				
	2013	2014	2015	2016	2017	2013	2014	2015	2016	2017	2013	2014	2015	2016	2017
Trimethoprim (J01EA)															
0-6	0.07	0.07	0.06	0.06	0.06	10.0	9.2	8.1	7.5	7.8	7.6	6.9	6.1	5.6	5.8
7-19	0.05	0.04	0.04	0.03	0.03	3.3	2.8	2.3	1.9	1.9	2.7	2.2	1.8	1.6	1.4
20-64	0.11	0.10	0.09	0.07	0.06	4.5	3.9	3.3	2.6	2.2	3.5	3.0	2.5	1.9	1.6
65-79	0.39	0.34	0.31	0.25	0.24	15.5	13.5	11.8	9.5	9.0	10.7	9.2	8.1	6.5	5.9
80-	0.83	0.71	0.69	0.62	0.58	41.5	35.5	32.7	30.3	28.4	21.4	18.8	17.1	14.2	12.9
All age groups	0.17	0.15	0.14	0.12	0.11	8.3	7.2	6.4	5.4	5.0	5.7	4.9	4.3	3.5	3.2
Trimethoprim with sulphonamides (J01EE)															
0-6	0.09	0.09	0.08	0.07	0.09	10.2	9.6	8.7	8.1	10.3	6.2	5.7	4.8	4.6	6.6
7-19	0.10	0.10	0.10	0.10	0.11	3.8	3.8	3.8	3.8	4.6	2.1	2.0	1.9	1.8	2.3
20-64	0.20	0.20	0.21	0.20	0.20	4.6	4.8	4.8	4.9	5.1	2.6	2.7	2.6	2.7	2.8
65-79	0.56	0.57	0.60	0.62	0.62	12.4	13.0	13.2	13.7	14.5	8.4	8.6	8.4	8.9	9.2
80-	0.51	0.51	0.53	0.55	0.54	13.0	13.2	13.1	14.0	14.9	9.7	9.9	9.7	10.3	10.7
All age groups	0.25	0.25	0.26	0.26	0.26	6.7	6.8	6.8	6.9	7.4	4.0	4.0	3.9	4.0	4.4
Macrolides (J01FA)															
0-6	0.26	0.26	0.23	0.25	0.26	12.1	12.4	11.1	11.6	12.4	9.5	9.7	8.5	9.0	9.5
7-19	0.24	0.22	0.21	0.22	0.22	8.3	8.6	8.3	8.7	9.3	5.8	6.1	5.7	6.1	6.5
20-64	0.27	0.24	0.23	0.23	0.21	8.7	9.1	8.9	8.4	8.2	6.4	6.8	6.5	6.3	6.3
65-79	0.33	0.30	0.30	0.29	0.32	8.7	9.0	9.0	8.3	9.0	5.6	5.9	5.7	5.4	5.7
80-	0.20	0.19	0.21	0.22	0.22	5.7	5.8	6.5	6.3	6.6	4.0	4.0	4.2	4.0	4.4
All age groups	0.27	0.25	0.24	0.24	0.24	8.9	9.2	9.0	8.9	9.2	6.3	6.7	6.3	6.2	6.4
Lincosamides (J01FF)															
0-6	0.02	0.02	0.02	0.02	0.04	5.0	5.1	4.7	5.0	7.7	3.7	3.6	3.3	3.7	5.7
7-19	0.11	0.11	0.11	0.11	0.12	7.4	7.3	7.1	7.2	7.7	5.9	5.7	5.4	5.7	6.0
20-64	0.31	0.31	0.30	0.30	0.29	15.4	14.7	14.5	14.3	13.6	12.2	11.5	11.3	11.4	10.8
65-79	0.58	0.56	0.57	0.56	0.56	24.3	22.9	23.0	22.5	21.9	16.8	15.7	15.3	15.6	15.1
80-	0.71	0.73	0.72	0.72	0.75	29.9	29.9	30.2	30.0	30.0	18.9	18.9	18.6	18.8	18.5
All age groups	0.32	0.32	0.32	0.32	0.31	15.6	14.9	14.8	14.8	14.5	11.6	11.0	10.8	10.9	10.7
Fluoroquinolones (J01MA)															
0-6	0.02	0.02	0.02	0.02	0.02	0.9	0.8	0.7	0.8	1.0	0.5	0.4	0.5	0.5	0.6
7-19	0.11	0.10	0.11	0.10	0.10	3.6	3.4	3.8	3.3	3.5	2.9	2.7	3.0	2.5	2.7
20-64	0.62	0.59	0.57	0.55	0.52	19.7	18.9	18.4	17.6	16.8	14.4	13.8	13.3	12.8	12.2
65-79	1.64	1.61	1.58	1.53	1.47	55.7	54.8	53.6	51.7	50.0	38.6	37.6	35.6	35.2	34.0
80-	2.00	1.95	1.91	1.90	1.83	73.7	72.5	71.0	70.1	67.3	52.6	51.4	49.8	49.1	47.2
All age groups	0.71	0.69	0.68	0.66	0.63	23.8	23.3	22.9	22.1	21.2	16.9	16.4	15.9	15.5	14.8
Nitrofurantoin (J01XE)															
0-6	0.05	0.06	0.05	0.06	0.06	7.1	7.2	7.1	7.4	8.0	5.1	5.2	5.2	5.5	6.1
7-19	0.13	0.13	0.12	0.12	0.12	10.1	9.8	9.2	9.1	9.2	8.6	8.3	7.8	7.7	7.8
20-64	0.30	0.31	0.31	0.31	0.32	20.5	21.1	20.9	20.9	21.5	16.6	17.0	16.7	16.8	17.2
65-79	0.72	0.74	0.76	0.76	0.78	44.0	44.9	45.2	45.2	45.7	31.9	32.5	31.7	32.2	32.4
80-	1.23	1.30	1.35	1.38	1.44	80.6	84.0	87.0	87.7	90.4	51.6	53.8	53.8	53.1	53.7
All age groups	0.37	0.38	0.38	0.39	0.40	24.5	25.1	25.2	25.3	25.9	18.4	18.9	18.6	18.7	19.0
All agents (J01 excl. methenamine)															
0-6	5.43	5.15	4.75	5.05	4.69	382.4	367.2	339.0	351.0	325.8	232.0	222.7	206.4	213.2	200.2
7-19	8.33	7.75	7.43	7.62	7.45	232.7	217.8	211.8	214.1	206.5	152.1	141.8	136.1	138.9	133.6
20-64	11.19	10.62	10.38	10.04	9.80	294.4	280.8	275.2	267.2	260.9	184.9	175.8	171.3	168.4	164.8
65-79	17.28	16.55	16.54	16.06	16.08	489.2	468.7	466.3	450.0	449.0	258.1	246.5	238.9	235.4	236.2
80-	20.22	19.95	20.34	20.10	20.30	654.2	640.3	645.9	634.7	634.1	314.7	307.8	306.7	301.2	301.5
All age groups	11.74	11.20	11.04	10.86	10.62	342.7	328.0	322.8	317.7	308.9	201.0	191.7	186.0	184.5	180.7

Antibiotic consumption in children

In 2017 the total sales of antibiotics to children aged 0-6 years decreased by 7.2%, from 351 to 326 prescriptions per 1 000 children and year, Table 1.2. The greatest decrease occurred in quarter three where the sales decreased by 11.5% compared with the same period in 2016. The sales of antibiotics commonly used to treat RTI decreased by 11.7% during 2017, Table 1.2. However, antibiotics commonly used to treat UTI and SSTI increased in all quarters of 2017. The greatest decrease in 2017 in the age group 0-6 years was seen for cephalosporins (J01DB-DE), that decreased by 85.8% due to low availability of these products. This is described more in depth in the In Focus: "Avaliability of antibiotics".

In the end of 2016, the number of laboratory verified cases of Influenza (Public Health Agency of Sweden, 2017) and the number of reported Respiratory syncytial virus-cases (RSV) (Public Health Agency of Sweden, 2017) were greater than in 2015. In addition, the Influenza and RSV season started earlier in autumn than the year before. Together this lead to more Influenza and RSV cases in 2016 compared with 2015, which might be an explanation to the increased sales of RTI antibiotics in 2016. This increase did not continue in 2017, Table 1.2.

The decreased sales were seen in 19 out of 21 counties. There are great national variations in antibiotic sales to children 0-6 years, from 379 prescriptions per 1 000 children and year in Stockholm County to 166 in Jämtland County, Figure 1.13.

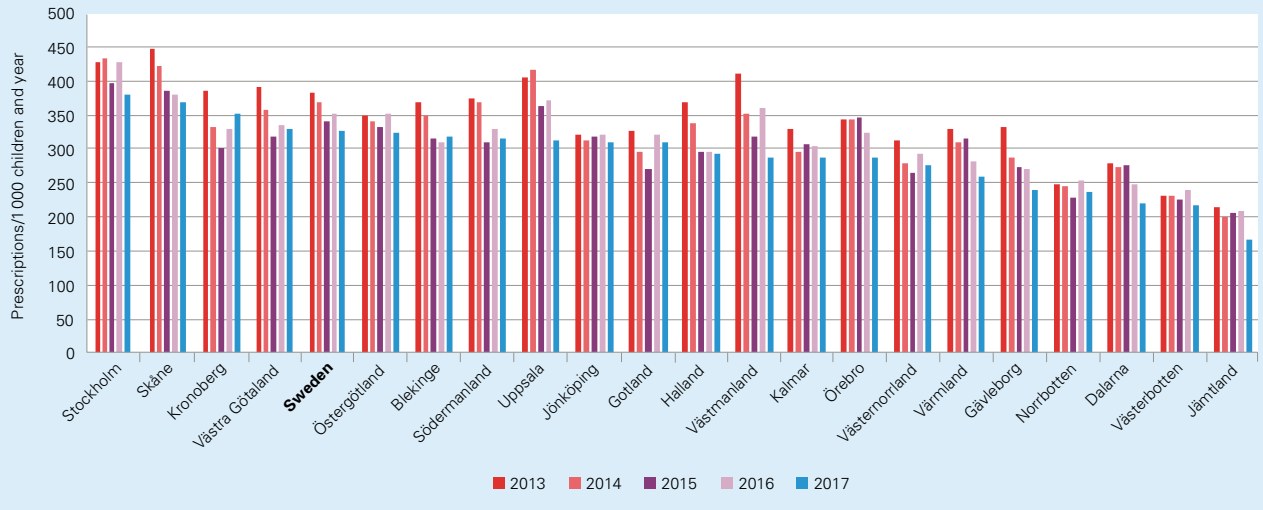
Different kinds of penicillins are the most commonly prescribed antibiotics in this age group and penicillin V (J01CE02), amoxicillin (J01CA04) and flucloxacillin (J01CF05) represent 60.2%, 11.6% and 8.4% respectively of the total sales in this age group in 2017, Table 1.1.

Over the years, the total sales of antibiotics to children aged 0-6 years have decreased by 56.3%, from 746 prescriptions per 1 000 children and year in 2000 to 326 in 2017. The great decrease in antibiotic sales to children, seen over time, can be explained by a more appropriate antibiotic use in Sweden. New recommendations for treatment of acute otitis media were launched by Strama, the Swedish strategic programme against antibiotic resistance, and the Swedish Medical Products Agency in 2010 (Medical Products Agency & Strama, 2010). The new recommendations have been attracting attention from professionals and the public, which may have influenced the antibiotic use in young children.
In Sweden, the proportion of children (0-6 years) treated with at least one course of antibiotics in 2017 was 20%, which is

TABLE 1.2. The sales of antibiotics to children 0-6 years in outpatient care, for different periods in 2017 compared to the same periods in 2016. The sales are measured in prescriptions/1 000 children and year. The difference between 2016 and 2017 is measured as percentage.

	J01 excl. methenamine			RTI antibiotics			UTI antibiotics			SSTI antibiotics		
	2016	2017	Difference in percent	2016	2017	Difference in percent	2016	2017	Difference in percent	2016	2017	Difference in percent
January-March	105	104	-0.9%	93.3	89.2	-4.4%	4.2	4.3	3.0%	5.7	8.1	42.6%
April-June	87.0	78.5	-9.8%	73.9	63.2	-14.5%	3.8	4.3	12.6%	7.2	8.4	17.3%
July-September	63.9	56.6	-11.5%	50.0	40.3	-19.4%	4.2	4.7	10.6%	8.0	9.2	14.5%
October-December	94.8	86.6	-8.7%	79.7	69.4	-12.8%	4.7	5.0	5.7%	8.0	9.2	14.7%
January-December	351	326	-7.2%	297	262	-11.7%	16.9	18.2	7.8%	28.9	34.9	20.7%

FIGURE 1.13. Sales of antibiotics (J01 excl. methenamine) on prescriptions to children 0-6 years, per county and in Sweden 2013-2017, prescriptions/1 000 children and year. The data are sorted according to the use in 2017.



less than in 2016, Figure 1.14. The proportion decreased in 20 out of 21 counties during 2017 and it ranges from 228 users per 1 000 children in Stockholm County to 112 users per 1 000 children in Jämtland County, Figure 1.14.

County data

In 2017, 18.1% of the Swedish population was treated with at least one course of antibiotics, compared to 2016 when 18.5% of the population was treated, Table 1.1. However, the proportion of people treated with antibiotics varies within Sweden, from 20.0% in Gotland County to 14.3% in Västerbotten County. In total, the proportion of patients treated decreased in 15 out of 21 counties in 2017, Figure 1.15. The proportion of people treated with antibiotics during the last five years has decreased by 2.0 percentage points since 2013. The same number for children is 3.2, Table 1.3.

In 2017, the average sales of antibiotics in outpatient care measured in prescriptions per 1 000 inhabitants in Sweden was 309. To reach the Swedish long term target of 250 prescriptions per 1 000 inhabitants and year, the antibiotic use in Sweden still must be reduced by 23.6%, Figure 1.16.

TABLE 1.3. The proportion (%) of children 0-6 years and the proportion (%) of people treated with at least one course of antibiotics (J01 excl. methenamine) in 2013-2017.

	2013	2014	2015	2016	2017	Difference 2013-2017
Children 0-6	23.2	22.2	20.6	21.3	20.0	3.2%
Total population	20.1	19.1	18.5	18.4	18.1	2.0%

FIGURE 1.14. The proportion (%) of children 0-6 years treated with at least one course of antibiotics (J01 excl. methenamine) in 2013-2017.

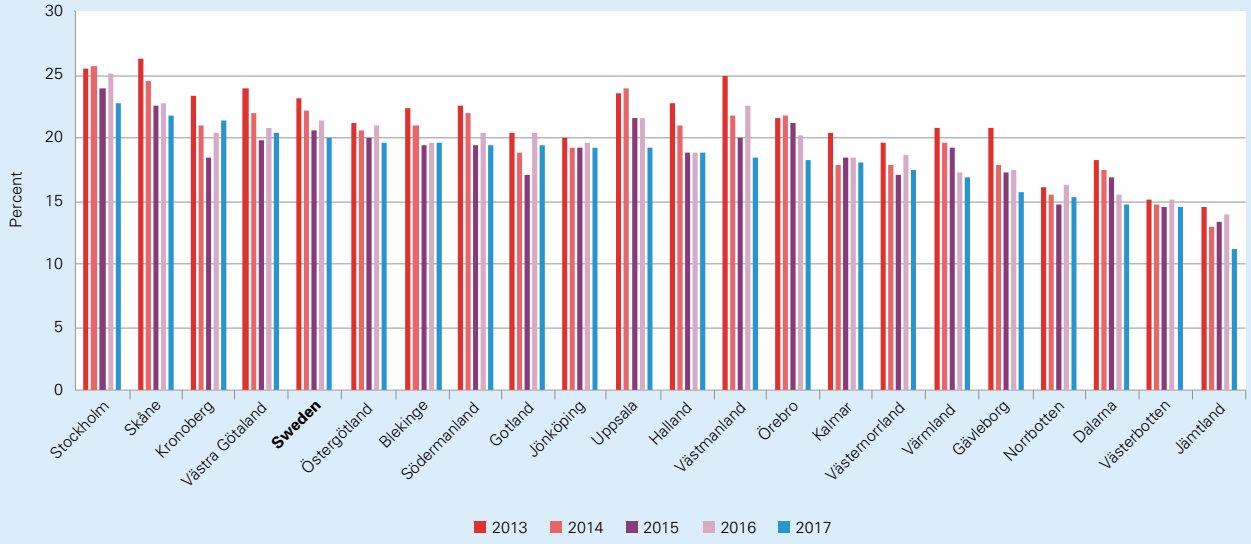
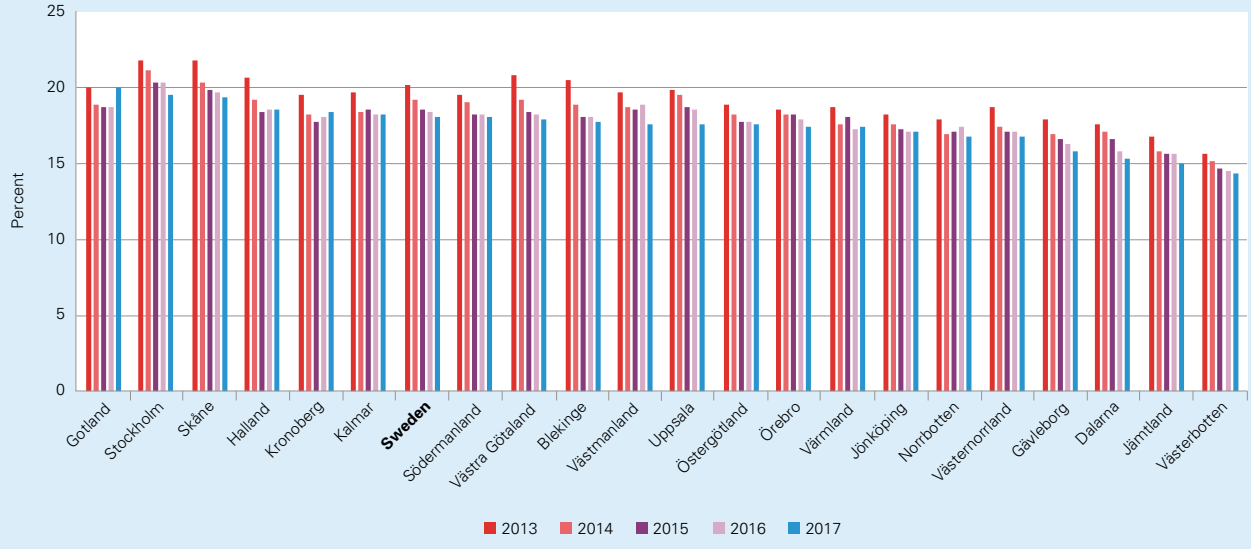


FIGURE 1.15. The proportion (%) of people treated with at least one course of antibiotics (J01 excl. methenamine) in 2013-2017.



In 2017, the number of prescriptions per 1 000 inhabitants was reduced in 19 out of 21 counties, Figure 1.16. One reason for the great decrease in antibiotic sales in all counties in Sweden during the latest years might be the patient safety initiative that started in 2011 and continued until the end of 2014. This was a governmental performance-based initiative, partly focusing on optimizing the antibiotic use through financial incentives. Read more about the agreement and evaluation on antibiotic use in relation to the initiative in Swedres-Svarm 2014 chapter "National campaign for improved patient safety" (Swedres-Svarm 2014, 2015).

However, there are still great regional differences in Sweden and prescriptions per 1 000 inhabitants range from 353 in Gotland County to 246 in Västerbotten County, Figure 1.16.

The great variation between counties is probably not explained by differences in morbidity (Hedin K, Andre M, et al. 2006). The differences are more likely explained by factors such as different availability of healthcare and overuse of antibiotics. Factors influencing antibiotic prescription in Swedish healthcare centres has been investigated in a study, see results in the report "Vad påverkar allmänläkare vid förskrivning av antibiotika?" on the webpage of the Public Health Agency of Sweden (Public Health Agency of Sweden, 2014).

Earlier studies in Sweden have shown overuse of antibiotics in RTI (Mölstad S, Andre M, et al. 2009, Neumark T et al. 2009). Notably, the greatest differences in the sales of antibiotics between counties relate to treatment of RTI. Over time, the regional differences within Sweden have decreased, which can be explained by a more appropriate antibiotic use.

As mentioned in earlier editions of Swedres-Svarm, Strama has proposed two qualitative targets for antibiotic prescribing in outpatient care:

1. At least 80% of antibiotics commonly used to treat respiratory tract infections in children aged 0-6 years should be penicillin V (J01CE02). The numerator is penicillin V (J01CE02) and the denominator is amoxicillin (J01CA04), penicillin V (J01CE02), amoxicillin-clavulanate (J01CR02), cephalosporins (J01DB-DE) and macrolides (J01FA).

In 2017 the proportion of penicillin V was 74% on a national level, compared with 70% in 2016. Värmland County had the greatest proportion, 82%, and Gotland County the lowest, 71%, Figure 1.17.

FIGURE 1.17. Proportion penicillin V of antibiotics commonly used to treat respiratory tract infections in children 0-6 years, per county, 2016-2017. The red line indicates Strama's goal at minimum 80% penicillin V.

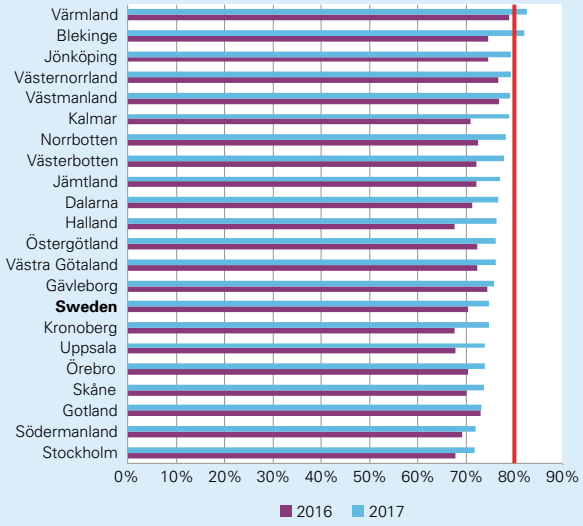
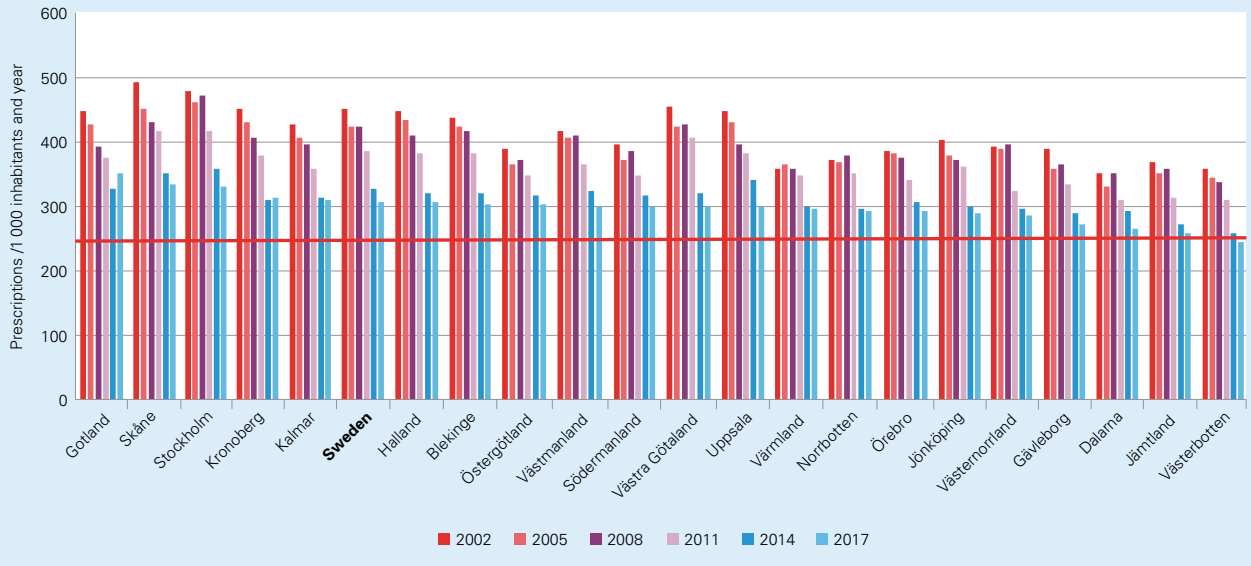


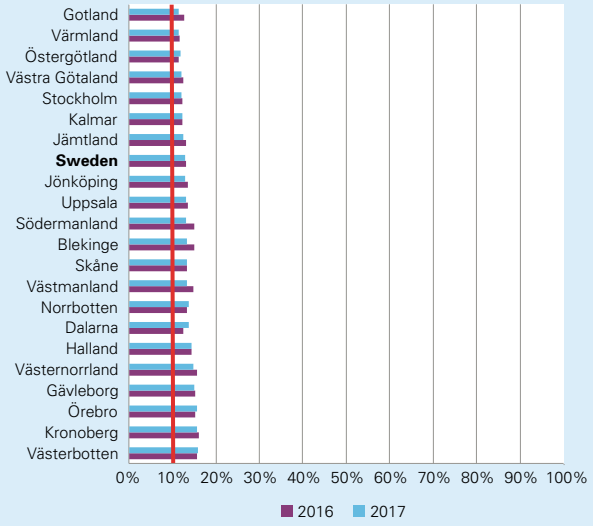
FIGURE 1.16. Sales of antibiotics in outpatient care 2002-2017, prescriptions/1 000 inhabitants and year. The red line indicates the Swedish long term target of 250 prescriptions/1 000 inhabitants and year. The data are sorted according to the sales in 2017. The figure shows every third year.



2. The proportion of fluoroquinolones should not exceed 10% of antibiotics commonly prescribed to treat urinary tract infections in women 18-79 years. The numerator is ciprofloxacin (J01MA02) and norfloxacin (J01MA06) and the denominator is pivmecillinam (J01CA08), trimethoprim (J01EA01), ciprofloxacin (J01MA02), norfloxacin (J01MA06) and nitrofurantoin (J01XE01).

The average proportion of fluoroquinolones in Sweden in 2017 was 13%. Västerbotten County had the highest proportion (16%) and Gotland County the lowest proportion (11%), Figure 1.18.

FIGURE 1.18. Proportion of fluoroquinolones of antibiotics commonly used to treat urinary tract infections in women 18-79 years, per county, 2016-2017. The red line indicates Strama's goal of maximum 10% fluoroquinolones.



Antibiotics in dentistry

In 2017 the sales of J01 and metronidazole (P01AB01) prescribed by dentists decreased by 4.8% compared with 2016. The sales decreased from 22 to 21 prescriptions per 1 000 inhabitants and year, Figure 1.19.

Penicillin V (J01CE02) is the most commonly prescribed antibiotic followed by amoxicillin (J01CA04) and clindamycin (J01FFA01). These antibiotic substances represent 73.0%, 9.0% and 8.2% respectively of all antibiotics prescribed by dentists. The greatest decrease in sales in 2017 was seen for erythromycin (15.6%) and clindamycin (9.2%), measured in prescriptions per 1 000 inhabitants and year. Amoxicillin has decreased by 22.2% between 2013 and 2017. The explanation for this might be the new stricter treatment recommendations for the use of antibiotic prophylaxis which was implemented in 2012. A big increase was seen for clindamycin between 2001 and 2011. However, since 2012, the trend has reversed and the sales of clindamycin have decreased each year.

The age group 65-79 years is the group with the highest consumption of antibiotics prescribed by dentists, followed by the age groups 20-64 years and 80 years and older. Between 2000 and 2007, an increase was seen in the consumption in all age groups, but since 2007 all age groups have decreased, Figure 1.20. One explanation to the increase in the age group 65-79 years between 2002 and 2008, might be the implementation of the reform "65+", which made complicated prosthetic treatment available at a lower cost to people over 65 years (Swedish National Board of Health and Welfare, 2011). In these treatments the use of antibiotics as profylaxis was common. The reform ended in 2008.

FIGURE 1.19. Sales of antibiotics prescribed by dentists in outpatient care, 2013-2017.

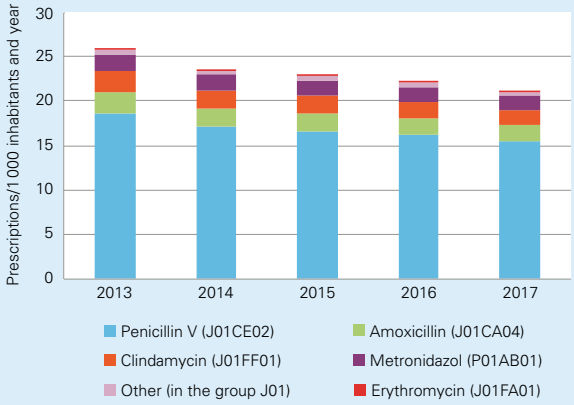


FIGURE 1.20. Sales of antibiotics (J01 and P01AB01) prescribed by dentists in outpatient care 2000-2017, prescriptions/1000 inhabitants and year, different age groups.

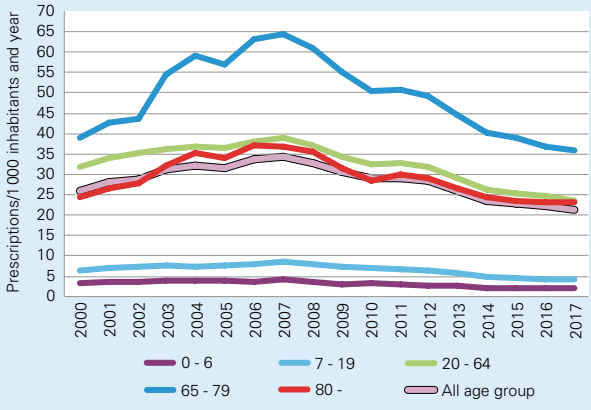
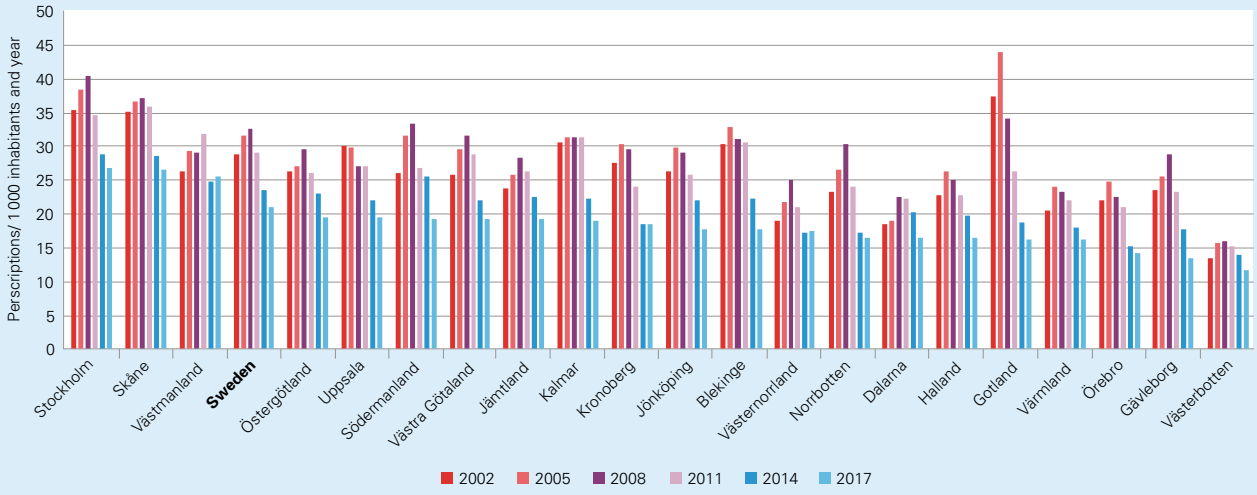


FIGURE 1.21. Sales of antibiotics prescribed by dentists in outpatient care per county, 2002-2017, antibiotics for systemic use (J01) and metronidazol (P01AB01). The data are sorted according to the sales in 2017. The figure shows every third year.



Dentists account for around 6% of all antibiotics prescribed in outpatient care in Sweden. The proportion varies between 4.1% and 7.5% in the different counties. The total sales of antibiotics (J01 and metronidazole), measured as prescriptions per 1 000 inhabitants and year, decreased in 19 of 21 counties in 2017 compared with 2016. There are great regional differences, greater than for outpatient care. Dentists in Stockholm County prescribe the most (27 prescriptions/1 000 inhabitants) and more than twice as much as Västerbotten County that prescribe the least (12 prescriptions/1 000 inhabitants) in 2017. The sales in all counties have decreased compared with 2002, after a peak in consumption in the years 2008 and 2011, Figure 1.21. There is no official explanation for the differences.

Antibiotics in hospital care

Sales data in this chapter are presented as: 1) all antibiotics sold by requisitions, below mentioned as hospital care, which gives a general view over use and trends, and 2) antibiotics sold by requisitions to acute care hospitals only, here called Swedish acute care hospitals, which provides a more detailed analysis.

The total antibiotic sale to hospital care includes sales data from all Swedish hospitals, including acute care hospitals, as well as nursing homes and other caregivers that order their antibiotics through requisition. In nursing homes, antibiotics can be bought either through requisition or by prescriptions to individual residents, something that varies between nursing homes and among counties. If bought by prescription, data are included in primary health care statistics, presented in the section "Antibiotics in outpatient care". At national level the proportion of antibiotics in hospital care sold to acute care hospitals is 70%. In some counties, almost 100% of all antibiotics in hospital care are sold to acute care hospitals and in other counties, the proportion is as low as 54%.

Antibiotic consumption in hospitals

The total antibiotic sale to hospital care increased in Sweden between 2000 and 2007 and has since then been relatively stable. In 2017 the sales decreased slightly, to 1.53 DDD per 1 000 inhabitants and day, compared with 2016. The sales of antibiotics (J01 excl. methenamine) increased by 29.7% between 2000 and 2012, from 1.18 to 1.63 DDD per 1000 inhabitants and day, Figure 1.22. However, since 2012, the sales have not increased.

FIGURE 1.22. Antibiotic consumption (J01 excl. methenamine) in hospital care 2000-2017, DDD/1 000 inhabitants and day.

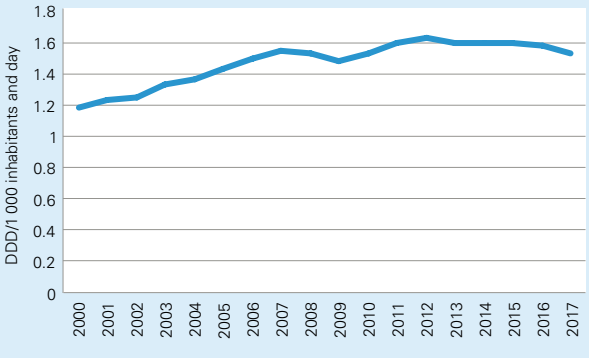
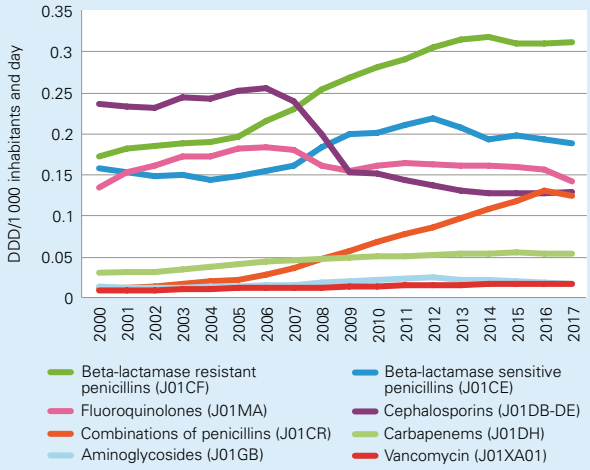


Figure 1.23 includes all sales on requisition measured as DDD per 1000 inhabitants and day. The figure shows a decrease of cephalosporins over the years and an increasing trend of more narrow spectrum antibiotics, for instance beta-lactamase resistant penicillins, of which flucloxacillin represents the biggest part. There were no major changes during 2017 compared with 2016 in any of the antibiotic groups. However, fluoroquinolones decreased slightly as well as the group with combinations of penicillins, in which Piperacillin with tazobactam (J01CR05) represents the biggest part, Figure 1.23. The decrease in this group might be explained by shortages of the substances, more about this in the section about acute care hospitals and in the "In focus"-section on "Availability of antibiotics".

The Strama network, together with local drug and therapeutic committees have promoted the following changes in antibiotic policy in Swedish hospitals: 1) moderately severe (CRB-65 0-1) community acquired pneumonia (CAP) should be treated with narrow spectrum penicillins; 2) surgical prophylaxis should normally be given as one dose. In high-risk situations, treatment can be given during 24 h maximum with few exceptions; 3) uncomplicated lower urinary tract infections in women should be treated with pivmecillinam or nitrofurantoin, including hospital inpatients, whereas the use of fluoroquinolones should be restricted; 4) extended spectrum cephalosporins and fluoroquinolones should not be used in situations where treatment with a narrow spectrum penicillin is an alternative (Hanberger H et al., 2014). This can be reflected in the statistics and is visible in figure 1.23.

FIGURE 1.23. Antibiotic groups often used within hospital care 2000-2017, DDD/1 000 inhabitants and day.



Antibiotic consumption in Swedish acute care hospitals

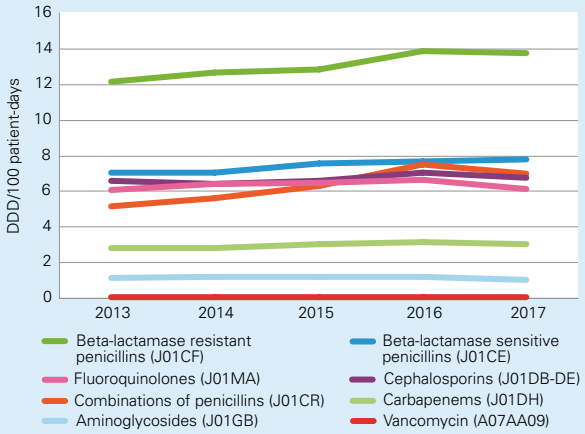
Data from acute care hospitals show that the consumption of antibiotics was slightly lower in 2017 compared with 2016 measured both as DDD per 100 patient-days and as DDD per 100 admissions, Table 1.4.

TABLE 1.4. DDD/100 patient-days and DDD/100 admissions in somatic medical care in Swedish acute care hospitals 2013-2017. Dalarna County is excluded from hospital data in 2017.

	DDD/100 admissions					DDD/100 patient-days				
	2013	2014	2015	2016	2017*	2013	2014	2015	2016	2017*
Tetracyclines (J01AA)	23.3	23.9	23.9	22.2	20.7	5.2	5.4	5.4	5.0	4.7
Penicillins with extended spectrum (J01CA)	31.8	33.1	33.9	33.4	32.6	7.2	7.4	7.7	7.6	7.4
Beta-lactamase sensitive penicillins (J01CE)	32.2	32.4	34.3	33.8	34.4	7.3	7.3	7.8	7.7	7.8
Beta-lactamase resistent penicillins (J01CF)	55.9	58.5	59.0	61.0	60.4	12.6	13.1	13.4	13.9	13.7
Combinations of penicillins (J01CR)	23.5	25.6	28.5	32.9	30.8	5.3	5.7	6.5	7.5	7.0
Cephalosporins (J01DB-DE)	30.4	29.5	30.2	31.1	29.6	6.8	6.6	6.8	7.1	6.7
Carbapenems (J01DH)	13.0	13.1	13.8	13.9	13.3	2.9	2.9	3.1	3.2	3.0
Trimethoprim (J01EA)	2.0	1.8	1.8	1.1	0.7	0.4	0.4	0.4	0.2	0.2
Trimethoprim with sulphonamides (J01EE)	10.6	10.6	10.7	11.7	11.0	2.4	2.4	2.4	2.7	2.5
Macrolides (J01FA)	4.5	4.4	4.9	5.4	5.5	1.0	1.0	1.1	1.2	1.2
Lincosamides (J01FF)	8.8	8.7	8.5	8.7	8.3	2.0	1.9	1.9	2.0	1.9
Aminoglycosides (J01GB)	5.2	5.4	5.3	5.2	4.6	1.2	1.2	1.2	1.2	1.0
Fluoroquinolones (J01MA)	28.1	29.7	29.7	29.3	26.9	6.3	6.7	6.7	6.7	6.1
Glycopeptides (J01XA)	4.3	4.5	4.7	4.8	4.7	1.0	1.0	1.1	1,1	1.1
Imidazole derivates (J01XD)	5.4	4.6	4.4	4.1	4.2	1.2	1.0	1.0	0.9	1.0
Nitrofurantoin (J01XE)	2.3	2.4	2.2	2.3	2.2	0.5	0.5	0.5	0.5	0.5
Vancomycin (A07AA09)	0.3	0.3	0.3	0.3	0.3	0.1	0.1	0.1	0.1	0.1
Pivmecillinam (J01CA08)	8.9	9.5	9.5	8.8	8.2	2.0	2.1	2.1	2.0	1.9
Piperacillin and tazobactam (J01CR05)	17.6	20.8	22.6	26.0	23.0	4.0	4.7	5.1	5.9	5.2
Moxifloxacin (J01MA14)	1.7	1.8	1.7	1.9	2.0	0.4	0.4	0.4	0.4	0.4
Methenamine (J01XX05)	2.4	2.4	2.4	2.0	1.9	0.5	0.5	0.5	0.4	0.4
Linezolid (J01XX08)	0.5	0.6	0.6	0.9	0.8	0.1	0.1	0.1	0.2	0.2
All agents (J01)	284.4	292.5	299.9	305.3	293.9	64.1	65.6	67.9	69.4	66.9

*Denominator data from 2016

FIGURE 1.24. Antibiotic groups often used within Swedish acute care hospitals 2013-2017 DDD/100 patient-days. Dalarna County is excluded from the hospital data in 2017.



In Figure 1.24 the most frequent groups of antibiotics used in Swedish acute care hospitals are presented. Trend analyses show a significant increase of the consumption of beta-lactamase resistant penicillins, beta-lactamase sensitive penicillins and combinations of penicillins over the last five years ($p < 0.001$). Piperacillin with tazobactam accounts for about 75% of the sales of combinations of penicillins (J01CR) in acute care hospitals. These agents have in many situations replaced the cephalosporins, for which no significant change in sales the last five years is seen ($p > 0.001$). Furthermore, there is a significant decreasing trend for the use of fluoroquinolones and aminoglycosides since 2016 and 2014 respectively ($p < 0.001$ for both antibiotic groups). A significant increase in sales was also seen for vancomycin. The sales of carbapenems increased significantly between 2013 and 2016, however a slight decrease in sales 2017 compared with 2016 might suggest a change of trend. In Table 1.5, the use measured in DDD per 100 patient-days can be seen as numbers as well as possible significances of the changes over the years.

TABLE 1.5. The changes in use in antibiotic groups often used within Swedish acute care hospitals, DDD/100 patient-days. The column on the right indicates if the trend over time is significant (** = $p < 0.001$) or Not Significant (N.S.) using trend analysis. Dalarna County is excluded from the hospital data in 2017.

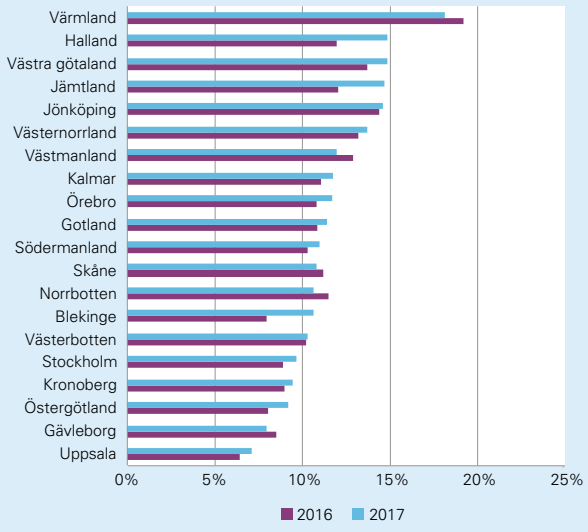
	2013	2014	2015	2016	2017	Sign.
Beta-lactamase resistant penicillins (J01CF)	12.1	12.7	12.9	13.9	13.7	**
Beta-lactamase sensitive penicillins (J01CE)	7.0	7.1	7.5	7.7	7.8	**
Combinations of penicillins (J01CR)	5.2	5.6	6.3	7.5	7.0	**
Cephalosporins (J01DB-DE)	6.6	6.4	6.6	7.1	6.7	N.S.
Fluoroquinolones (J01MA)	6.1	6.4	6.5	6.7	6.1	**
Carbapenems (J01DH)	2.8	2.8	3.0	3.2	3.0	**
Aminoglycosides (J01GB)	1.2	1.2	1.2	1.2	1.0	**
Vancomycin (A07AA09)	0.1	0.1	0.1	0.1	0.1	**

From 2013 to 2016, combinations of penicillins was steadily increasing, measured in DDD per 100 patient-days. However, in 2017 a decrease of 7% is seen which might be explained by insufficient availability after an explosion in a factory producing raw materials for piperacillin with tazobactam in October 2016.

The increase of piperacillin with tazobactam during earlier years is probably a result of an increased number of infections with ESBL. To minimize the selection of ESBL producing bacteria, a decreased use of 2nd and 3rd generation's cephalosporins is recommended in Sweden and piperacillin with tazobactam have in many situations replaced the cephalosporins. Invasive infections caused by ESBL-producing Escherichia coli and Klebsiella pneumonia have increased, but the proportion of pathogens resistant to third-generation cephalosporins causing invasive infections is still very low in a European and international perspective.

Since 2008 and still today the largest group of antibiotics in Swedish acute care hospitals is the beta-lactamase resistant penicillins (J01CF), with 13.7 DDD per 100 patient-days in 2017. A large proportion of the use consists of surgical prophylaxis (even though the hospital use in Sweden to a large extent has gone from a multi-dose to a single-dose prophylaxis). The use of fluoroquinolones (J01MA) accounts for 9.2% of all antibiotics in acute care hospitals and has been at the same level since 2008. In 2017 the use of flouroquinolones decreased by 8.0% compared with 2016. One explanation to the decrease in this group might be that the resistance is quite extensive.

FIGURE 1.25. Percentage of narrow spectrum penicillins (penicillin V and G, J01CE) of all antibiotics in Swedish acute care hospitals 2016 and 2017, per county. Dalarna County is excluded from the hospital data in 2017.



According to available data, antibiotic consumption in Swedish acute care hospitals shows a wide variation between the counties in the use of narrow spectrum penicillins, ranging from 7.1% to 18.1% of the total acute care hospital consumption measured in DDDs, Figure 1.25. The use of narrow spectrum antibiotics increased in 15 of 20 counties (Dalarna County is excluded from the hospital data in 2017) in 2017 compared with 2016. There are, however, great differences in regards to dosages of penicillin G given between the counties. The DDD for penicillin G is 3.6 g, but in Sweden the dosage varies from 1g three times a day to 3g three times a day. Type of hospital and patient composition may also influence the statistics and should be taken into account when comparing these data. Uppsala, Stockholm, Västerbotten, Västra Götaland, Skåne, Östergötland and Örebro counties all have tertiary referral hospitals.

In acute care hospitals the use of cephalosporins varied between 3.9% and 13.9% during 2017, and the corresponding numbers for fluoroquinolones was 7.3% to 14.5%. Piperacillin-tazobactam varied between 4.4% and 11.0% and carbapenems between 2.2% and 7.1%, Figure 1.26. The proportion of all broad spectrum antibiotics (fluoroquinolones, cephalosporins, piperacillin with tazobactam and carbapenems) in Swedish acute care hospitals varied from 27.6% in Jönköping County, to 36.7% in Kronoberg County. In general, there are major differences in the distribution regarding which group of broad spectrum antibiotics that is used, but the overall consumption of broad spectrum antibiotics is quite similar between the counties.

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 2013 and 2017, were analysed for various groups of agents. There were 2 535 reports of side effects caused by the use of antibiotics during this period.

The following organ system groups received most reports related to the use of systemic antibiotic drugs (J01): skin- and subcutaneous tissue disorders (n=1229), gastrointestinal disorders (n=528), general disorders (n= 337), neurological reactions (n=303), respiratory disorders (n=207), immune system disorders (n=200), musculoskeletal disorders (n=159), investigations (n=137), hepato-biliary disorders (n=133), psychiatric disorders (n=97), renal and urinary disorders (n=94) and blood and lymphatic system disorders (n=71).

The majority of the reports (61 %) concern female patients, which is corresponding to the gender difference seen in the antibiotic use.

The ten antibiotic substances most commonly associated with adverse reactions in the last 5 years, unadjusted for consumption and regardless of the cause of the report, are presented in Table 1.6.

FIGURE 1.26. Percentage of broad spectrum antibiotics (fluoroquinolones, cephalosporins, piperacillin with tazobactam and carbapenems) of all antibiotics in Swedish acute care hospitals 2017, per county. Dalarna County is excluded from hospital data in 2017.

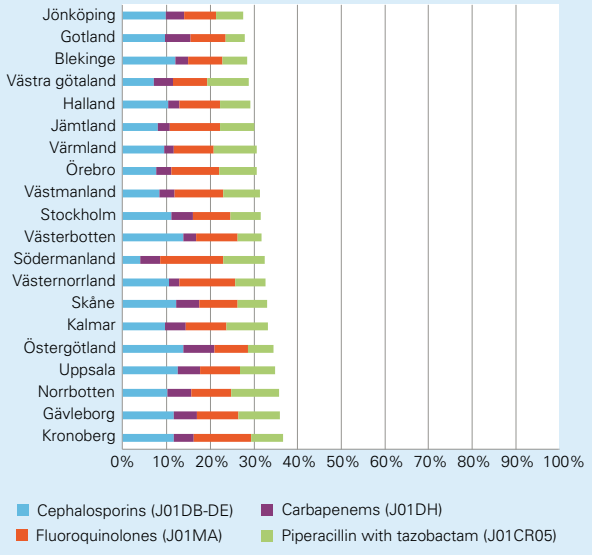


TABLE 1.6. Most reported adverse drug reactions related to antibiotic agents to the Swedish Medical Products Agency 2013-2017.

Antibiotic	Total number of adverse drug reaction reports 2013-2017	Number of 'serious' reports	Number of fatal cases
Phenoxymethyl-penicillin	307	115	0
Flucloxacillin	284	148	9
Ciprofloxacin	264	162	3
Clindamycin	204	99	4
Nitrofurantoin	203	97	3
Sulfamethoxazole and trimethoprim	149	103	1
Amoxicillin	145	57	0
Piperacillin and enzyme inhibitor	118	79	3
Doxycycline	118	44	0
Cefotaxime	90	45	3

Availability of antibiotics

In 2017, insufficient availability of several antibiotic substances was seen in Sweden, Table 1. This introduces challenges in regards to treatment options and is particulary concerning from a patient safety perspective. Insufficient availability of an antibiotic substance might for example result in that the prescribing doctor have to administer an intravenous antibiotic instead of an oral treatment. This demands more resources from the healthcare system with human resources and hospitalisation of the patient. A shortage situation can also lead to the involuntary use of an antibiotic with a broader spectrum than necessary, which might lead to unwanted ecological disturbances of the microbiota of the patient. Finding an appropriate alternative can take time, which costs human resources, and delays the start of treatment. Children are especially vulnerable to poor availability of antibiotics, as many children have trouble swallowing tablets, resulting in fewer treatment options.

Initiatives to approach insufficient availability of antibiotics

In 2015, the Public Health Agency of Sweden was, in collaboration with the Dental and Pharmaceutical Benefits Agency, commissioned by the Government to propose a model for making available both new and old antibiotics where national availability is insufficient. The commission was reported to the Ministry of Health and Social Affairs on 1 December 2017 (1). The Public Health Agency of Sweden has since initiated a pre-study for a possible pilot study. Programråd Strama is also engaged in discussions regarding the problems with insufficient availability.

Table 1. Reported insufficient availabilty of antibiotics until March 2018 (3).

Product(ATC)	Formulation	Strength	Date of information about insufficient availability
Ceftibuten (J01DD14)			Deregistered May 2017
Eusaprim forte (J01EE01)	Tablet	160mg/800mg	March 2018
Piperacillin/tazobactam (J01CR05)	Intravenous	2g/0.25g, 4g/0.5g	April 2017
Furadantin (J01XE01)	Tablet	5 mg	Dec 2017
Furadantin (J01XE01)	Tablet	50 mg	Dec 2017
Cefadroxil (J01DB05)	Oral susp	100 mg/ml	Sep 2017
Spektramox (J01CR02)	Powder oral susp	50+12,5 mg/ml (1:4)	Jan 2018
Spektramox (J01CR02)	Powder oral susp	80+11.97 mg/ml (1:7)	March 2018

Initiative of multisectorial collaboration with participants from the academia, the healthcare sector, governments and the industry has been taken.

All Marketing Authorisation Holders are obligated to report any insufficient availability of pharmaceutical products on the Swedish market to the Swedish Medical Products Agency (MPA). This information is published at the MPAs webpage continuously (2). Insufficient availability is also published by the governmentally owned pharmacy chain Apoteket AB on their webpage www.apoteket.se. The lists are frequently updated and outdated shortages are removed. There is no national compilation of previous occurance of insufficient availability at hand at this moment.

Fact box. Consequences of insufficient avaliability of antibiotics

Substance/formulations	Examples of consequences within health care during insufficient avaliability
Ceftibuten	Used for UTIs when quinolones or trimethoprim/sulfamethoxazole are inappropriate i.e. first-line treatment of febrile UTI in pregnant women and in children Intravenous antibiotics may be used
Eusaprim forte	Wide range of use and difficult to replace for certain patient groups, i.e. prophylaxis against *Pneomocystis jirovecii* in immunocompromised patients
Piperacillin/tazobactam	A broad-spectrum beta-lactam-beta-lactamase inhibitor combination with anti-pseudomonas effect Used as first-line treatment for nosocomial pneumonia, neutropenic fever and intraabdominal infections May be replaced by carbapenems in situations with insufficient availability
Furadantin	First-line treatment of cystitis and also used for prophylaxis against UTI The second-most sold UTI antibiotic in Sweden A shortage may increase the use of quinolones
Cefadroxil oral susp	First generation oral cephalosporin Oral suspension is used for children and others who cannot use tablets Used for skin and soft tissue infections and as second-line treatment for tonsillitis
Spektramox oral susp	Amoxicillin and a beta-lactamase inhibitor Oral suspension is used for children and others who cannot use tablets First-line treatment for infections caused by betalactamase-producing *Haemophilus influenzae* and *Moraxella catarrhalis*

References:

1. The Public Health Agency. Avaliability of antibiotics. In Swedish. 2017. https://www.folkhalsomyndigheten.se/publicerat-material/publikationsarkiv/t/tillganglighet-till-antibiotika/

2. The Medical Products Agency. Avaliability notifications – in the occation of temporary shortage of a medical product. In Swedish. 2018. https://lakemedelsverket.se/OVRIGA-SIDOR/Restnoteringar/

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.

Briefly on data sources and methodology

In Sweden, all veterinary medicinal products are sold by pharmacies. All pharmacies are obliged to report all sales of medicinal and veterinary medicinal products to the eHealth Agency who maintains a database. As the result of a new interpretation of existing legislation on confidentiality, it has not been possible for SVA to obtain raw data per product for calculation to kg active substance and subsequent analyses from the eHealth Agency. Therefore, the Public Health Agency of Sweden has performed the calculations with methodological support from SVA. To facilitate, a few products with limited sales, sold on special license, were excluded from the material. The data source is the same as before, i.e. information in the database of the eHealth Agency on sales from pharmacies to animal owners (prescriptions dispensed) or to veterinarians (requisition).

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

Completeness of data

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

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

Trends in animal populations

Changes in the numbers of animals may affect trends in statistics on consumption of antibiotics. Compared to 2008, the number of pigs slaughtered in 2017 has decreased by 16%, while the number of broilers has increased by 34%. The number of dairy cows decreased by 10% during the same period. The number of horses was estimated to 355 500 in 2016. The number of dogs was estimated to 784 000 in 2012 and 729 000 in 2006. Further details on animal numbers and data sources are found in Demographics and denominator data in this report.

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

ATCvet code	Antimicrobial class	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
QJ01AA, QG01A	Tetracyclines	1 649	1 174	1 115	1 073	881	935	787	685	515	521
QJ01BA	Amphenicols					<1	3	7	11	36	21
QJ01CE, -R, QJ51	Benzylpenicillin[b]	7 758	7 721	7 546	6 696	6 362	5 954	5 509	5 861	5 997	5 940
QJ01CA, QJ01CR	Aminopenicillins	938	1 068	907	723	649	645	635	642	677	640
QJ01D	Cephalosporins	820	738	575	498	410	330	299	267	242	210
QA07AA, QJ01G, -R, QJ51R	Aminoglycosides and polymixins	643	609	557	503	483	341	378	414	385	357
QA07AB, QJ01E	Sulphonamides	2 303	2 128	1 998	1 867	1 813	1707	1 699	1 634	1 643	1 678
QJ01E	Trimethoprim & derivatives	416	379	357	338	329	320	314	313	318	326
QJ01F	Macrolides & lincosamides	1 096	988	739	648	632	564	484	485	472	514
QJ01MA	Fluoroquinolones	169	164	148	120	106	52	45	34	30	26
QJ01XX92, - 94	Pleuromutilins	572	398	174	140	99	126	114	122	228	78
Total		**16 364**	**15 368**	**14 117**	**12 606**	**11 763**	**10 975**	**10 270**	**10 468**	**10 543**	**10 310**

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

Overall sales

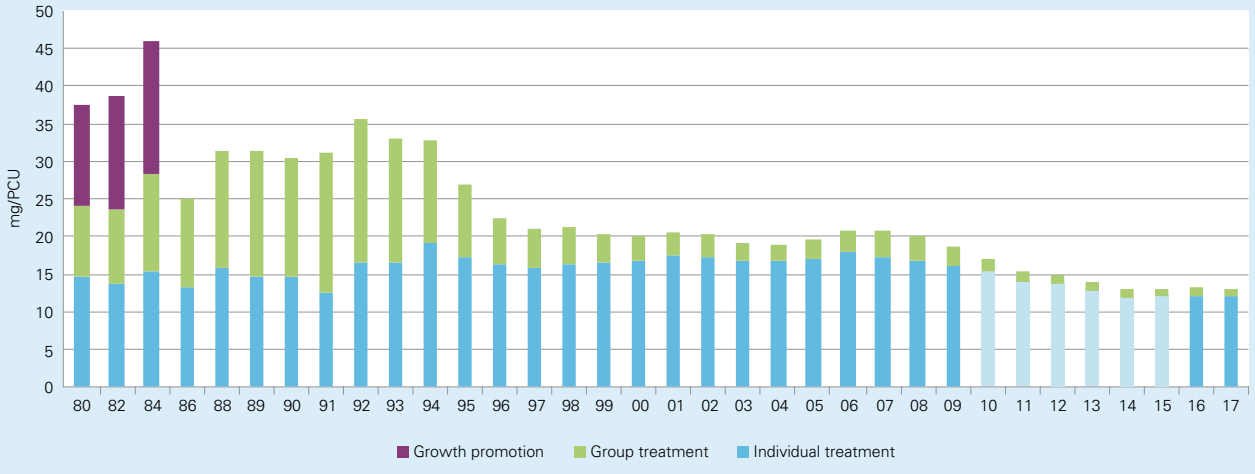
The total yearly sales of antibiotics for animals over the last decade are presented in Table 2.1. The potencies of different antibiotics are not equal and therefore, each class should be evaluated separately.

Of the overall sales expressed as kg active substance, more than 90% are products formulated for treatment of individual animals (injectables, tablets, intramammaries) and less than 10% for treatment of groups or flocks (premixes, oral powders, solutions for in water medication). In 2017, the total reported sales from Swedish pharmacies of antibiotics for animals were 10 310 kg, of which 57% was benzylpenicillin. The corresponding figures for 2008 were 16 364 kg and 47%.

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 PCU-figures for 2016 as a proxy for 2017. The overall sales have decreased by around two thirds compared to the average figures for 1980-1984 (i.e. before the Swedish ban on growth promoting antimicrobials in 1986). This is explained first by the removal of growth promoting antimicrobials in 1986, followed by a major gradual decrease from the mid-90s of the sales of veterinary products for medication via feed or water (group medication), followed by a decrease of sales of injectable products in the past decade.

The WHO classifies 3rd generation cephalosporins, fluoroquinolones and polymyxins as "highly prioritised critically important antimicrobials" (WHO, 2017). In 2017, the sales of these three classes of antibiotics were 0.003, 0.032 and 0.07 mg/PCU, respectively. This represent decreases since 2008 by 89%, 84% and 46%, respectively. For the 3rd generation cephalosporins and fluoroquinolones, the decrease is partly explained by a regulation limiting veterinarians' rights to prescribe this types of antimicrobials (SJVFS 2013:42). As to polymyxins, the recent findings of transferable resistance to colistin were communicated to stakeholders during 2016. An awareness among prescribers of the importance of this class of antimicrobials for public health, and of the potential consequences of transferable resistance, is a probable explanation for the observed decrease.

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



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

Improved surveillance of antibiotic resistance and antibiotic consumption in humans and animals

Nothing is so good that it cannot be made better; this goes for antibiotic resistance (AMR) and antibiotic consumption (AMC) surveillance as well. Increased knowledge through strengthened surveillance is one of the goal in the Swedish governments' strategy on the Swedish work against antibiotic resistance.

Since 2016 the Public Health Agency and the National Veterinary Institute (SVA) are collaborating in a project financed by the Swedish Civil Contingencies Agency (MSB) with the aim to strengthen the ability to early detection and surveillance of antibiotic resistance and bacterial zoonosis. The most important parts of the project includes:

- develop a national all-covering surveillance systems for antibiotic resistance in humans (Svebar),
- rebuild a surveillance system covering the use of antibiotics and health care associated infections in humans to enable national compilation of data (Infektionsverktyget) and,
- build a voluntary network for privately owned veterinary laboratories that perform microbiology and antibiotic susceptibility testing.

A national all-covering surveillance of AMR through Svebar

Svebar is a surveillance system for early detection and national surveillance of antibiotic resistance and a unique collaboration between the clinical microbiology laboratories in Sweden and The Public Health Agency. The aims with Svebar are firstly to provide functions for early warnings for serious types of antimicrobial resistance and to automatically collect all results from clinical microbiology laboratories that are of relevance to antibiotic resistance. A centralized compilation of reports on antibiotic resistance data that can be used both at the local and national-level is also of importance. Moreover, to aid the process of national consensus regarding which types of resistance that are to be considered serious. Svebar is developed and owned by the Public Health Agency. The data are owned by the individual participating laboratory. Reporting to Svebar is voluntary; but all laboratories have agreed to participate. Currently (Mars 22, 2018) 19 out of 26 laboratories deliver data to Svebar, covering approximately 88 % of the population. As part of the MSB-project the Public Health Agency are visiting the laboratories to assure that technical and practical obstacles are addressed so that all can deliver data by the end of 2018. Hence will Svebar be a full-cover national surveillance system for antibiotic resistance by 2019.

National data on the use of antibiotics and health care associated infections

Infektionsverktyget is a surveillance system for health care associated infections (HAIs) and the use of antibiotics. It is owned by Inera. It was developed and implemented 6 years ago (2012) in a large part of the Swedish hospitals as a tool for local improvement work aiming at preventing health care associated infections and improving the rational use of antibiotics. National data on HAIs and diagnoses linked antibiotic prescribing is however currently not available in Sweden. As part of this MSB-project the Public Health Agency has financed a rebuild of Infektionsverktyget so that the data can be complied on a national level.

A voluntary network for veterinary laboratories

A voluntary network for privately owned veterinary laboratories that perform microbiology and antibiotic susceptibility testing was formed in October 2016. The network is a part of the MSB-project and coordinated by the National Veterinary Institute (SVA). The aim of the network is to share knowledge between laboratories and thereby increase the general level of competence of the participants. Another aim is to harmonize quality assurance (QA) within the network. High competence and QA will raise the analytical quality and ensure more reliable data for the surveillance of antibiotic resistance and zoonoses. This is beneficial for the society and for veterinarians in clinical practice as well as for the welfare of animals. The network also strengthens coordination and communication between authorities and the private sector.

So far twelve private laboratories have joined the network. To attain the aim of the network, several activities are implemented, e.g. yearly meetings; yearly proficiency tests; web-based platform for chat and exchange of knowledge; newsletters with up-to-date information in the field and individually targeted education of personnel. Moreover, personnel from SVA have performed on-site visits to other labs in the network for discussions on e.g. methodology and QA. The contact and communication between the laboratories and experts at SVA have increased substantially since the network was launched in 2016. The network has become a key player within the field of susceptibility testing in the veterinary sector.

Antibiotic resistance in humans

Overview of surveillance systems

The national surveillance systems collect data from two different sources: notifiable diseases and data from clinical samples, which are submitted voluntarily. The clinical samples are mostly from patients with suspected infections, whereas for the notifiable diseases a large proportion of the samples are taken for screening or case finding purposes.

Notifiable diseases

For humans four bacterial types of antibiotic resistance are included in the Swedish Communicable Diseases Act. These are *Staphylococcus aureus* resistant to methicillin (MRSA), *Streptococcus pneumoniae* with reduced susceptibility or resistance to penicillin (PNSP), *Enterococcus faecalis* and *Enterococcus faecium* resistant to vancomycin (*vanA* or *vanB*, VRE), and Enterobacteriaceae carrying ESBL or $ESBL_{CARBA}$. As in previous years, the reports of ESBLs have outnumbered the other three types manifold.

Voluntary surveillance based on clinical samples

Svebar

From 2015 and onwards, all voluntary data on clinical isolates from humans have been collected through Svebar. This is a system that automatically collects all culture results from participating clinical microbiology laboratories. Currently 19 laboratories deliver data to Svebar. It is not possible to deduplicate Svebar data since patient identification is not permitted in the system. Consequently, duplicate findings from blood and other samples will be reported. For unusual resistance types, this can result in differences in proportion of resistance compared to previous years so all resistance trends should be interpreted with caution. Data used and analysed for volontary surveillance are based on data from ten (2015, 2016) and eleven (2017) laboratories. These laboratories delivered validated and correct data for all years. The eight remaining laboratories now delivering data to Svebar have either not been connected the entire timeperiod or needs further data validation.

Isolates from blood cultures reported to ECDC/EARS-Net

EARS-Net started in 1998 as EARSS (the European Antimicrobial Resistance Surveillance System) with data from blood cultures on *Staphylococcus aureus*, and *Streptococcus pneumoniae*, and now includes eight species. Sweden participated already the first year. The coordination and validation of results from the participating Swedish laboratories is done by the Public Health Agency of Sweden. Data for EARS-Net 2017 was collected through Svebar and a total of 11 laboratories were included as they delivered data from the entire year. In general, the proportions of resistance to clinically important antibiotics were low, and this has been the typical situation for Sweden all through the EARSS/EARS-Net history. The resistance trends from 2015 and onwards should be interpreted with caution since patients infected with multiresistant isolates tend to be sampled more often, and deduplication of data from Svebar is not possible.

ResNet

Prior to 2015, the national surveillance programme on antibiotic resistance, ResNet, was used to collect data on seven bacterial species. From 2015 and onwards, yearly data based on SIR reported by the clinical microbiology laboratories to Svebar were used. In the web-based software ResNet, zone-diameters were reported in aggregated form by the clinical microbiology laboratories participating. Data were presented in the form of resistance levels in their respective geographical areas on a map of Sweden as well as individual zone histogram graphs as a tool for internal quality assurance. *S. pneumoniae* and *H. influenzae*, commonly causing respiratory tract infections have been included since 1994. *Escherichia coli* from urine and *S. aureus* from skin and soft-tissue infections was included in 2002. In 2005, *Klebsiella pneumoniae* mainly from urine was included. *Pseudomonas aeruginosa* was included in 2009.

Microbiological characterization program

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

Overview of sampling and culture results

Denominator data have been collected since 2001 on a voluntary basis from the microbiology laboratories in Sweden and reported each year in Swedres-Svarm as background data. The reporting laboratories, this year 24 out of 25, cover more than 95 percent of the population. Some modifications of the data collection have been made during the years, for instance were analyses of toxinpositive *C. difficile* included year 2008, urine cultures analyses included year 2009 and positive blood culture analyses included year 2010. Complete data for 2017 are given in the section Demographics and denominator data.

In the following figure 3.1 the annual numbers of requested analyses per 100 000 inhabitants are presented for: blood culture, MRB screening culture, general culture, throat culture, nasopharynx culture, urine culture, and *C. difficile*. 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 and MRB screening cultures requested annually per 100 000 inhabitants have increased continuously, except for MRB-screen which decreasesed the last years. Changes in screening practices in the counties and variation in sampling due to outbreaks could explain some of this decline. 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.

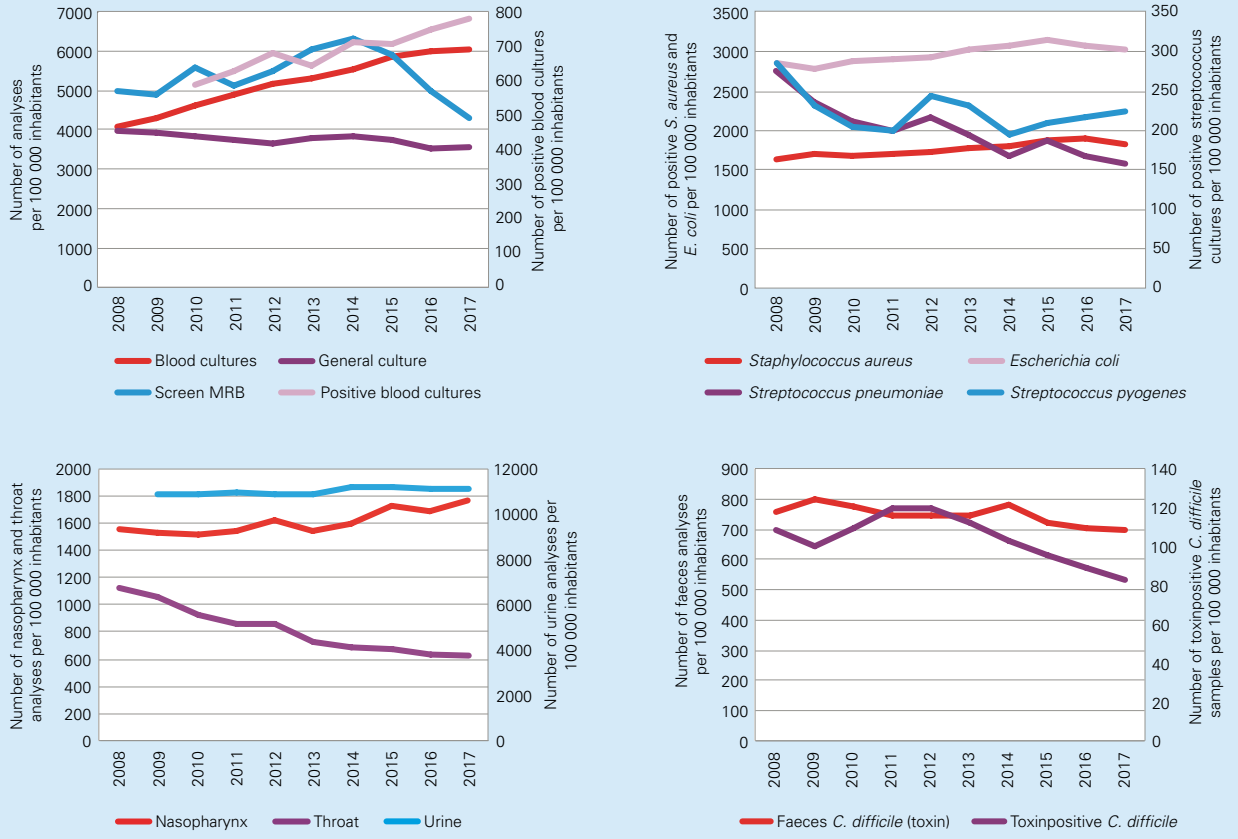
Escherichia coli, Klebsiella pneumoniae, and Enterobacteriaceae with ESBL and ESBL$_{CARBA}$

Mandatory reporting of ESBL-producing Enterobacteriaceae

Background

ESBL-producing Enterobacteriaceae has been notifiable by clinical laboratories according to the Communicable Diseases Act since February 2007. As there is no clinical reporting, information on ESBL cases is limited to data on age, gender and sample type. From 2010, the definition of ESBL included not only classical ESBLs (=ESBL$_A$), which are inhibited by clavulanic acid, but also plasmid-mediated AmpC-betalactamases (= ESBL$_M$) and metallo-betalactamases /carbapenemases (= ESBL$_{CARBA}$). In March 2012 the notifications of bacteria with ESBL$_{CARBA}$ were extended to include both a laboratory and a clinical report, additionally contact tracing became mandatory.

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



Notifications of ESBL according to the Communicable Disease Act

A total of 10 084 cases were notified in 2017, a decrease with 5% compared to 2016. The national incidence was 100 cases per 100 000 inhabitants. Eleven out of 21 Swedish counties reported fewer cases. The highest incidence was found in Blekinge county (201 cases per 100 000 inhabitants; Figure 3.2) and the lowest incidence in Östergötland county. There was a nearly three-fold difference in incidence between the counties. The large variation in incidence between counties could partly be explained by different local practices for sampling and screening but also in the number of people who recently arrived in Sweden.

As in previous years the most commonly reported species was *E. coli* found in 86% of all cases, followed by *K. pneumoniae* with 10% (Table 3.1).

ESBL-producing bacteria were most often found in urine samples (n=6 135, 61%). The second and third most common sources were fecal and rectal samples with 18% (n=1 807) and 10% (n=988) respectively. Sampling from feces and rectum for screening purposes has increased in recent years but 2017 the number of screening samples decreased with 23% compared to 2016 (Figure 3.3). Isolates from blood and wound samples constituted four percent and two percent, respectively, and isolates were from other samples in five percent of the cases. In 2017, 594 cases with ESBL-producing bacteria were reported as invasive infections, compared to 609 cases

TABLE 3.1. Distribution of species among human cases of ESBL-producing Enterobacteriaceae 2017.

Species	Number of cases	Proportion, %
Escherichia coli	8 989	86
Klebsiella pneumoniae	1 004	9,6
Proteus mirabilis	61	0,6
Citrobacter species	28	0,3
Shigella species	28	0,3
Salmonella species	8	0,1
Enterobacteriaceae (not specified or species not reported)	289	2.8
Total number reported	**10 407**[a]	

[a]In 301 patients two or more ESBL-producing species were reported resulting in a higher number of isolates than number of cases reported.

FIGURE 3.2. The incidence (cases/100 000 inhabitants) of ESBL-producing Enterobacteriaceae in Swedish counties 2017, in relation to type of sample.

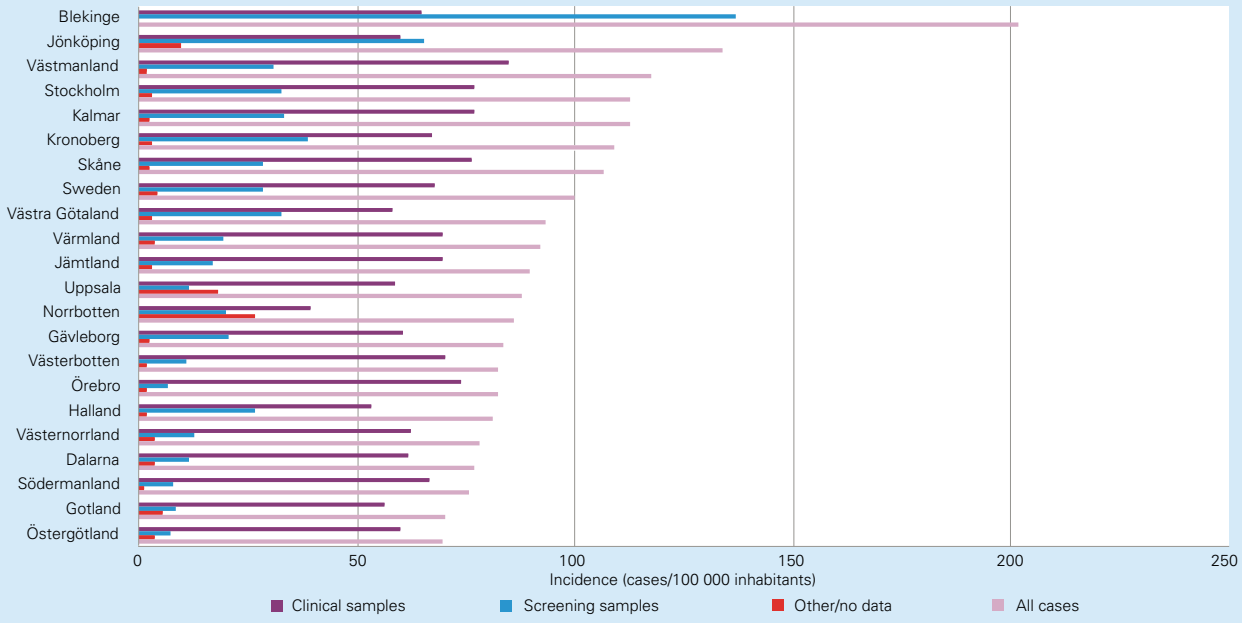
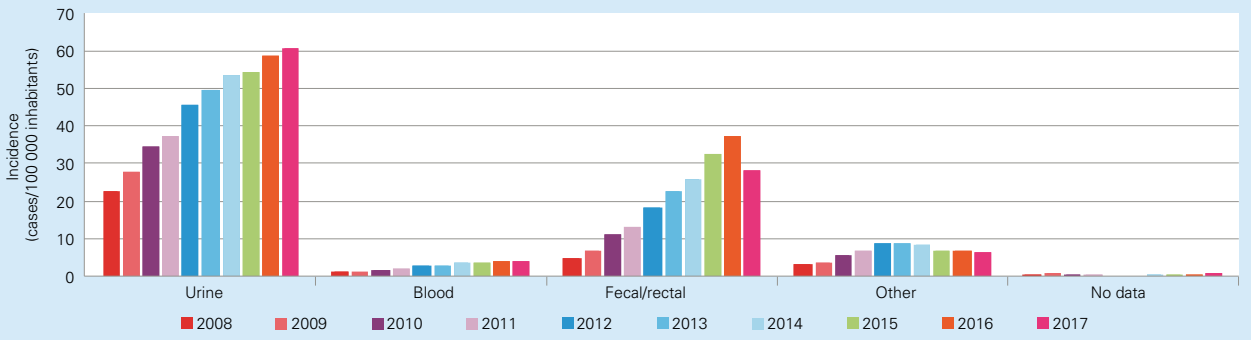


FIGURE 3.3. Incidence (cases/100 000 inhabitants) per sample type of notified human cases of ESBL-producing Enterobacteriaceae 2008-2017.



2016. Among these, 474 were new cases for 2017 and 120 were known carriers of ESBL, notified during previous years.

In 2017, 6 580 cases with ESBL-producing Enterobacteriaceae were reported from women and 3 504 cases from men. The gender distribution has not changed significantly since the surveillance started. The incidence was highest in the age group <1 year (318), followed by the age group 80 years and older (279) (Figure 3.4). In most of the other age groups the incidence remained at a lower but slightly decreasing level. Among the elderly urinary tract infection is a common bacterial infection which could explain the higher incidence in this group. The high incidence in neonates is probably a result of screening practices at neonatal units and contact tracing for new cases.

The incidence in age and gender groups for both *E. coli* and *K. pneumoniae* reflects the expected occurrence of urinary tract infection in the different groups (Figure 3.5). ESBL-producing *E. coli* were derived from women in 67% of the cases. They had a median age of 48 years compared to 62 years for men. The *K. pneumoniae* ESBL cases were more equally distributed between sexes, with median ages of 59 years for women and 65 years for men.

FIGURE 3.4. Incidence (cases/100 000 inhabitants) per age group of notified human cases of ESBL-producing Enterobacteriaceae 2008-2017.

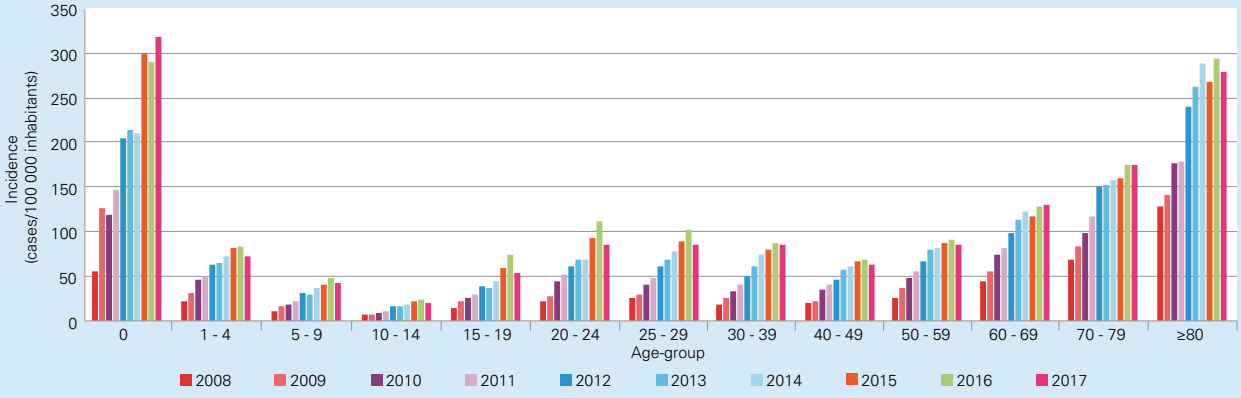
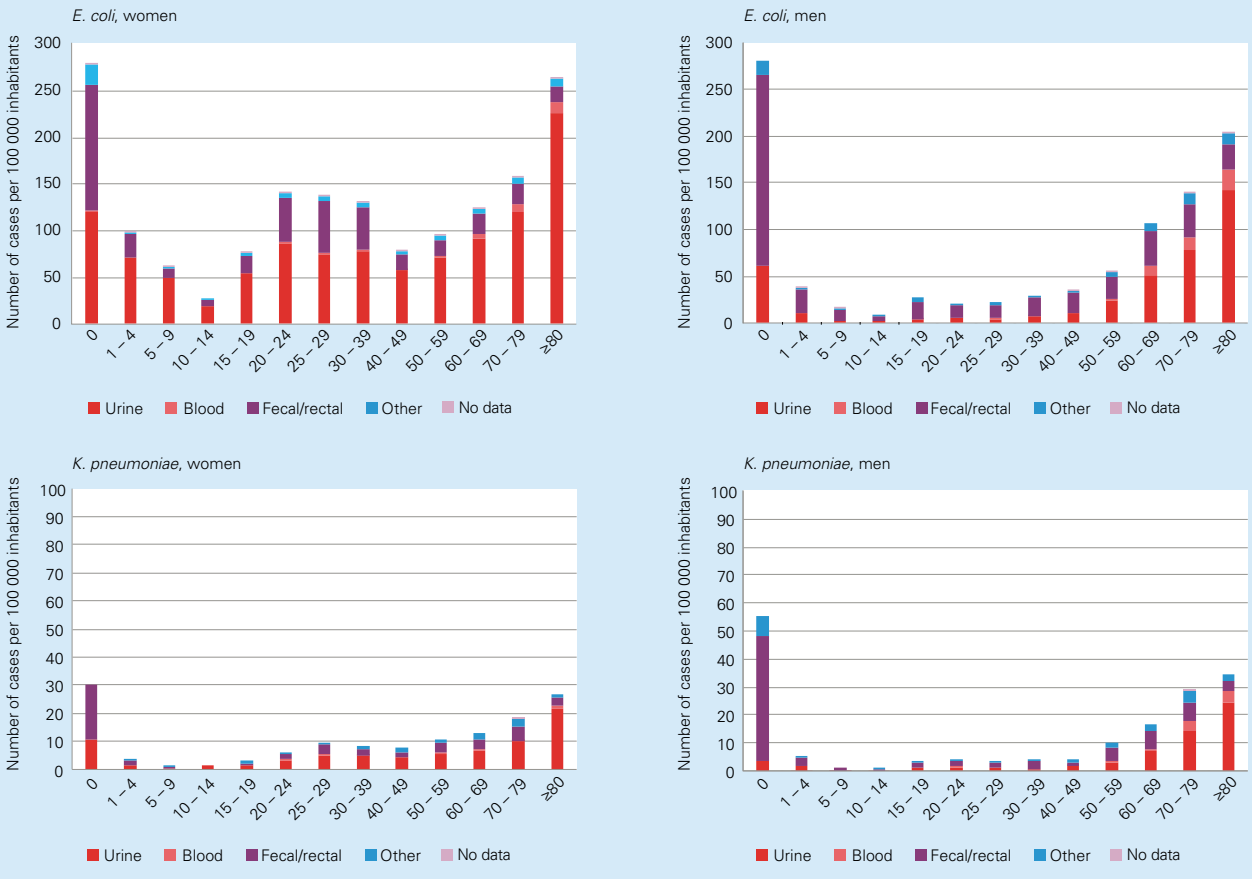


FIGURE 3.5. Age, gender and sample type distribution of human cases of ESBL-producing *E. coli* and *K. pneumoniae* 2017.



Outbreak investigations

In 2017, one larger outbreak with ESBL-producing *E. coli* at a neonatal unit was reported. A total of 26 patients were affected. Other small clusters with both ESBL-producing *K. pneumoniae* and *E. coli* have been noted at both neonatal units and other units in different parts of Sweden during 2017, but outbreaks are not consistently reported.

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

Background

ESBL$_{CARBA}$ of clinical importance belong to one of three kinds, either KPC (K. pneumoniae Carbapenemase)/IMI (imipenem-hydrolyzing β-lactamase), MBLs (Metallo-betalactamases, i.e. NDM, VIM and IMP) or certain OXA-enzymes. In Sweden, all enzymes with carbapenemase activity are denoted ESBL$_{CARBA}$ (Giske et al., 2009).

Notifications of ESBL$_{CARBA}$ according to the Communicable Disease Act

In 2017, 116 new cases with an ESBL$_{CARBA}$-producing Enterobacteriaceae were reported, compared to 127 new cases in 2016. Cases were reported from nineteen Swedish counties with 41% (47 cases) of the cases being reported from Stockholm. Of all cases, 17% (n=20) were reported as domestic and 80% (n=93) as acquired abroad (Figure 3.6). The five most common countries for acquisistion abroad were Turkey (n=9), Egypt (n=8), India (n=8), Iraq (n=7) and Serbia (n=7).

A majority of the domestic cases in 2017, were identified during investigation of clinical symptoms in contrast to year 2015 when several cases were identified in targeted screening at neonatal units (Figure 3.7). Screening after hospitalisation abroad continues to be the leading cause of identification of ESBL$_{CARBA}$-producing Enterobacteriaceae among cases acquired abroad. The number of domestic cases with hospital acquired ESBL$_{CARBA}$ remained at the same level as in 2016 but for seven of the domestic cases information of acquisition was missing (Figure 3.8). Hospital acquired infection dominated among imported cases but increased from 58 to 72 compared to 2016 and for seven cases data on acquisition were missing.

FIGURE 3.7. Indications for sampling of domestic cases of ESBL$_{CARBA}$ producing Enterobacteriaceae in humans in Sweden 2012-2017. Number of reported cases each year is shown in brackets.

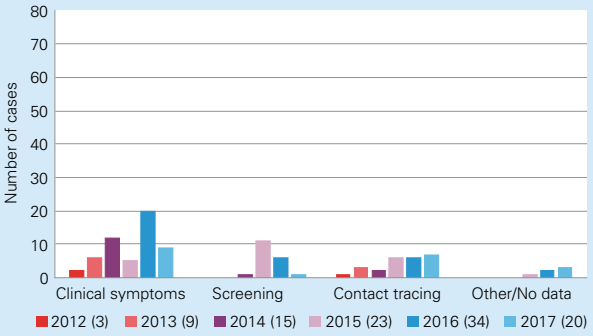


FIGURE 3.6. Number of human cases of ESBL$_{CARBA}$ annually notified as acquired in Sweden and abroad, 2008-2017.

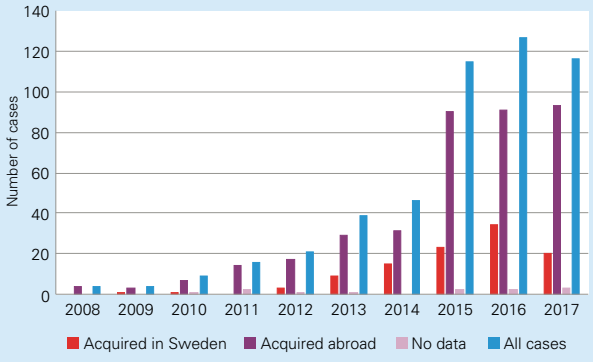
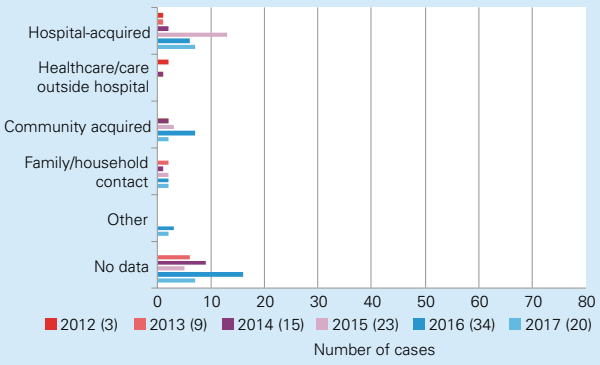


FIGURE 3.8. Epidemiological classification of human cases of ESBL$_{CARBA}$ producing Enterobacteriaceae acquired in Sweden 2012-2017. Number of reported cases each year is shown in brackets.



The $ESBL_{CARBA}$-producing Enterobacteriaceae were identified in fecal/rectal samples (n=82), urine (n=23), wound (n=4), respiratory samples (n=2), blood (n=2), and for three cases sample material was not specified. The cases were nearly equally distributed between gender, and the median ages were 44 and 68 years for women and men, respectively.

Outbreak investigations

During 2017 one hospital outbreak with $ESBL_{CARBA}$-producing *E. coli* with OXA-48 was identified and confirmed with whole genome sequencing at the Public Health Agency of Sweden. A total of five cases were linked to the outbreak.

Epidemiological typing of $ESBL_{CARBA}$

Since November 2015, epidemiological typing of ESBL has been performed with whole genome sequencing (WGS). All $ESBL_{CARBA}$ isolates from notified cases in 2017 have been characterised using this methodology. The most common carbapenemase-producing Enterobacteriaceae was *E. coli* accounting for 60% of all cases, followed by *K. pneumoniae* with 33%. Genes coding for carbapenem resistance have also been detected in several other species of Enterobacteriaceae. The dominating enzyme type in 2017 was OXA-48 and this enzyme was detected in *E. coli* and *K. pneumoniae* isolates, in most cases together with CTX-M (=$ESBL_A$). Table 3.2 shows

TABLE 3.2. Number of isolates (n) in different species among human cases with $ESBL_{CARBA}$ divided by subtypes.

Enzyme	Subtype	*E. coli* (n=77)	*K. pneumoniae* (n=41)	Other Enterobacteriaceae (n=17)
VIM	VIM-1-like	0	0	4
OXA-48+NDM	OXA-181 + NDM-5	2	0	0
	OXA-48 + NDM-1	0	3	1
	OXA-232 + NDM-1	0	1	0
	OXA-181 + NDM-1	0	1	0
OXA-48	OXA-48	25	8	5
	OXA-181	6	8	0
	OXA-244	14	0	0
	OXA-245	0	1	0
	OXA-162	0	1	0
	OXA-232	0	1	0
NDM	NDM-1	5	9	5
	NDM-5	22	2	0
	NDM-6	1	0	0
	NDM-7	1	0	1
KPC	KPC-2	1	3	0
	KPC-3	0	3	0
IMP+GES	IMP-14 + GES-5	0	0	1

TABLE 3.3. Number of isolates among human cases with $ESBL_{CARBA}$ sorted by species and percent resistance.

	KPC-MBL positive isolates			OXA-48-like positive isolates		
	E. coli % R	*K. pneumoniae* % R	Other Enterobacteriaceae % R	*E. coli* % R	*K. pneumoniae* % R	Other Enterobacteriaceae % R
Antibiotic	**n=30**	**n=17**	**n=11**	**n=45**	**n=19**	**n=5**
Cefotaxime	100	100	100	87	84	60
Ceftazidime	100	100	100	69	84	60
Mecillinam	50	47	67[b]	20	21	-
Trimethoprim	87	82	100	76	58	60
Nitrofurantoin	3	-	-	7	-	-
Meropenem	70	41	36	4	37	0
Gentamicin	47	59	73	47	53	40
Tobramycin	53	100	100	33	74	60
Amikacin	30	37	55	11	11	40
Piperacillin/ tazobactam	100	100	82	100	100	100
Cefoxitin	97	100	91	49	68	80
Imipenem[a]	13	18	45	0	5	0
Ciprofloxacin[a]	87	100	82	49	100	60

[a]Gradient test, [b]calculated on three *P. mirabilis* isolates

the different subtypes of $ESBL_{CARBA}$-enzymes. For the OXA-48 group OXA-48 was most common followed by OXA-244. For the NDM group NDM-5 was most common. Isolates with $ESBL_{CARBA}$ very often carry multiple resistance genes, leaving very few options for antibiotic treatment.

Apart from the genotypic analysis phenotypic susceptibility testing was performed on all $ESBL_{CARBA}$ isolates. Resistance (R) to all the tested antibiotics for both *E. coli* and *K. pneumoniae* are summarized in Table 3.3. Resistance to imipenem and meropenem were higher among KPC-MBL isolates compared to OXA-48 isolates. The majority of the *E. coli* isolates were sensitive to nitrofurantoin, only 3% of the KPC-MBL and 7% of the OXA-48 isolates were resistant.

Characterization of *K. pneumoniae* and *E. coli* from urine in Sweden; a national microbial surveillance program, 2007-2015

The epidemiology of ESBL-producing Enterobacteriaceae, especially the two most common species *E. coli* and *K. pneumoniae*, is monitored in a national surveillance program. The aim is to understand the genetics of the bacterial strains as well as what types of enzymes that cause resistance to beta-lactam antibiotics. By collecting isolates regularly, and performing phenotypic and genotypic analyses, we have achieved a better understanding of the epidemiology of these resistant bacteria. All laboratories in Sweden have since 2007 been asked to collect consecutive cefadroxil-resistant *E. coli* and *K. pneumoniae* isolates from urine samples every second year during a one-month period. The isolates are sent to the Public Health Agency for further analysis. The result of the 2017 collection will be presented in Swedres-Svarm 2018.

In 2007, 87% and 98% of $ESBL_A$ positive isolates were detected for submitted *E. coli* and *K. pneumoniae* respectively. Compared to 2015 the share decreased to 81% and 93%, with the lowest proportion identified 2011 with 76% and 70% $ESBL_A$ positive isolates of *E. coli* and *K. pneumoniae* respectively (Figure 3.9 and 3.10). The share of submitted cefadroxil resistant *E. coli* and *K. pneumoniae* that were ESBL-negative in the genotypic screen was highest in 2011 with 18% and 24% respectively.

Among the $ESBL_A$, CTX-Ms from group 1, was the most prevalent enzyme, followed by CTX-Ms from group 9. The most commonly found genes among the $ESBL_M$ positive *E. coli* isolates over the years was of the type CIT. A slight increase was seen for $ESBL_M$ positive isolates from 4.2% to 5.6% (2007-2015). A few isolates were detected with both $ESBL_A$ and $ESBL_M$ (13 *E. coli* and 3 *K. pneumoniae* isolates).

Two $ESBL_{CARBA}$ producing genes was also identified, NDM together with CTX-M group 1 in *K. pneumoniae* 2013 and OXA-48 together with DHA in *E. coli* 2015.

Three isolates harboring the *mcr* gene, causing resistance to colistin, were identified in 2015 (two *E. coli* and one *K. pneumoniae*). It is of great importance to identify the *mcr* gene in an early stage to prevent national spread. In the *K. pneumoniae* isolate the *mcr* gene was identified together with CTX-M group 1, and in the two *E. coli* isolates the gene was identified with CTX-M group 1 and CTX-M- group 9 respectively.

FIGURE 3.9. Distribution of ESBL classes among cefadroxil resistant *E. coli* between 2007 and 2015.

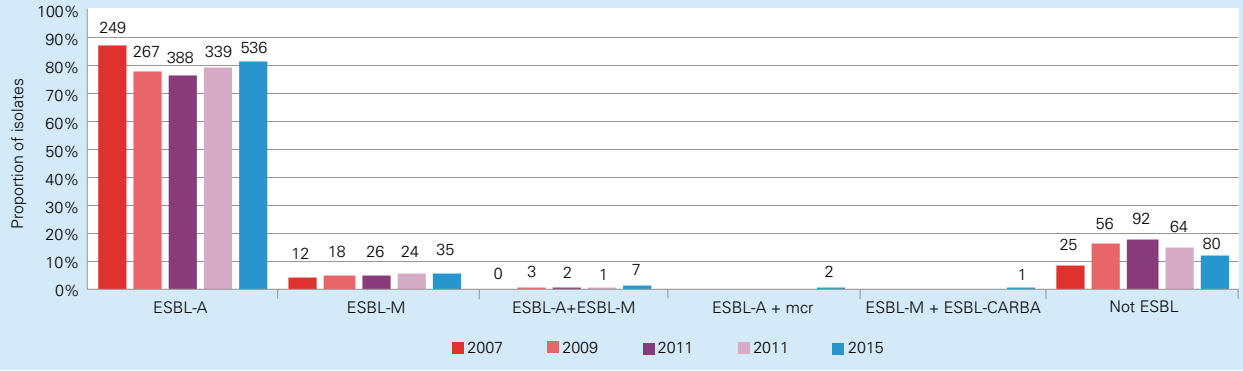


FIGURE 3.10. Distribution of ESBL classes among cefadroxil resistant *K. pneumoniae* between 2007 and 2015. Number of isolates are given above bars.

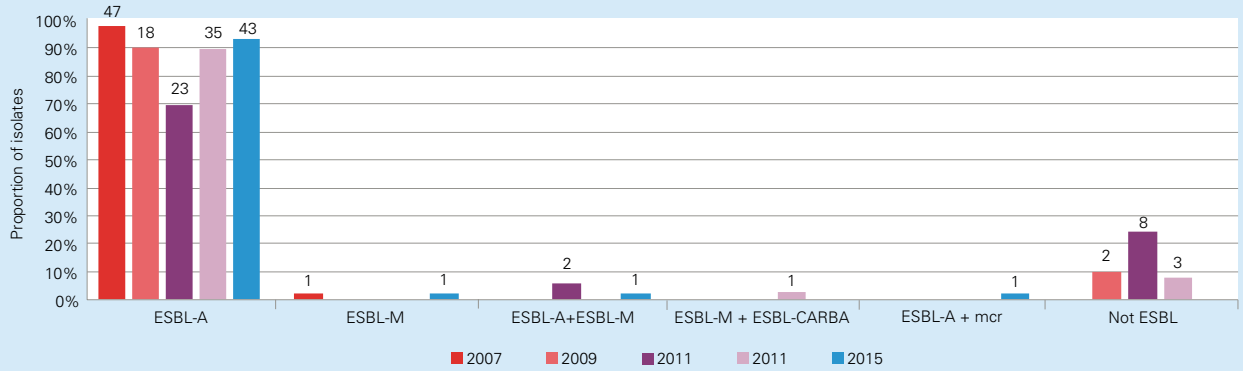


TABLE 3.4. Antibiotic resistance of *E. coli* and *K. pneumoniae* with $ESBL_A$ within the national microbial surveillance program 2007-2015. Number of isolates are given in brackets.

	E. coli, % R					*K. pneumoniae*, % R				
Antibiotic	**2007** (n=249)	**2009** (n=270)	**2011** (n=390)	**2013** (n=339)	**2015** (n=536)	**2007** (n=47)	**2009** (n=18)	**2009** (n=25)	**2013** (n=36)	**2015** (n=43)
Cefotaxime	96	100	99	100	100	96	100	100	100	100
Ceftazidime	49	67	73	76	79	60	89	88	86	95
Piperacillin/tazobactam	5	7	15	8	8	19	0	36	33	21
Imipenem	nt	0	0	0	0	nt	0	0	3	0
Meropenem	nt	0	0	0	0	nt	0	0	3	0
Gentamicin	31	44	40	34	33	26	50	44	47	40
Tobramycin	21	47	47	34	34	15	44	80	58	51
Amikacin	0	7	1	1	1	0	22	8	0	0
Ciprofloxacin	77	66	61	58	66	53	50	68	47	51
Nitrofurantoin	6	8	3	6	2	nt	nt	nt	nt	nt
Trimethoprim	71	73	71	67	63	77	78	88	81	88
Tigecycline	nt	0	0	1	0	nt	0	12	0	0
Mecillinam	3	12	7	7	5	4	39	16	17	14
Ertapenem	0	3	1	1	2	0	0	0	17	2

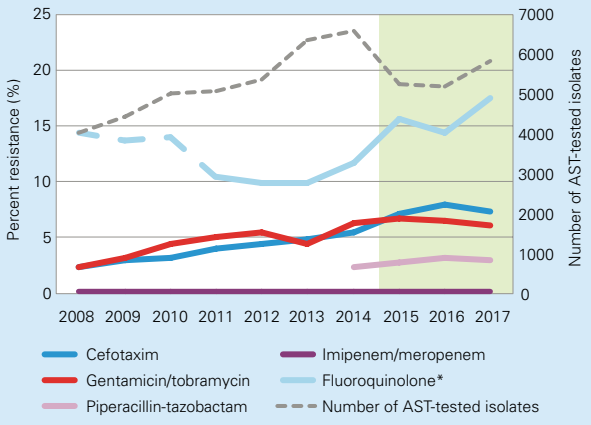
Apart from the genotypic analysis phenotypic susceptibility testing was performed on all isolates with an ESBL gene. Resistance (R) to all the tested antibiotics for both *E. coli* and *K. pneumoniae* from the five collections are summarized in Table 3.4. An increase of resistance to ceftazidime were identified, from 49% to 79% among the *E. coli* and 60% to 95% among the *K. pneumoniae* isolates. A slight decrease of resistance to trimethoprim and ciprofloxacin in *E. coli* isolates were seen.

Escherichia coli, clinical isolates from blood and urine

Resistance data on *Escherichia coli* reported to EARS-Net

From 2008 to 2014, deduplicated data on invasive infections from 18-21 laboratories (depending of the year) were used. From 2015 and onwards, yearly (non deduplicated) data based on SIR reported to Svebar were used.The number of isolates of *E. coli* (n=5 810) were much greater than the number for the other pathogens reported to EARS-Net. The level of resistance for *E. coli* to the antibiotics included in EARS are shown in Figure 3.11. The resistance to third-generation cephalosporins was around 7%. Resistance to fluoroquinolones is now on a level of 18% and an increase is seen over the past years. The high levels of fluoroquinolone resistance seen prior to 2011, was due to the use of nalidixic acid for detection of this resistance, which was replaced with ciprofloxacin in 2011. The carbapenem resistance remains at a very low level.

FIGURE 3.11. Antibiotic resistance in *E. coli* isolates from bloodstream infections included in EARS-Net surveillance during the years 2008-2017.



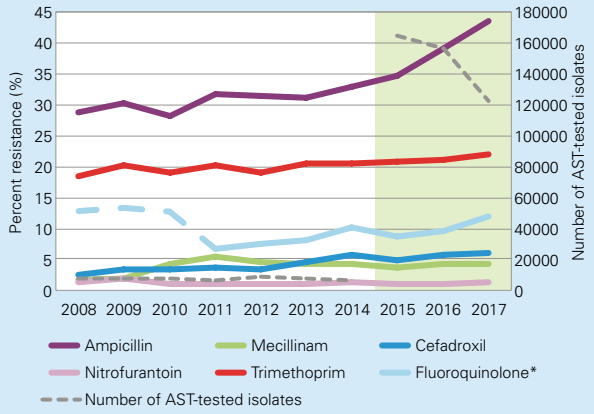
*Prior to 2011, nalidixic acid was used for detection of fluoroquinolone resistance in Enterobacteriaceae. From 2011, ciprofloxacin was used.

Resistance data on *Escherichia coli* from urine

From 2008 to 2014, zone-diameter data from the national surveillance programme on antibiotic resistance ResNet were used. From 2015 and onwards, yearly data based on SIR reported to Svebar were used. Resistance to commonly prescribed oral antibiotics for treatment of urinarytract infections (UTI) caused by *E. coli* are monitored. Resistance levels remained stable. Cefadroxil resistance is used as an indicator

for presence of genes coding for ESBLs. The high levels of fluoroquinolone resistance seen prior to 2011, was due to the use of nalidixic acid for detection of this resistance, which was replaced with ciprofloxacin in 2011 (Figure 3.12). Resistance to amoxicillin-clavulanic acid and piperacillin-tazobactam was 26% and 3.4% respectively. These resistance proportions are based on a selected population already resistant to cefadroxil.

FIGURE 3.12. Resistance rates for antibiotics commonly used to treat urinary tract infections, *E. coli* 2008-2017.



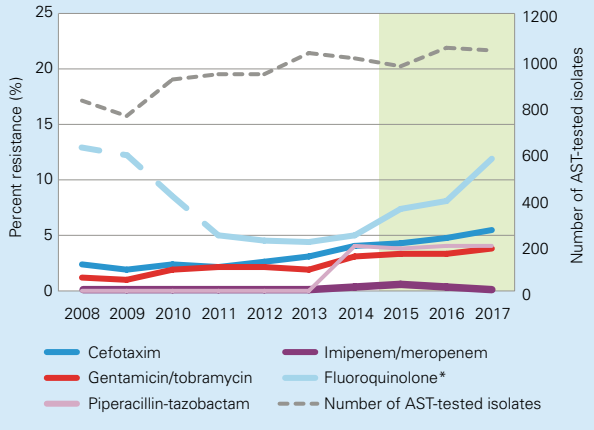
*Prior to 2011, nalidixic acid was used for detection of fluoroquinolone resistance in Enterobacteriaceae. From 2011, ciprofloxacin was used.

Klebsiella pneumoniae, clinical isolates from blood and urine

Klebsiella pneumoniae reported to EARS-Net

From 2008 to 2014, deduplicated data on invasive infections from 18-21 laboratories (depending of the year) were used. From 2015 and onwards, yearly (non deduplicated) data based on SIR reported to Svebar were used. The proportion of resistance for *K. pneumoniae* to the antibiotic combinations defined by EARS are shown in Figure 3.13. The resistance to third-generation cephalosporins is quite stable over time. In 2017, the fluoroquinolone resistance increased to 12% compared to 8% in 2016. The high levels of fluoroquinolone resistance seen prior to 2011, was due to the use of nalidixic acid for detection of this resistance, which was replaced with ciprofloxacin in 2011. The carbapenem resistance remains at a very low level (0.1%).

FIGURE 3.13. Antibiotic resistance in *K. pneumoniae* isolates from bloodstream infections included in EARS-Net surveillance during the years 2008-2017.

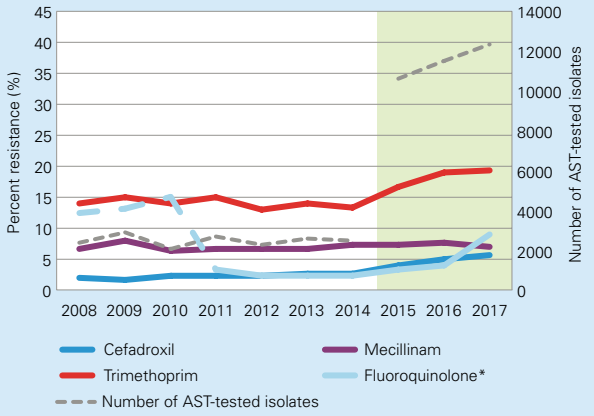


*Prior to 2011, nalidixic acid was used for detection of fluoroquinolone resistance in Enterobacteriaceae. From 2011, ciprofloxacin was used.

Klebsiella pneumoniae from urine

From 2008 to 2014, zone-diameter data from the national surveillance programme on antibiotic resistance ResNet were used. From 2015 and onwards, yearly data based on SIR reported to Svebar were used. In 2017, the resistance levels for all tested antibiotics remained at approximately the same levels as seen in 2016 with exception for fluoroquinolone resistance (Figure 3.14). The high levels of fluoroquinolone resistance seen prior to 2011, was due to the use of nalidixic acid for detection of this resistance, which was replaced with ciprofloxacin in 2011. Resistance to amoxicillin-clavulanic acid and piperacillin-tazobactam was 13% and 7% respectively. These resistance proportions are based on a selected population already resistant to cefadroxil.

FIGURE 3.14. Resistance rates for antibiotics commonly used to treat urinary tract infections, *K. pneumoniae* 2008-2017.



*Prior to 2011, nalidixic acid was used for detection of fluoroquinolone resistance in Enterobacteriaceae. From 2011, ciprofloxacin was used.

Genomic-based surveillance of carbapenem-resistant and/or colistin-resistant Enterobacteriaceae at the EU-level (EURGen-CCRE)

Background

The emergence of multidrug-resistant Gram-negative bacteria is mainly the result of horizontal gene transmission by mobile genetic elements (e.g., plasmids) and the spread of specific bacterial clones. The global epidemics of extended-spectrum beta-lactamases, carbapenemases and of the recently discovered mobile colistin resistance (mcr-1) gene are typical examples of such plasmid-mediated resistance epidemics.

Carbapenem and colistin both represent antibiotics of last resort. The use of these drugs have increased during the last years as a consequence of the emerging cephalosporin resistant (ESBL-producing) Gram negative bacteria. Colistin was excluded from human medicine in many countries during the 1970s due to toxicity. However, the drug was continuously used in veterinary medicine and for growth promotion in the meat industry. Hence, the selection pressure has persisted. The increased clinical use now drives dissemination of this resistance in a highly undesirable way.

In 2012, ECDC launched the European Survey on Carbapenemase-Producing Enterobacteriaceae (EuSCAPE) project to gain insights into the occurrence, epidemiology and the spread of carbapenemase-producing Enterobacteriaceae (CPE) and to build laboratory capacity for diagnosis and surveillance of CPE in Europe. The EuSCAPE project demonstrated the feasibility of conducting integrated epidemiological and microbiological sentinel multi-center structured surveys and of collecting comparable quality-assessed data suitable for EU level analyses.

Surveillance has traditionally been based on phenotypic antimicrobial susceptibility testing. However, with the fast development of genomic tools new opportunities opens up for extensive genetic investigations. Genomic characterization combined with epidemiological data provide information with higher resolution.

ECDC has developed a study protocol for future European whole genome sequencing (WGS)-based surveillance of carbapenem- and/or colistin-resistant Enterobacteriaceae based on the model of the EuSCAPE project. This new protocol describes the design of structured multi-centre molecular epidemiological surveys of the prevalence and distribution of carbapenem-resistant and/or colistin-resistant Enterobacteriaceae (CCRE-surveys).

Objectives

The primary public health objective of this type of EU-wide WGS-based surveillance is:

- To determine the occurrence, geographic distribution and the population dynamics of high-risk carbapenem-resistant and/or colistin resistant Enterobacteriaceae clones and/or transmissible resistance / genetic elements of critical public health importance in Europe in order to inform risk assessment, prevention and control policies.

The secondary objectives are:

- To identify the epidemiological risk factors for infection or colonisation with carbapenem-resistant and/or colistin-resistant Enterobacteriaceae at bacterial clonal and sub-genomic level;

- To support the Member States in developing technical capability and proficiency for genomic-based surveillance and risk assessment of multidrug-resistant bacteria with epidemic potential.

Project outline

The project is coordinated by a consortium from the Public Health Agency of Sweden (PHAS), Karolinska University Hospital (KUH) and EUCAST Development Laboratory (EDL). This includes coordination of the European Antimicrobial Resistance Genes Surveillance Network (EURGen-Net) and of the first CCRE survey. In preparation for the CCRE survey training and quality assessment services will be conducted.

Representatives of 37 countries in the EU/EEA, will form the EURGen-Net and participate in training activities as well as the CCRE survey. A scientific advisory board is engaged to provide an overview of the current epidemiologic situation of carbapenem and colistin-resistant Enterobacteriaceae in Europe. The scientific advisory board will also be consulted on all scientific questions related to the implementation of the CCRE survey.

The project is divided into three work areas:

- Coordination of the European Antimicrobial Resistance Genes Surveillance Network (EURGen-Net) and of the first carbapenem and/or colistin-resistant Enterobacteriaceae (CCRE) survey.

- Assessment, development and training on the methodology of carbapenem and colistin susceptibility testing.

- Provision of external quality assessment (EQA) of phenotypic and genotypic carbapenem and colistin resistance testing of Enterobacteriaceae.

During **the first year** the consortium will review the field of carbapenem and colistin susceptibility and mechanisms of resistance. Consensus protocols and laboratory manuals for characterization of carbapenem resistance/carbapenemase producers and colistin resistance will be produced and distributed within the network. These manuals will guide the performance of antibiotic susceptibility testing (AST) and resistance mechanism identification within the CCRE survey.

A survey measuring the capacity of colistin and carbapenem AST as well as genotypic characterization of colistin in the EU/EEA will be conducted. This will be followed by a training workshop focusing on the capacity of colistin and carbapenem AST to which the National Technical Coordinators will be invited. After the training workshop an external quality assessment (EQA) to evaluate the implementation of the recommended diagnostic tools for colistin resistance will be performed.

The National Technical Coordinators representing each of the 37 countries will be asked to recruit local hospitals and their associated laboratories according to NUTS-2 (Nomenclature of Territorial Units for Statistics) for a relevant geographical distribution.

Participating National Reference Laboratories will be certified and invited to participate in the large CCRE survey that takes place during six months **the second year**.

In order to perform the CCRE survey data collection forms and a database where the information can be stored for further analysis will be created. An analysis plan for the epidemiological data collection will be prepared.

The CCRE survey is expected to yield approximately 6000 *K. pneumoniae* and *E. coli* isolates that will be extensively characterized using phenotypic and genotypic methods including whole genome sequencing (WGS).

During **the third and final year** of the project data analysis will be the main focus, as well as communication of results in various ways such as reports, peer reviewed publications etc.

Staphylococcus aureus including MRSA

Mandatory reporting of methicillin resistant *Staphylococcus aureus*

MRSA has been notifiable according to the Communicable Disease Act since year 2000. Infection control programmes for MRSA have been developed and implemented locally under supervision of the County Medical Officers (CMO) and infection control teams. The programmes are based on early case-finding through screening of patients with risk factors and, in cases of confirmed MRSA, contact tracing combined with infection control measures such as hospital care in single rooms of patients with clinical infection caused by MRSA and campaigns on basic hygiene precautions.

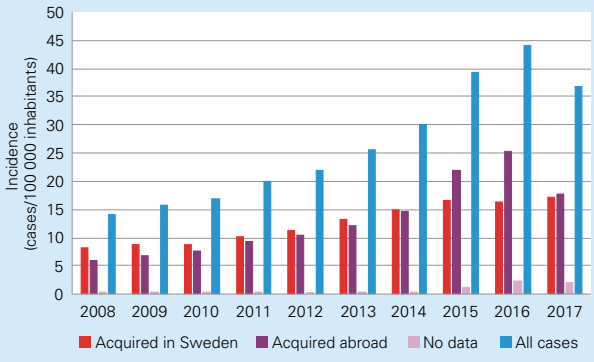
Notifications of MRSA according to the Communicable Disease Act

In 2017 a total of 3 735 cases of MRSA were notified, a decrease by 667 cases (15%), see Figure 3.15. This is the first reported decrease since MRSA became notifiable.

The national incidence, based on yearly number of cases, decreased from 44 cases per 100 000 inhabitants to 37 cases per 100 000 inhabitants between 2016 and 2017. The decrease was seen primarily among cases with MRSA acquired abroad.

The highest incidence was seen in Kalmar (72), while the lowest incidence was seen in Gävleborg (23), Figure 3.16. Different screening and contact tracing practices and uneven distribution between counties of people seeking political asylum are probable explanations to the large variation in incidence between counties.

FIGURE 3.15. The incidence (cases/100 000 inhabitants) of human cases of MRSA acquired in Sweden and acquired abroad, year 2008–2017.



In 2017, 47% (n=1 743) of all reported MRSA were acquired in Sweden and 48% (n=1 789) were acquired abroad. The five most common countries were Syria (n=423), Iraq (n=172), Afghanistan (n=68), Turkey (n=63) and Philippines (n=62). For approximately five percent (n=203) country of infection was missing ("No data"). The most commonly reported indication for sampling among domestic cases was investigation of clinical symptoms (50%) and contact tracing (37%), see Figure 3.17. Among imported cases screening remains the most common indication for sampling (45%) followed by clinical symptoms and contact tracing, data not shown. Overall, the majority of samples from investigations of clinical symptoms were wound samples (66%).

Among samples from screening (n=1 055), throat swabs and nasal swabs were most common (34% and 30%, respectively). Invasive MRSA infection was reported in 55 cases during 2017 compared to 44 cases during 2016. Out of them were 51 cases newly notified 2017 and 4 cases in patients already known to carry MRSA.

Community acquired infections continue to be most common among all cases in 2017, Figure 3.18. A higher proportion of hospital acquired MRSA was noted among cases of MRSA acquired abroad (22%) than among cases acquired in Sweden (7%). The proportion of cases with MRSA acquired in healthcare/care outside hospital was low for both domestic (4%) and imported (7%) cases. Sixteen percent of the

FIGURE 3.16. The incidence (cases/100 000 inhabitants) of human cases of MRSA in Swedish counties 2017, in relation to indication for sampling.

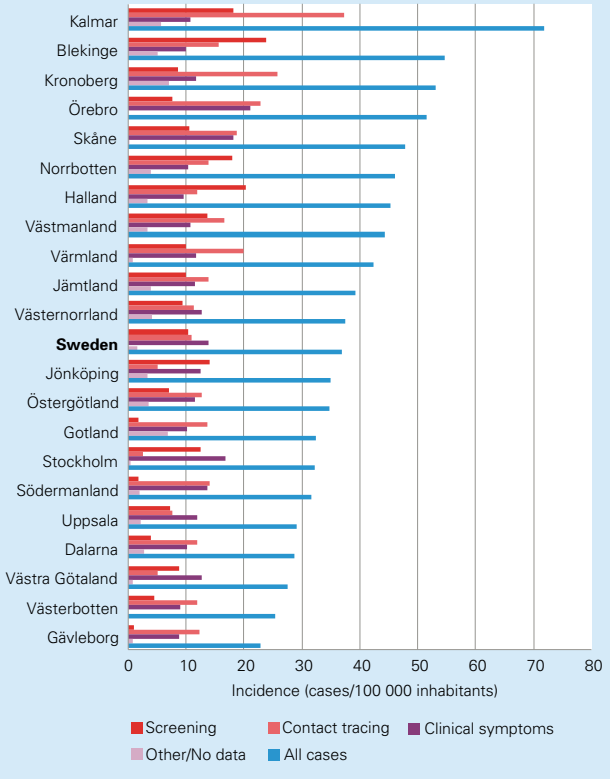


FIGURE 3.17. Indications for sampling of human MRSA cases acquired in Sweden year 2008-2017. Presented as incidence. A figure on cases acquired abroad is provided as attachment in the PDF-file.

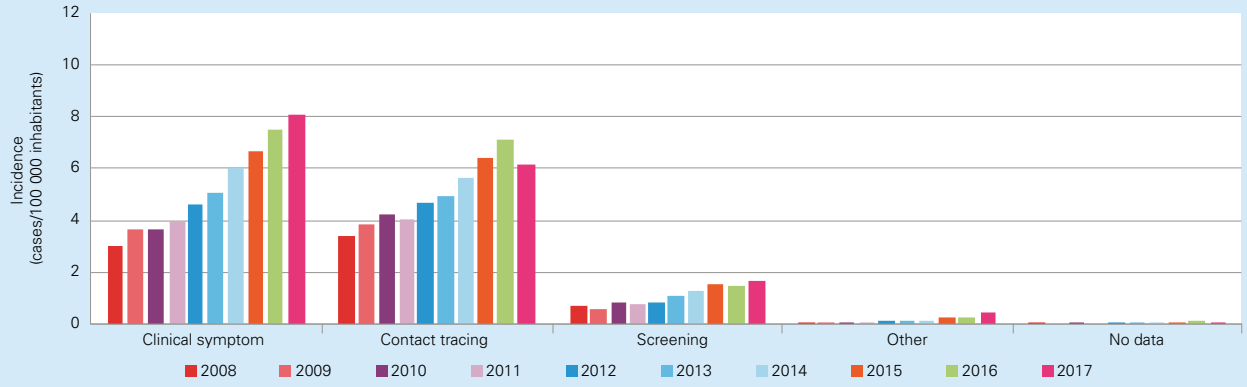
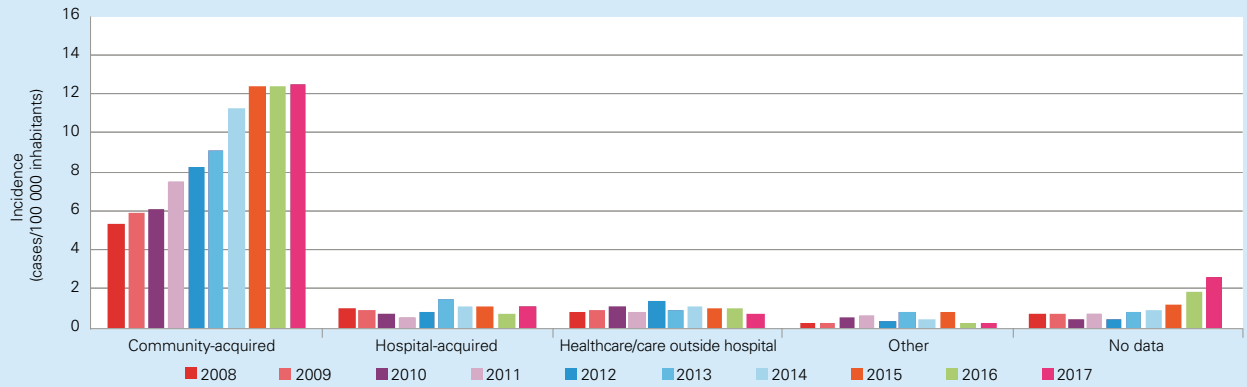


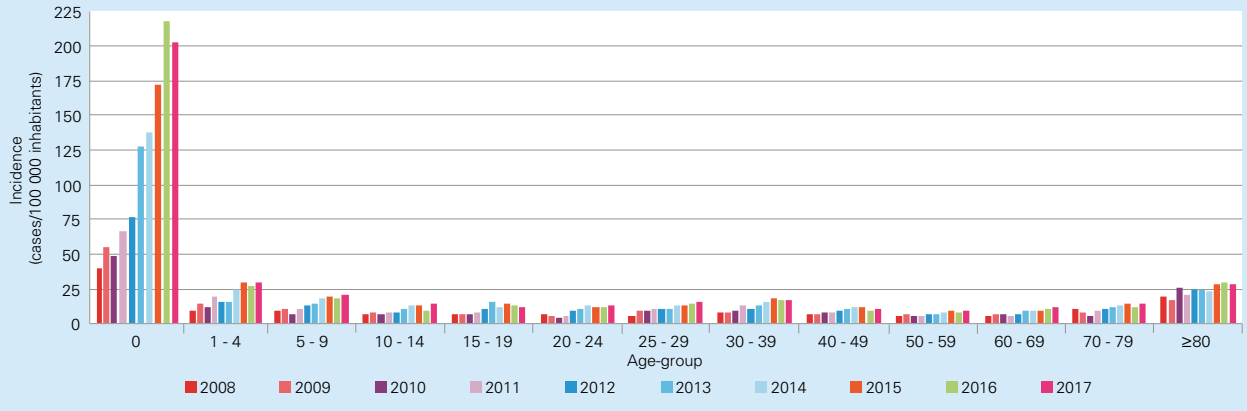
FIGURE 3.18. Epidemiological classification of cases of MRSA acquired in Sweden, year 2008-2017. Presented as incidence (cases/100 000 inhabitants). A figure on cases acquired abroad is provided as attachment in the PDF-file.



imported cases, and 15% of the domestic cases, lacked information on acquisition. The classification is based on information in the clinical notifications and subsequent investigations by the CMOs.

Among the domestic MRSA cases 2017, the incidence was highest in the age group <1 year (203), followed by the age group 1–4 years (30). The incidence of MRSA among the 0 year old was 12 times higher than the overall incidence for domestic cases (17). In the other age groups the incidence remained at similar level as in 2016, with a range from 9.2 to 28 cases per 100 000 inhabitants. Out of the 237 MRSA cases among <1 year olds 124 (52%) were detected through contact tracing, 63 (27%) by screening and 44 (19%) by clinical symptoms. One in six were healthcare related (n=39, 16%), 21 of these were part of 2 neonatal outbreaks comprising 5 or more cases, 179 cases (76%) were community acquired.

FIGURE 3.19. Incidence of MRSA acquired in Sweden, 2008-2017 among different age groups.



Outbreak investigations

During 2017, one larger outbreak involving neonatal units was reported with cases in four different counties. In all, 24 cases were linked with epidemiological information and whole genome sequencing (*spa*-type t304). Another outbreak also at a neonatal unit involved seven cases (*spa*-type t386). Several smaller outbreaks with two to four cases were reported both from hospital and healthcare institutions outside hopsitals during 2017.

Epidemiological typing of MRSA

The method used for epidemiological typing of MRSA isolates sent to the Public Health Agency of Sweden is *spa*-typing. This is a DNA sequence based method with a standardized, unambiguous and internationally well recognized nomenclature (http://spaserver.ridom.de/). In addition, PVL status (absence/presence of genes coding for PVL) of each isolate is determined and used as an epidemiological marker that differentiates MRSA variants within *spa*-types. Nationwide typing results were available for MRSA isolates from 97% of the notified cases for the period January–June (n=1 766). All but eight of the isolates were typable. A total of 327 *spa*-types were recorded.

The ten most common *spa*-types were: t304 (n=208), t223 (n=177), t127 (n=127), t002 (n=93), t008 (n=67), t386 (n=56), t044 (n=55), t019 (n=53), t437 (n=38) och t688 (n=34). A total of 51% (n=908) of the notified cases had an MRSA with a top ten *spa*-type.

The distribution of the top ten *spa*-types and information on PVL-status, is shown for isolates from cases with MRSA acquired in Sweden (n=848) and abroad (n=870), respectively, in Figure 3.20. All ten *spa*-types were seen among both domestic and imported cases. Information regarding where the MRSA was acquired was missing for 100 cases.

The distribution of the top ten *spa*-types in relation to epidemiological classification is shown in Figure 3.21. For all ten *spa*-types, acquisition in the community was most common. For one of the *spa*-types, t688, there were no reported cases with hospital acquired MRSA. Among MRSA acquired in hospital, t304 and t386 were the most common *spa*-types, and for MRSA acquired in healthcare/care outside hospital, t002 was most commonly seen.

Figure 3.22 A and B show the proportion of each of the top ten *spa*-types per year for 2008-2017. In total 18 *spa*-types have been among the top ten during one or more years. In 2008, t002 was the most common *spa*-type (121 cases) and in 2017 as in 2016, t304 was the most common (208 cases, Jan-Jun). Four *spa*-types, t002, t008, t044 and t127, have been among the top ten during the whole period.

FIGURE 3.21. The ten most common *spa*-types 2017 in relation to epidemiological classification of human MRSA. Presented as proportion (%) of all cases.

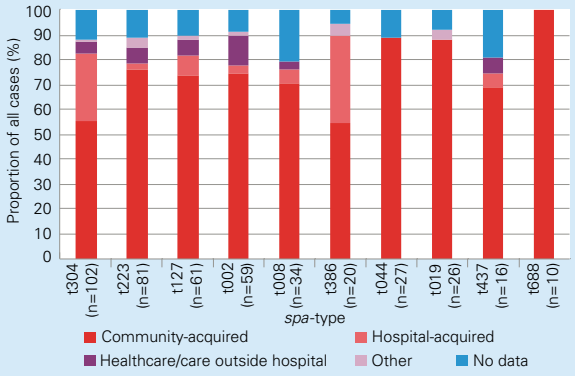


FIGURE 3.20. The ten most common *spa*-types with PVL status for MRSA aquired in Sweden and abroad, January–June 2017.

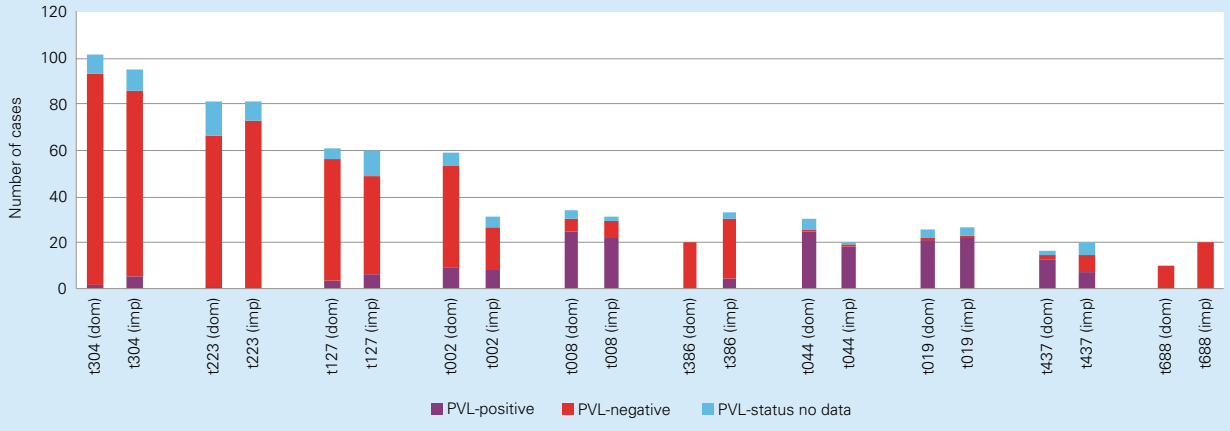
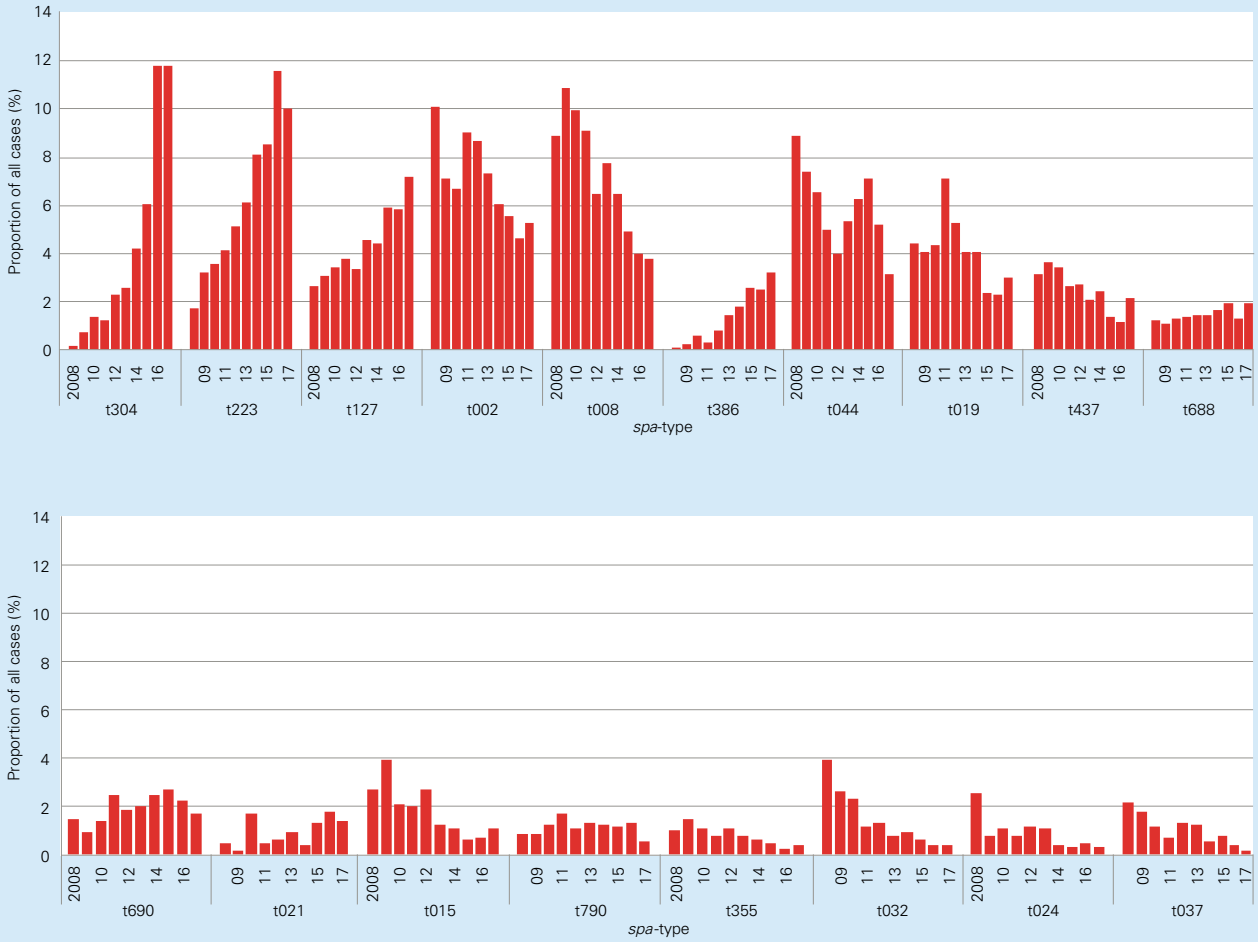


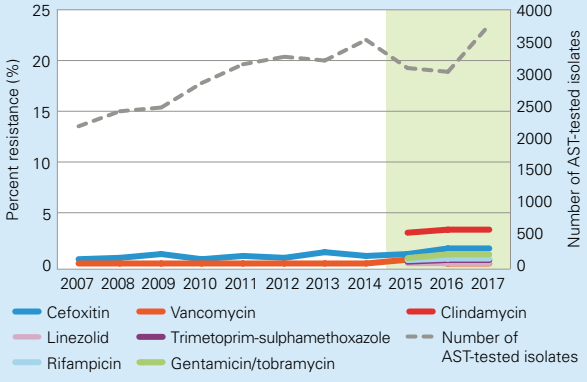
FIGURE 3.22 A AND B. The most common *spa*-types among MRSA in humans year 2008-2017. Presented as proportion of all cases.



Staphylococcus aureus reported to EARS-Net

From 2008 to 2014, deduplicated data on invasive infections from 18-21 laboratories (depending of the year) were used. From 2015 and onwards, yearly (non deduplicated) data based on SIR reported to Svebar were used. The rate of MRSA in blood has been steady through the years and was 1.5% in 2017 (indicated by cefoxitin resistance) (Figure 3.23). Antibiotic susceptibility to vancomycin is not routinely preformed on cefoxitin susceptible *S. aureus*. In 2017, 313 out of 3 746 (8%) isolates were tested for vancomycin resistance with no resistance detected.

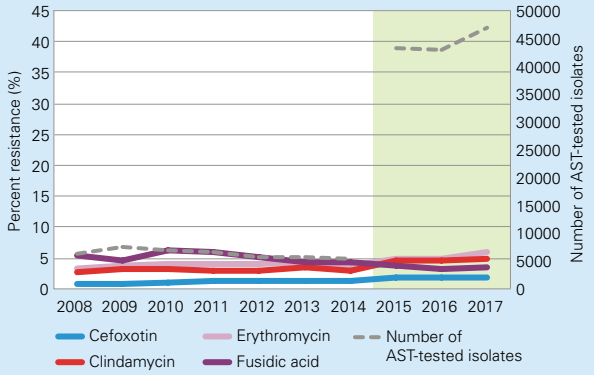
FIGURE 3.23. Antibiotic resistance in *S. aureus* isolates from bloodstream infections included in EARS-Net surveillance during the years 2008-2017.



Staphylococcus aureus from skin and soft tissue infections

From 2008 to 2014, zone-diameter data from the national surveillance programme on antibiotic resistance ResNet were used. From 2015 and onwards, yearly data based on SIR reported to Svebar were used. The frequency of MRSA in skin and soft tissue infections (cefoxitin used as test compound) has increased slowly and reached 1.8% in 2017. Resistance to aminoglycosides was still only 1% (Figure 3.24).

FIGURE 3.24. Resistance rates for *S. aureus* from skin and soft tissue infections 2008-2017.



Antibiotic resistance in MRSA

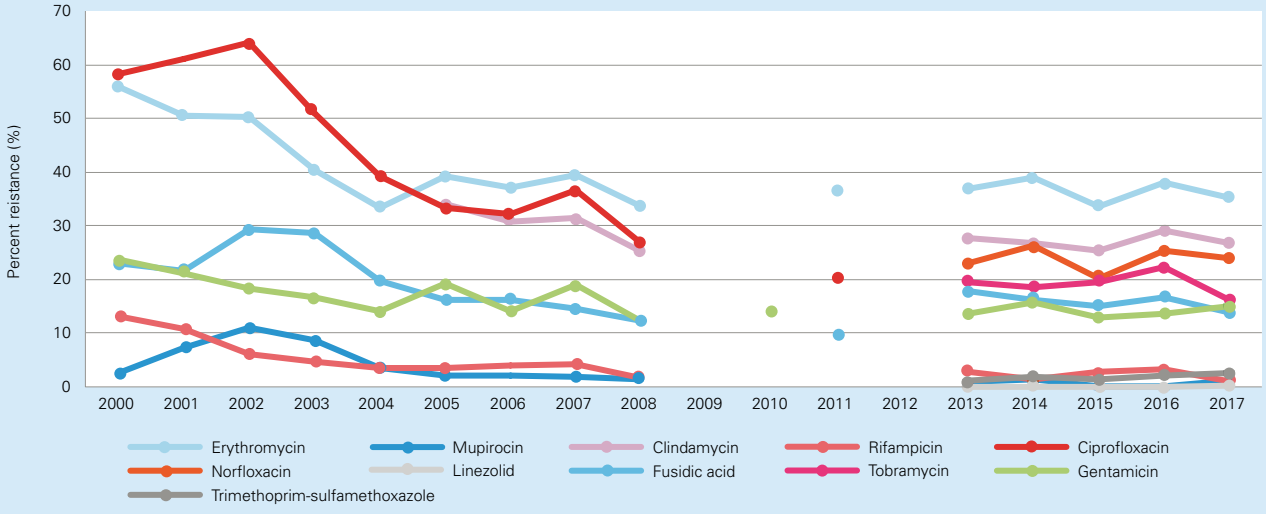
In previous Swedres – Svarm reports, antibiotic resistance in MRSA was, with the exception of 2009, reported until 2011. Here the data from previous reports are summarized and results from Svebar for 2013-17 are added. The results from 2000-2011 were based on all MRSA isolates sent for epidemiological typing and include all MRSA-cases, irrespective of the indication for culture. This included all isolates except those from two or three laboratories.

In the data from Svebar only results from samples obtained for clinical diagnostic purposes were selected, i.e. results from screening and case-finding were excluded. The previous data were case-based whereas the data from Svebar may contain duplicate results from patients. Culture results from Svebar are presented in Table 3.5. The proportion of resistance among MRSA is shown in Figure 3.25. It is interesting to note that despite the difference between the periods in how data were obtained, the proportions of resistance among MRSA to other antibiotics remain at similar levels. The decrease in resistance seen for several antibiotics between 2000 and 2004 reflects the shift from hospital to community acquired MRSA strains.

TABLE 3.5. Number of *S. aureus* and MRSA from clinical cultures and the proportion of MRSA for 2013 – 2017

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

FIGURE 3.25. Antibiotic resistance in clinical isolates of MRSA.



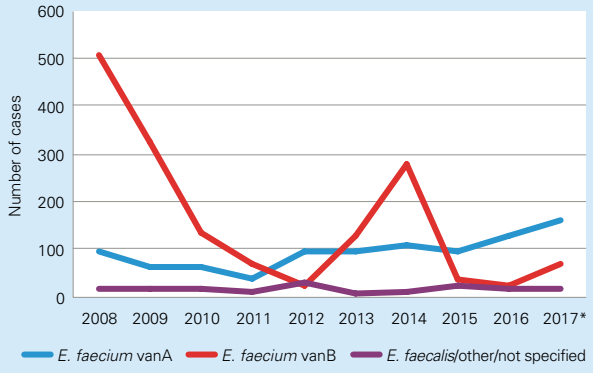
Enterococcus faecalis and *Enterococcus faecium* including VRE

Mandatory reporting of vancomycin resistant enterococci

Background

Vancomycin resistant enterococci (VRE) are important causes of nosocomial infections in many parts of the world, usually involving high-risk populations frequently in contact with health-care such as immunocompromised and intensive care patients. Like MRSA, VRE were made notifiable according to the Swedish Communicable Disease Act in the year 2000 and since 2004 contact tracing is mandatory. The following presentation is based on data collected in the national web-based notification system SmiNet. In 2007 Stockholm County experienced the first and largest VRE outbreak with *E. faecium vanB*. This outbreak spread to counties surrounding Stockholm, it ended 2011 and included 872 cases. Before 2007 few cases of VRE were reported (18-35 cases per year). The following large outbreak of *E. faecium* with *vanB* occurred in Gävleborg County, 2013-2014, and included 314 cases. In general, strains of *E. faecium vanB* have caused large outbreaks while strains of *E. faecium vanA* have caused numerous minor outbreaks. However, from 2015 we see a change where *E. faecium vanA* are responsible for most outbreaks (Figure 3.26).

FIGURE 3.26. Number of cases of VRE and their corresponding van-type.



*A total of 27 isolates harbouring both *vanA* and *vanB*.

Notifications of VRE according to the Communicable Disease Act

244 cases were reported in 2017, over 50 percent increase compared to 2016 (n=165). For 2017, 153 cases (63%) were reported as acquired in Sweden and 86 cases (32%) as acquired abroad. Data are missing for five cases (Figure 3.27). VRE cases were reported from 15 of the 21 Swedish counties with a national incidence of 2.4 per 100 000 inhabitants. Six counties had a higher incidence than the national incidence, Örebro county (7.7), Värmland county (7.5), Halland county (5.9), Västmanland county (5.2), Stockholm county (4.0) och Kronoberg county (3.5). One hundred thirty-five (88%) of the cases with acquisition in Sweden and 74 (86%) of the cases acquired abroad were healthcare related. Most cases whom acquired VRE in Sweden were found through contact tracing (n=101) in contrast to cases acquired VRE abroad which was most often detected through screening (n=69) (Figure 3.28). Accordingly a majority of the isolates (n=216, 89%) were from feaces and rectum, and only 11 percent from urine, wound or other clinical samples. Two invasive VRE infections with *E. faecium* were reported in 2017. The VRE cases were unequally distributed between sexes (62% male and 38% female), with median ages of 67 years for men and 69.5 years for women. In 2017, 236 cases were reported as *E. faecium* and eight cases as *E. faecalis*. In two cases both *E. faecium vanA* and *E. faecalis vanA* could be isolated. The *vanA* genotype was most commonly found (n=161) among the VRE cases with *E. faecium* in 2017 (Figure 3.26).

FIGURE 3.27. Number of VRE cases and country of acquisition reported during ten years (2008-2017).

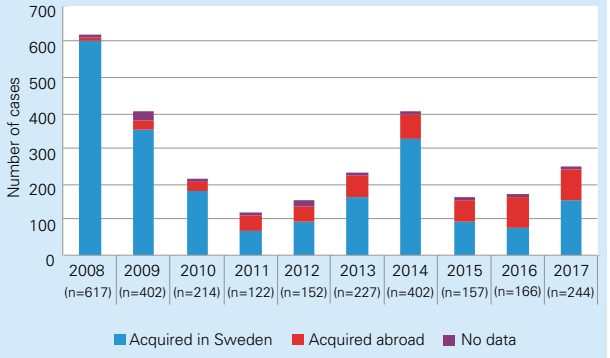
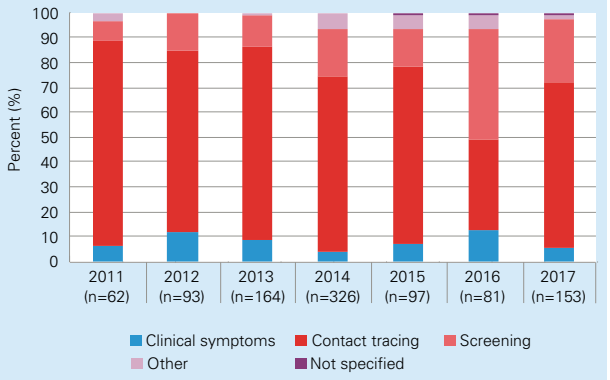


FIGURE 3.28. Source of VRE acquisition in Sweden 2011-2017.



Epidemiological typing of VRE in outbreaks

Since May 2016, epidemiological typing of VRE has been performed with whole genome sequencing (WGS) and "single nucleotide polymorphism" SNPs based analysis and multilocus sequence typing (MLST). 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).

Epidemiological typing of VRE is an important tool in the extensive work needed to take the necessary infection control measures when a spread of VRE is identified. In 2017, ten hospital-related outbreaks were reported. Four outbreaks were large (over 25 cases), while the other six included small scatters (two-four cases). Three of the major outbreaks belonged to ST203 and ST80, these sequence types are known in the literature to cause major hospital-related outbreaks, belonging to the clonal complex (CC) 17. One outbreak in Stockholm county included 48 cases of *E. faecium vanA* (SE-EfmA-1207, ST203). Another large outbreak caused by *E. faecium vanB* (SE-EfmB(A)-1612, ST80) spread from Värmland county to Örebro county and included 42 cases. The third large outbreak origniated from Denmark and resulted in a national spread from Västra Götaland County to Halland County with 27 cases. This *E. faecium* harboured both *vanA* and *vanB* (SE-EfmA/B-1704, ST80). A forth outbreak in Västmanland county with *E. faecium vanA* (SE-EfmA-1608, ST552) started in spring 2016 and ended late in 2017, included 29 cases (Figure 3.29).

A total of 43% of all VRE cases 2017 belonged to ST80, including two of the outbreaks mentioned above as well as 20% of all unique *E. faecium* isolates. The diversity of sequence types is high among *E. faecium* classified as unique. (Figure 3.29).

Enterococcus faecalis and *Enterococcus faecium* reported to EARS-Net

From 2008 to 2014, deduplicated data on invasive infections from 18-21 laboratories (depending of the year) were used. From 2015 and onwards, yearly (non deduplicated) data based on SIR reported to Svebar were used. Enterococci causes considerably fewer bloodstream infections than *E. coli*. All *E. faecium* isolates were susceptible to vancomycin while the resistance for *E. faecalis* was 0.5% (n=4). The high-level aminoglycoside resistance (HLAR) remained stable for both *E. faecium* and *E. faecalis*. (Figures 3.30 and 3.31)

FIGURE 3.30. Antibiotic resistance in *E. faecalis* isolates from bloodstream infections included in EARS-Net surveillance during the years 2008-2017.

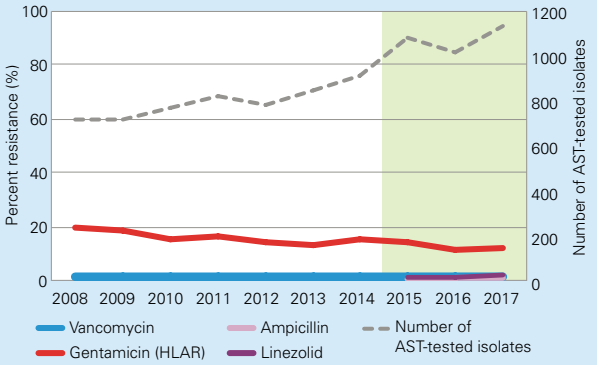


FIGURE 3.31. Antibiotic resistance in *E. faecium* isolates from bloodstream infections included in EARS-Net surveillance during the years 2008-2017.

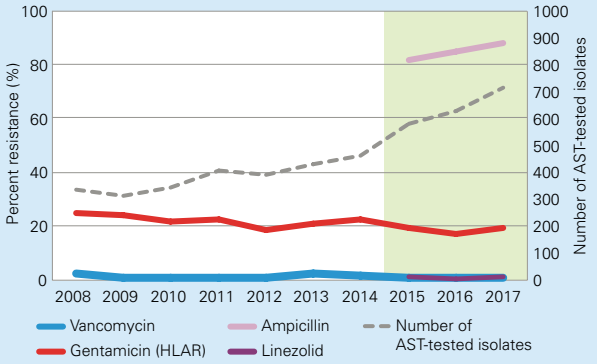
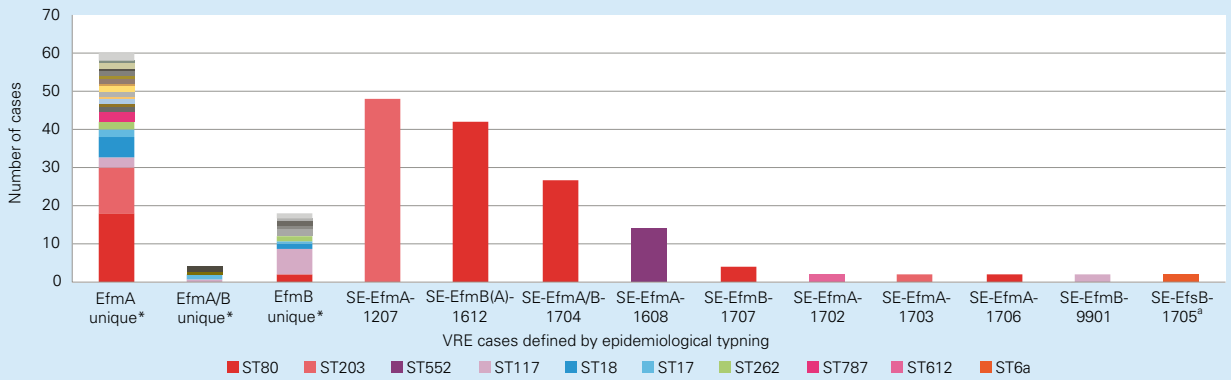


FIGURE 3.29. Distribution of sequence types among the VRE cases in 2017.



*High diversity among the unique VRE cases is seen by the many STs in this group (one ST represents one colour).
[a]A different MLST scheme is used for *E. faecalis*.

Streptococcus pneumoniae including PNSP

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

Background

S. pneumoniae with reduced susceptibility to penicillin (PNSP, defined as MIC ≥ 0.5 mg/L) became notifiable according to the Communicable Disease Act in 1996. In May 2012, a revised case definition was introduced, stating that only PNSP with MIC of penicillin >1 mg/L were now notifiable and the identified cases subjected to contact tracing.

Notifications according to the Communicable Disease Act

In 2017, a total of 61 PNSP cases (PcG MIC > 1mg/L) were reported in Sweden including five cases of invasive infections (blood and cerebrospinal fluid). A majority of the cases had been infected in Sweden (n=42, 69%) and thirteen percent of the cases in a foreign country (n=8). For the remaining eleven cases, no country of acquisition was given (18%). The incidence of PNSP in Sweden 2017 was 0.6 cases per 100 000 inhabitants and year. Figure 3.32 shows the number of cases and incidence for each age group. PNSP was most common in the age group 50-59 years (21%) in contrast to earlier years when most cases were found among age groups 0-4 years. Of the reported cases in 2017, 57% were male and 43% female. PNSP were reported from 16 of 21 Swedish counties, with Stockholm (n=12), Södermanland county (n=7), Västra Götaland county (n=6), Örebro county (n=5) and Västmanland county (n=4) accounting for 56% of all notifications. The remaining nine counties reported 1-3 cases each. PNSP was most often found in cultures from the nasopharynx (57%). Twelve isolates were found in sputum/ bronchoalveolar lavage (18%) and no data were reported for nine cases (15%). In 50 cases (82%) the detection of PNSP was due to clinical symptoms. Two cases were detected through contact tracing (3%) and five cases through targeted screening (8%). The information was missing for the remaining four cases (7%).

Serotype distribution of pneumococcal isolates with PcG MIC > 1 mg/L

A total of 55 isolates with PcG MIC > 1 mg/L were sent to the Public Health Agency of Sweden for serotyping during 2017. Of these, 33 isolates (60%) belonged to serotypes included in the conjugate vaccines used for children in the national vaccination programme. Isolates with high PcG MIC-values were found in 7 out of 15 serotypes (Figure 3.33). The five invasive cases were caused by PNSP belonging to serotype 14, 19F, 9N and 10A. In order to follow and evaluate the effect of vaccination against pneumococcal disease and to identify spread of antibiotic resistant clones, the Public Health Agency of Sweden has continued to collect and perform serotyping on PNSP isolates according to the previous definition. In 2017, about 317 isolates with a PcG MIC ≥ 0.5 mg/L were collected, which is approximately the same amount as in 2016. Of these, 40% constituted types included in the conjugate vaccines used for children in the national vaccination programme.

FIGURE 3.32. Number of cases and incicence per age group for PNSP acquisition 2017.

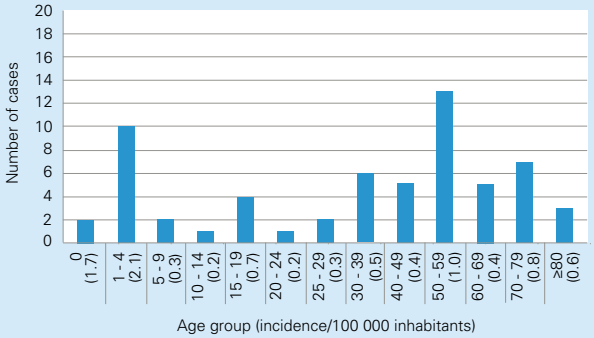
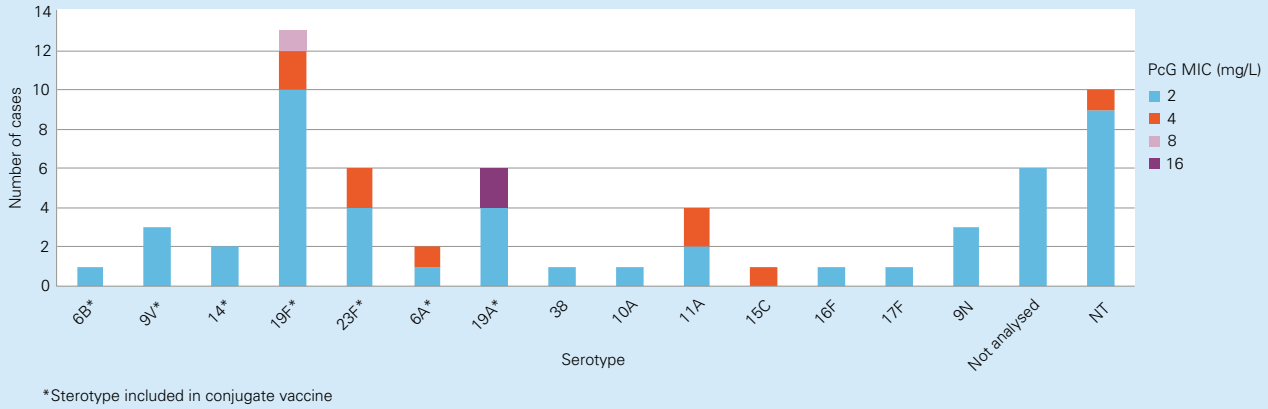


FIGURE 3.33. Distribution of MICs among PNSP with PcG MIC > 1 mg/L.



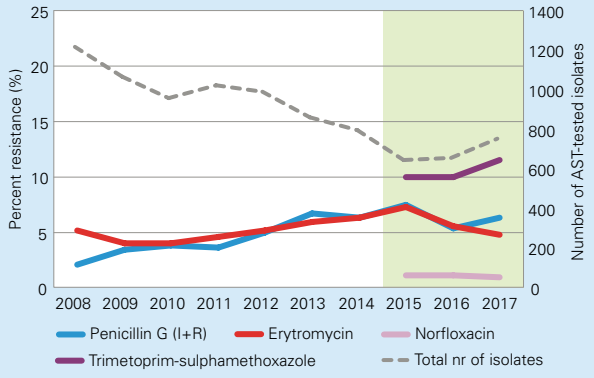
*Sterotype included in conjugate vaccine

Streptococcus pneumoniae, clinical isolates from blood and respiratory specimens

Streptococcus pneumoniae reported to EARS-Net

From 2008 to 2014, deduplicated data on invasive pneumococcal infections from 18-21 laboratories (depending of the year) were used. From 2015 and onwards, yearly (non deduplicated) data based on SIR reporing from Svebar were used. The proportion of PcG non-susceptible isolates was 6% in 2017 and the erythromycin resistance decreased to below 5% (Figure 3.34). In 2017, the number of invasive pneumococcal disease cases reported to SmiNet was 1 368. During the last ten years, the number of reported cases varied from 1 159 to 1 789.

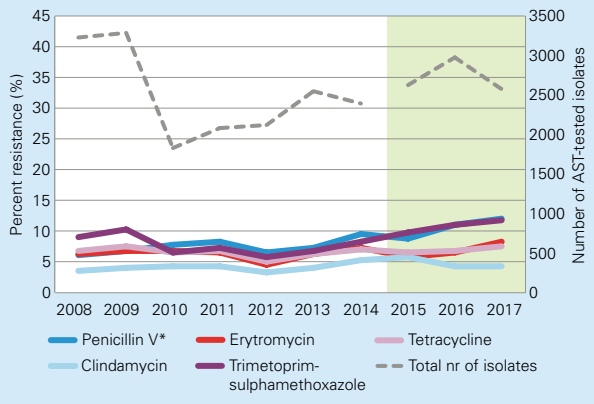
FIGURE 3.34. Antibiotic resistance in *S. pneumoniae* isolates from bloodstream infections included in EARS-Net surveillance during the years 2008-2017.



Streptococcus pneumoniae from nasopharyngeal cultures

From 2008 to 2014, zone-diameter data from the national surveillance programme on antibiotic resistance ResNet were used. From 2015 and onwards, yearly data based on SIR reporing to Svebar were used. The clinical laboratories have tested isolates for susceptibility to penicillin by means of oxacillin 1 µg screen disk. Since 2012, there has been a slow increase in the proportions of resistance for all tested antibiotics with the exception of clindamycin (Figure 3.35). Only 31% of the isolates were tested for norfloxacin resistance which was 2.5% in 2017.

FIGURE 3.35. Proportion of resistance to antibiotics commonly used to treat respiratory tract infections, *S. pneumoniae* 2008-2017.



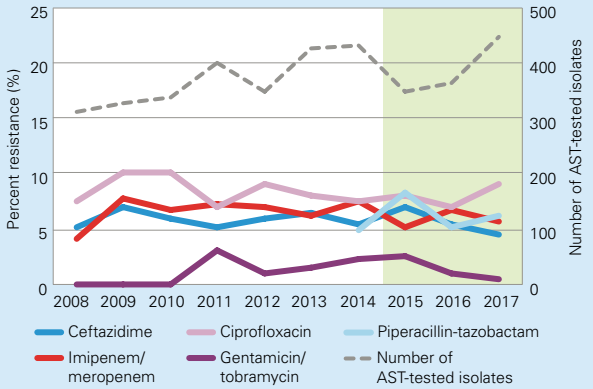
*Based on susceptibility testing using oxacillin.

Pseudomonas aeruginosa and *Acinetobacter* spp.

Pseudomonas aeruginosa and _Acinetobacter_ spp. reported to EARS-Net

From 2008 to 2014, deduplicated data on invasive infections from 18-21 laboratories (depending of the year) were used. From 2015 and onwards, yearly (non deduplicated) data based on SIR reported to Svebar were used. The proportion of resistance for *P. aeruginosa* to the antibiotics reported to EARS are shown in Figure 3.36. The resistance to ceftazidime (4.5%) is due to other mechanisms than ESBL production, and the resistance proportions are quite stable over time.

FIGURE 3.36. Antibiotic resistance in *P. aeruginosa* isolates from bloodstream infections included in EARS-Net surveillance during the years 2008-2017.



During 2017, a total of 54 isolates of *Acinetobacter* spp. from blood was reported to Svebar. No carbapenem-resistance was found (Table 3.6). Septicemia caused by *Acinetobacter* is still rare in Sweden compared to other countries in Europe where multiresistant *Acinetobacter* is a problematic pathogen in hospitals. Sweden has reported *Acinetobacter* spp. to EARS-Net since 2014.

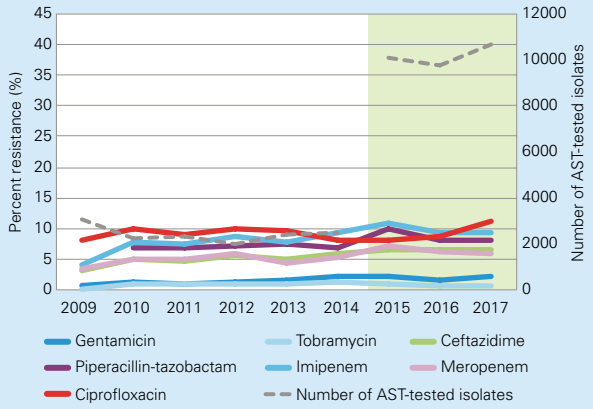
TABLE 3.6. Antibiotic resistance in *Acinetobacter* species isolates from bloodstream infections included in EARS-Net surveillance during the years 2014-2017.

		2014		2015		2016		2017	
Species	**Antibiotic**	**n**	**% R**	**n**	**% R**	**n**	**% R**	**n**	**% R**
Acinetobacter species	**Number of AST-tested isolates**	**59**		**41**		**54**		**54**	
	Meropenem		3.4		0		1.9		0
	Ciprofloxacin				0		5.6		0
	Colistin				0		0		0
	Gentamicin				0		7		0
	Trimethoprim-sulfonamide				5.1		5.7		0

Resistance data on *Pseudomonas aeruginosa*

From 2008 to 2014, zone-diameter data from the national surveillance programme on antibiotic resistance ResNet were used. From 2015 and onwards, yearly data based on SIR reported to Svebar were used. All *P. aeruginosa* isolates with the exclusion of respiratory isolates are included. Four beta-lactam antibiotics are tested; one cephalosporin, one penicillin-inhibitor combination, and two carbapenems. For all of them, the rates of resistance have been more or less stable since 2010. For the carbapenems, resistance to imipenem continues to be higher (9.4%) than to meropenem (5.9%). The resistance to ciprofloxacin increaced in 2017 compared to 2016 (Figure 3.37).

FIGURE 3.37. Proportion of resistance to four groups of antibiotics tested against *P. aeruginosa* 2009-2017.



Clostridium difficile

The *Clostridium difficile* surveillance programme in Sweden

The national surveillance program for *C. difficile* includes both a voluntary laboratory reporting system of all new cases of *C. difficile* infection (CDI) and a determination of resistance and epidemiological typing of isolates from the clinical microbiology laboratories. All *C. difficile* strains isolated during week no. 11-12 and 39-40 were sent to the Public Health Agency of Sweden for typing by PCR ribotyping and antibiotic susceptibility testing. Primarily metronidazole and vancomycin resistance was monitored, i.e. the recommended treatment choices for CDI. However, since use of antibiotics is a risk factor for acquiring CDI we also tested susceptibility to other antibiotics as an indicator of selective pressure, currently moxifloxacin, clindamycin and erythromycin. All isolates were tested using E-test on fastidious Mueller Hinton agar.

Incidence of CDI

In 2017, 6 466 new CDI cases were reported corresponding to an incidence of 64 cases per 100 000 inhabitants (Figure 3.38) a decrease with 11% compared to 2015. The mean incidence of new CDI cases per 10 000 patient-days for 2017 was 10 cases/10 000 patient-days (patient-days data are from 2016) (Figure 3.39).

FIGURE 3.38. Incidence of new cases of CDI (cases per 100 000 inhabitants) in Swedish counties 2015-2017, arranged in ascending order according to incidence rates for 2017.

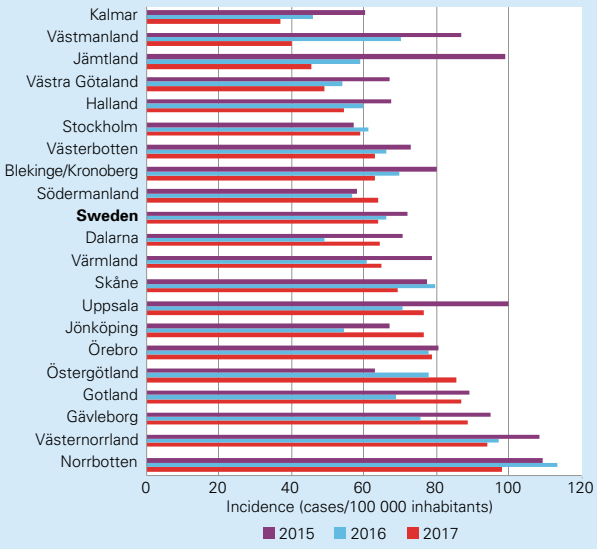
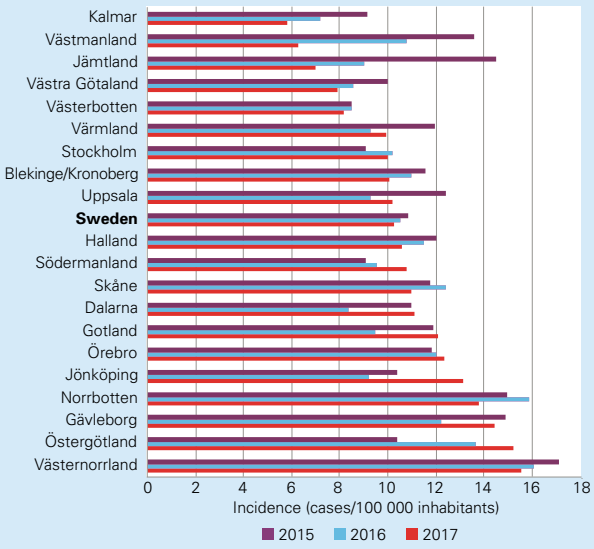


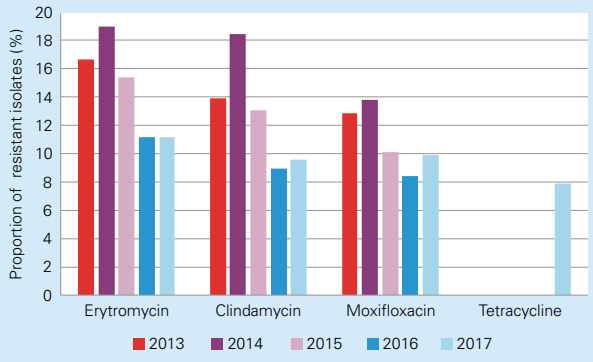
FIGURE 3.39. Incidence of new cases of CDI (cases per 10 000 patient-days) in Swedish counties 2015-2017, arranged in ascending order according to incidence rates for 2017. (Incidence of cases for 2017 is calculated using patient-days for 2016).



Antibiotic resistance in *Clostridium difficile* isolates 2017

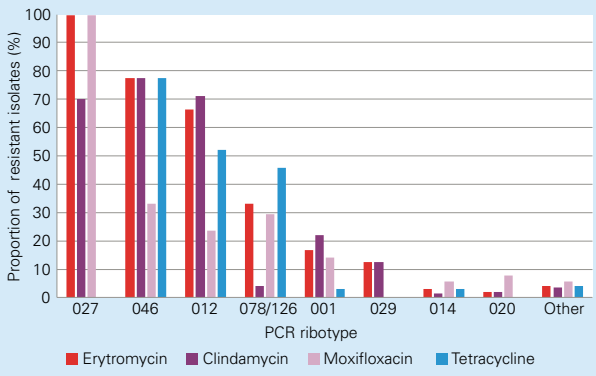
In 2017 the proportion of isolates resistant to the three indicator antibiotics moxifloxacin, erythromycin, clindamycin was around 10 percent, i.e. similar to that in 2016 (fig 3.40). A reduction in the number of resistant isolates has occurred since 2013-2014. Tetracycline was introduced as a fourth indicator antibiotics during 2017 and the proportion of resistance was similar to the other three.

FIGURE 3.40. Percentage of *C. difficile* isolates 2013-2017 resistant to erythromycin, clindamycin, moxifloxacin or tetracycline.



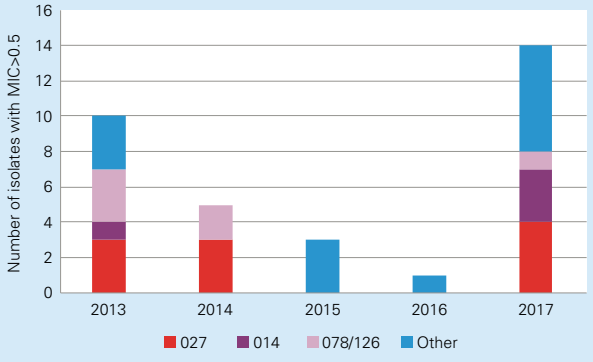
As previous years, resistance against the indicator antibiotics was mainly associated with certain types (Figure 3.41). With the exception of PCR ribotype 078/126 we have observed a reduction in the number of PCR ribotypes 012 and 046, which have been previously associated with resistance to all three antibiotics. A few isolates of the outbreak-related type 027 were found in 2017, mainly in the county of Gävleborg where it caused a minor outbreak.

FIGURE 3.41. Proportion of *C. difficile* isolates resistant to indicator antibiotics per PCR ribotype 2017.



No isolates were resistant to the treatment options metronadizole or vancomycin as classified using the current EUCAST breakpoints. However, certain types showed more frequently higher MICs against metronidazole although not classified as resistant types. Such higher MICs and or types may be associated with higher recurrence rates. One of these types was e.g. the very rare and outbreak-related PCR ribotype 027 (Figure 3.42).

FIGURE 3.42. Number of *C. difficile* isolates with higher MICs (> 0.5 mg/L) against metronidazole during 2013-2017. A higher totalt number in 2017 is partly due to that the surveillance period was extended and more isolates were collected.

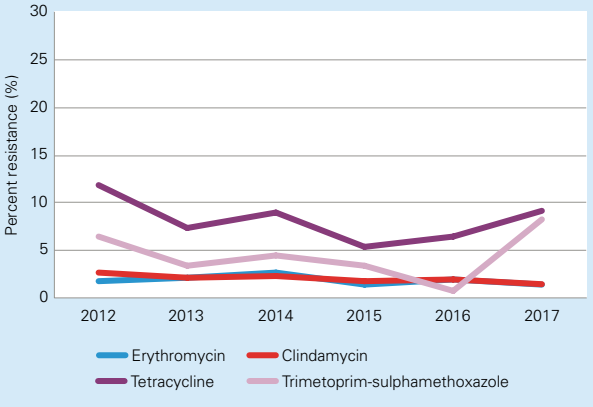


Streptococcus pyogenes, *Streptococcus agalactiae*, and *Haemophilus influenzae*

Streptococcus pyogenes, *Streptococcus agalactiae* and *Haemophilus influenzae* from blood

Resistance data for invasive *S. pyogenes* (iGAS) are collected yearly from the clinical microbiological laboratories through the microbial surveillance programme at the Public Health Agency of Sweden (Figure 3.43). Invasive *S. pyogenes* are notifiable according to the Communicable Disease Act and 668 cases were reported in 2017.

FIGURE 3.43. Antibiotic resistance in invasive isolates of *S. pyogenes* (iGAS) during six years (2012-2017).



For *S. agalactiae* (GBS) and *H. influenzae* deduplicated data on invasive infections from 2008 to 2014, collected from 18-21 laboratories (depending of the year) were used. From 2015 and onwards, yearly (non deduplicated) data based on SIR reported to Svebar were used. *S. agalactiae* is not included in the Communicable Disease Act, but it is an important pathogen in the context of pregnancy and child birth (Figure 3.44). Invasive isolates of *H. influenza* (n=178) are notifiable according to the Communicable Disease Act, but regardless of their antibiotic susceptibility. The antibiotic resistance is shown in Figure 3.45. In 2017, 229 cases of invasive *H. influenza* were reported.

FIGURE 3.44. Antibiotic resistance in invasive isolates of *S. agalactiae* (GBS) during ten years (2008-2017).

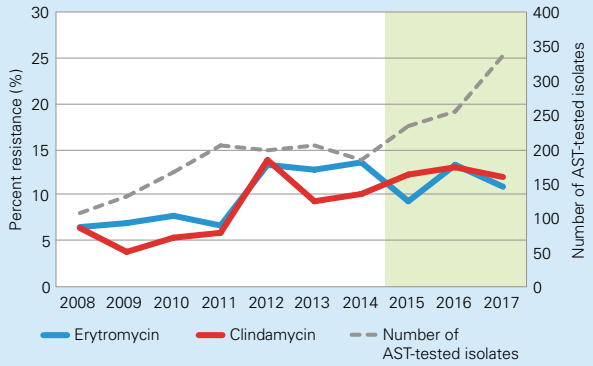
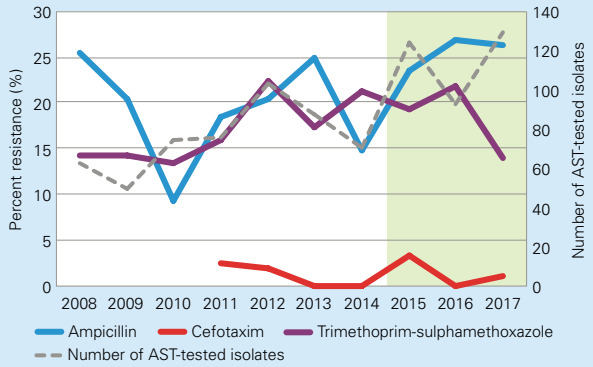


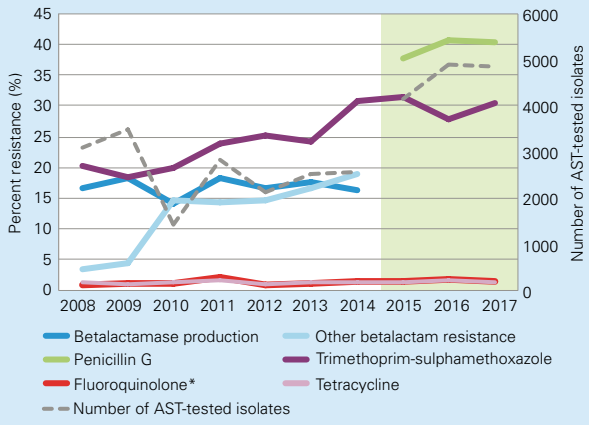
FIGURE 3.45. Antibiotic resistance in invasive isolates of *H. influenzae* during ten years (2008-2017).



Haemophilus influenzae from nasopharynx

From 2008 to 2014, zone-diameter data from the national surveillance programme on antibiotic resistance ResNet were used. From 2015 and onwards, yearly data based on SIR reported to Svebar were used. The high increase in resistance to trimethoprim-sulfonamide seen in 2014 remained at a relativelt steady level. Tetracycline resistance was still rare (1.1%) as was resistance to fluoroquinolones (1.6%), detected by the nalidixic acid screening disk (Figure 3.46). In 2010 methodological changes were introduced (for description see www.nordicast.org) which made results for beta-lactam resistance more difficult to interpret. This was resolved by adjusting the reporting routines. Laboratories were asked to report 6 mm inhibition zones of penicillin G for all beta-lactamase producing isolates, regardless of the actual zone diameter. Other mechanisms of beta-lactam resistance were then assumed if zones of penicillin G 1 unit disk measured 7-11 mm, allowing for a rough estimation of the frequency of beta-lactamase negative ampicillin resistant (BLNAR). It is not possible to deduce the resistance correlating to beta-lactamase production or the resistance due to BLNAR, which correlates to chromosomal resistance to cefalosporins, from 2015 and onwards since betalaktamase (+/-) data or zone-diameter (mm) is missing in Svebar for most of the penicillin G resistant isolates. The resistance to penicillin G was 40% (Figure 3.46) and the cefotaxim resistance was 1.5% in 2017.

FIGURE 3.46. Antibiotic resistance in *H. influenzae* during year 2008-2017.



*Nalidixic acid was used for detection of fluoroquinolone resistance.

Mycobacterium tuberculosis

During 2017 a total of 533 cases of tuberculosis (TB) were reported compared to 734 cases during 2016 which is a decrease of 27%. Out of the 533 cases 13 was already on TB treatment when arriving in Sweden.

The number and proportion of culture confirmed cases were 423 (79%) compared to 598 (82%) in 2016. *Mycobacterium bovis* was identified in three cases, *Mycobacterium africanum* in one case and *Mycobacterium tuberculosis* in 419 cases out of which for one it was not possible to do an analysis of resistance. The proportions of cases diagnosed with MDR-TB decreased from 3.7% (22/591) in 2016 to 2.6% (11/419). 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 50 patients corresponding to 11.9% of the 419 with culture confirmed *M. tuberculosis*, see Table 3.7. As always the most common resistance found was against isoniazid.

Among the cases born in Sweden 4.3% (2/46) of those with culture confirmed diagnosis had some kind of resistant TB (and two cases of M bovis). Of these two, there was one with MDR-TB infected outside of Sweden.

Of all the TB cases reported in Sweden 2017, 90% were born in another country. In total 377 in this group had a culture confirmed TB and 46 (12%) had some kind of resistance out of which 10 had MDR-TB.

Genetic typing of TB isolates has been performed in Sweden since the late 1990's. This is done to identify clusters of cases as clustering indicates possible ongoing spread and helps to identify missed opportunities of infection control. Since September 2016 the laboratory at the Public Health Agency of Sweden has changed from MIRU-VNTR to whole genome sequencing, a method that has a higher resolution and will reduce the risk of "false" clustering of cases with no connection. Of all the cases 14% (75/533) were considered as infected in Sweden and of the 349 cases analyzed with whole genome sequencing 78% were unique isolates not belonging to any cluster. In Gothenburg MIRU-VNTR is still used for typing but they plan to change to whole genome sequencing during 2018.

The proportion of patients with *M. tuberculosis* resistant against any antibiotics has decreased in 2017 including the proportion of MDR-TB.

FIGURE 3.47. Drug resistant *M. tuberculosis* in Sweden 2008 – 2017.

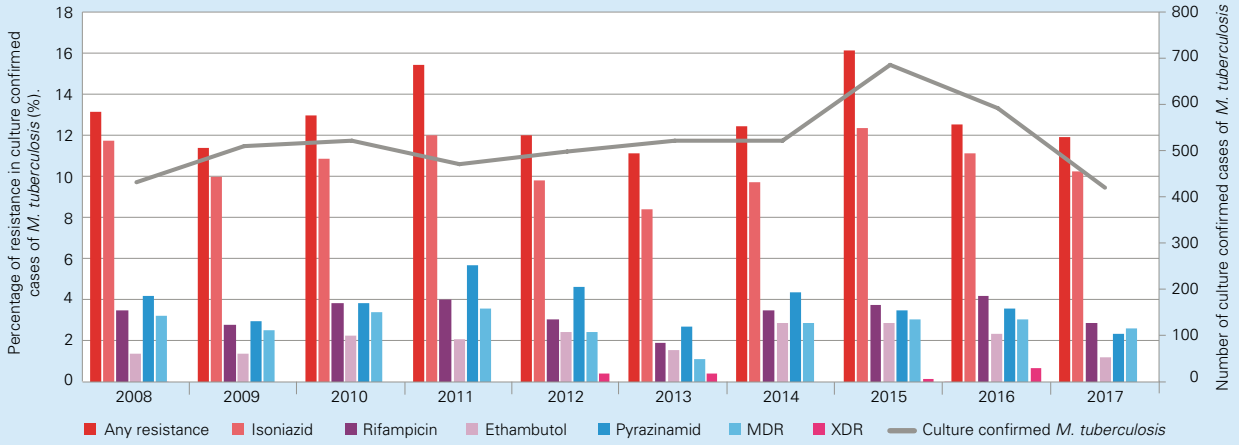


TABLE 3.7. Proportion of resistant isolated (%R) in cases with culture confirmed *M. tuberculosis*.

	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Culture confirmed *M. tuberculosis*	434	510	523	473	498	522	522	687	591	419
Any resistance	13.1%	11.4%	13.0%	15.4%	12.0%	11.1%	12.5%	16.2%	12.5%	11.9%
Isoniazid	11.8%	10.0%	10.9%	12.1%	9.8%	8.4%	9.8%	12.4%	11.2%	10.3%
Rifampicin	3.5%	2.7%	3.8%	4.0%	3.0%	1.9%	3.4%	3.8%	4.2%	2.9%
Ethambutol	1.4%	1.4%	2.3%	2.1%	2.4%	1.5%	2.9%	2.9%	2.4%	1.2%
Pyrazinamid	4.1%	2.9%	3.8%	5.7%	4.6%	2.7%	4.4%	3.5%	3.6%	2.4%
MDR	3.2%	2.5%	3.4%	3.6%	2.4%	1.1%	2.9%	3.1%	3.0%	2.6%
XDR	0.0%	0.0%	0.0%	0.0%	0.4%	0.4%	0.0%	0.1%	0.7%	0.0%

TABLE 3.8. Antibiotic resistance (%) in *N. gonorrhoeae* strains 2008-2017.

	2008 (n=447)	2009 (n=384)	2010 (n=618)	2011 (n=805)	2012 (n=877)	2013 (n=967)	2014 (n=384)	2015 (n=462)	2016 (n=601)	2017 (n=528)
Cefixime	1	5	6	8	10	4	2	2	1	<1 (0.6)
Ceftriaxone	<1	0	2	2	1	<1 (0.3)	<1 (0.3)	0	0	0
Azithromycin	13	6	12	11	10	13	9	10	3	5
Ciprofloxacin	63	75	56	55	62	53	60	53	53	47
Spectinomycin	0	0	0	0	0	0	0	0	0	0

Neisseria gonorrhoeae

Gonorrhoea is a notifiable infection and in 2017, 2 531 cases (25 cases per 100,000 inhabitants) of gonococcal infections were reported to the Public Health Agency of Sweden. This is a substantial (42%) increase compared to 2016 (1 777 cases, incidence: 18). Most of these cases were identified in the three largest counties of Sweden, which comprise the cities Stockholm, Gothenburg, and Malmö, respectively. The largest increase (63%), from 882 in 2016 to 1 436 in 2017, in the number of gonorrhoea cases was observed in Stockholm county. 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. Data from Stockholm and Skåne counties are not available at current date. In 2017, *N. gonorrhoeae* strains from 528 cases, corresponding to 21% of all reported cases, were fully characterised at the Swedish Reference Laboratory for Sexually Transmitted Infections.

Antimicrobial susceptibility testing was performed according to standardized and quality assured methodology using Etest for MIC determination of ceftriaxone, cefixime, azithromycin, spectinomycin, and ciprofloxacin. The used SIR criteria have been determined by The European Committee on Antimicrobial Susceptibility Testing (EUCAST).

In Table 3.8 the antibiotic resistance in gonococcal isolates (one isolate per case) cultured in 2017 are compared with those from 2008 to 2016. Briefly, the level of resistance to ciprofloxacin, which previously was used as first-line treatment for gonorrhoea, remains very high, i.e. 47% in 2017. The level of resistance to azithromycin was stably high (9-13%) from 2010 to 2015, significantly decreased to 3% in 2016, but increased again to 5% in 2017. The resistance to cefixime has decreased since 2012 (10%) and in 2017 it reached 0.6% resistance, which is the lowest level of cefixime resistance determined any year from 2008 to 2017. Furthermore, as in 2015 and 2016 no resistance to ceftriaxone was identified. This is exceedingly promising because ceftriaxone is the last remaining option for empirical antibiotic 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

Invasive meningococcal disease is a notifiable disease, and in 2017 a total of 49 clinical cases (0.5 cases per 100,000 inhabitants) of the disease were reported. In total, 45 clinical invasive isolates from blood, cerebrospinal fluid or puncture (one isolate per patient) were analysed at the Swedish National Reference Laboratory for *N. meningitidis* (an external body of the Public Health Agency of Sweden), Department of Laboratory Medicine, Clinical Microbiology, Örebro University Hospital.

Antimicrobial susceptibility testing was performed according to standardized and quality assured methodology using Etest for determination of MIC values for penicillin G, cefotaxime, meropenem, chloramphenicol, ciprofloxacin and rifampicin. Production of β-lactamase was examined by nitrocefin discs.

Seven (16%) isolates had an intermediate susceptibility to penicillin G (MIC > 0.064 mg/L), but no isolates where resistant (MIC > 0.25 mg/L). All isolates (100%) were susceptible to cefotaxime (MIC values of < 0.002-0.012 mg/L), meropenem (MICs: 0.003-0.032 mg/L), chloramphenicol (MICs: 0.25-1.5 mg/L), ciprofloxacin (0.002-0.008 mg/L), and rifampicin (MICs: 0.002-0.125 mg/L). None of the isolates obtained in 2017 produced β-lactamase, and in fact no β-lactamase-producing meningococcal isolate has ever been identified in Sweden.

Zoonotic pathogens: *Campylobacter* and *Salmonella*

Campylobacter

Campylobacter is a notifiable infection in Sweden and a total of 10 608 cases were reported in 2017. Approximately 60% of all these cases were persons infected domestically and 40% while travelling abroad. During 2016 and the first six months of 2017 there was a marked increase in domestic cases. This was linked to an increase of *Campylobacter jejuni* in Swedish chicken flocks.

In the national surveillance program, isolates from domestic cases are collected twice during the year (week 11 and 34). The focus of the epidemiological typing, with whole-genome sequencing, is species identification and cluster analysis to identify potential outbreaks. National data on antibiotic susceptibility in *Campylobacter* spp. from humans have largely been missing. A few clinical microbiological laboratories have been monitoring the local resistance rates (see Swedres/Svarm 2011). Antibiotic susceptibility results have also been presented, in the last years of Swedres, originating from laboratories reporting data from blood cultures. These data have been from less than 10 clinical microbiological laboratories and the number of *Campylobacter* isolates have been low.

Antimicrobial susceptibility data from faecal samples, reported to Svebar from 11 laboratories during 2017, were compiled. A total of 6 127 *Campylobacter* spp. isolates were reported. Most isolates were reported as *C. jejuni/coli*, with 4 097 reported isolates, followed by *C. jejuni* (n=1 809), *C. coli* (n=115), *Campylobacter* spp. (n=100), *C. upsaliensis* (n=5) and one isolate of *C. lari*.

The proportion of isolates with reported AST-results was low, except for *C. jejuni* where more results were present. From the selected laboratories 38-39% of the isolates had an AST in total, Table 3.9. The number of tested isolates in the selected laboratories varied, from 7-88% of all *C.jejuni* isolates. The resistance for ciprofloxacin was 37%, and 28% for tetracycline. Only three isolates were resistant to erythromycin, Table 3.9. Information on geographical origin of infection is lacking.

Salmonella

Infection with *Salmonella* is a notifiable diseases in Sweden and a total of 2 279 cases were reported in 2017. Approximately one-third of all cases were infected domestically and two-thirds while travelling abroad. The national surveillance program focus on epidemiological typing to identify potential outbreaks. Isolates from domestic cases are continuously sent to the Public Health Agency of Sweden for species identification, serotyping and for S. Typhimurium, monophasic *S.* Typhimurium och S. Enteritidis multiple-locus variable number tandem repeat analysis is performed.

National data on antibiotic susceptibility in *Salmonella enterica* from humans have, the last years, been compiled from laboratories reporting data from blood cultures. These data have been from around 10 clinical microbiological laboratories and the number of invasive *Salmonella enterica* have been low.

Antimicrobial susceptibility data from faecal and urine samples reported to Svebar during 2017, from 11 laboratories, were compiled. A total of 1401 *Salmonella enterica* isolates were reported. *Salmonella* Typhi and *Salmonella* Paratyphi A were excluded in the analysis.

The antimicrobial susceptibility data are presented in Table 3.10. The highest resistance was seen for the quinolones (22%). The proportion of isolates tested for each antibiotic varied from one quarter to almost half of the reported *Salmonella enterica* isolates. Almost all isolates were susceptible to cefotaxime, ceftazidime and meropenem respectivly. The number of tested isolates in each laboratory varied, from 5 percent to 100 percent of all isolates and laboratory.

It should also be noted that information is lacking regarding whether the isolates came from a person being infected domestically or abroad, which may affect the resistance profile since it reflects the situation at the geographical origin.

TABLE 3.9. Antimicrobial susceptibility in *Campylobacter jejuni* isolates (n=1809) from faecal samples reported to Svebar in 2017.

Antimicrobial	Resistance (%)	Number of tested isolates	Proportion of isolates tested (%)	Min-Max (%) of tested isolats per laboratory	Data from number of laboratories
Ciprofloxacin	37	700	39	7 - 88	6
Erythromycin	< 1	687	39	7 - 88	6
Tetracycline	28	701	38	9 - 88	5

TABLE 3.10. Antibiotic susceptibility in *Salmonella enterica.* isolates (n=1 401) from faecal and urine samples reported to Svebar in 2017. Sterotypes Typhi and Paratyphi A were excluded from the analysis.

Antimicrobial	Resistance (%)	Number of tested isolates	Proportion of isolates tested totally (%)	Min-Max (%) of tested isolats per laboratory	Data from number of laboratories
Azitromycin	3	335	24	5 - 54	4
Cefotaxim	< 1	656	47	7 - 90	10
Ceftazidim	< 1	599	43	7 - 90	9
Meropenem	0	546	39	7 - 90	7
Piperacillin-tazobactam	1	482	35	6 - 80	6
Quinolones	22	622	44	8 - 100	10
Trimethoprim-sulfamethoxazole	6	652	47	7 - 90	10

Antibiotic resistance in animals

Notifiable diseases

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

ESBL-producing Enterobacteriaceae

Farm animals

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

During 2017, samples of intestinal contents from healthy pigs (n=241) and healthy broilers (n=100) as well as samples of pork (n=295) and beef (n=286) 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 (n=228 for pork and n=249 for beef) and other countries (n=67 for pork and n=37 for beef). Isolates with reduced susceptibility were further investigated by molecular methods for presence of transferable genes coding for ESC resistance (for details see Material and methods, resistance in bacteria from animals).

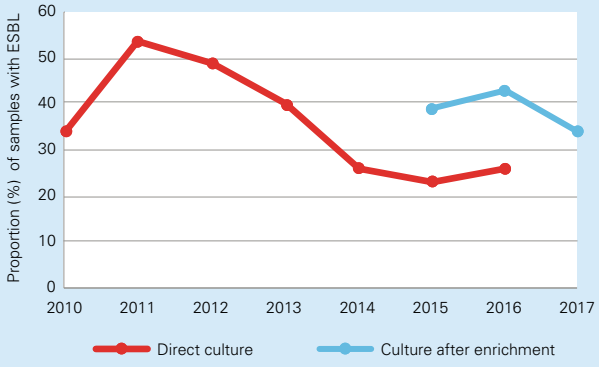
Escherichia coli with ESC-resistance was isolated from 29 (12%) of the samples of intestinal contents from pigs but in only 9 (4%) was a transferable gene coding for ESC resistance detected. All these were $ESBL_A$ and carried the genes $bla_{CTX\text{-}M\text{-}14}$, (n=6), $bla_{CTX\text{-}M\text{-}15}$ (n=2), or $bla_{CTX\text{-}M\text{-}55}$ (n=1). *Escherichia coli* with ESC-resistance was not isolated from any of the samples of pork. Carbapenem resistant *E. coli* was not isolated from any sample.

Regarding beef, *E. coli* with ESC-resistance was isolated from 3 (1%) of the samples and in 2 (<1%) were a transferable gene coding for ESC resistance detected. Both these were $ESBL_A$ and carried the genes $bla_{CTX\text{-}M\text{-}15}$ (n=1), or $bla_{CTX\text{-}M\text{-}27}$ (n=1). All these three samples were of Swedish origin. Carbapenem resistant *E. coli* was not isolated from any sample.

In 2017, *E. coli* with ESC-resistance was isolated from 40 (40%) of the samples of intestinal contents from broilers and in 34 (34%) were a transferable gene coding for ESC resistance detected. The majority (n=20) of these carried the $bla_{CMY\text{-}2}$-gene ($ESBL_M$) and all the remaining (n=14) isolates carried the $bla_{CTX\text{-}M\text{-}1}$-gene ($ESBL_A$). Thereby, the most common gene conferring ESC-resistance among *E. coli* in Swedish broiler production is once again $bla_{CMY\text{-}2}$ (Table 4.1). Carbapenem resistant *E. coli* was not isolated from any sample.

Due to differences in methodology during 2010-2017, changes in the proportion of broiler caecal samples positive for ESC resistant *E. coli* over time cannot be directly assessed (Figure 4.1). However, some comparison 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).

FIGURE 4.1. Proportion (%) of samples from broilers positive for *E. coli* with $ESBL_A$ or $ESBL_M$ from 2010 to 2017.



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.

However, for a number of years, funding from the Swedish Board of Agriculture has enabled SVA to perform confirmation of suspected ESC resistance in isolates of Enterobacteriaceae free of charge for referring laboratories. During 2017, 53 submitted isolates of Enterobacteriaceae with phenotypic resistance to ESCs were confirmed to produce $ESBL_A$ and/or $ESBL_M$ (Table 4.2). The isolates were from cats (n=5), dogs (n=17) and horses (n=31). This is comparable with the number of ESBL-producing Enterobacteriaceae confirmed in 2016.

Apart from resistance agains beta-lactams, including third generation cephalosporins, 46 isolates (87%) were also resistant to at least two other antibiotics, i.e. they were multiresistant. The most common resistances were streptomycin (79%), trimethoprim-sulphonamides (75%), gentamicin (72%), enrofloxacin (45%) and tetracyclin (45%). Resistance to nitrofurantoin was however uncommon (4%).

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

							Beta-lactamase (No. isolates)								
Animal species	**Matrix**	**Year**	**No. of samples**	**No. samples with ESC resist-ance**	**No. samples with $ESBL_A$ or $ESBL_M$**	**% samples with $ESBL_A$ or $ESBL_M$**	**CTX-M-1**	**CTX-M-3**	**CTX-M-14**	**CTX-M-15**	**CTX-M-27**	**CTX-M-55**	**TEM-52**	**SHV**	**CMY-2**
Broilers	Intestine	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[a]	39[a]	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	2017	249	3	2	<1				1	1				
Cattle[e]	Intestine	2015	103	5	0	0									
Cattle	Meat	2015	289	0	0	0									
Cattle[e]	Intestine	2013	202	3	1	<1				1					
Cattle[e]	Intestine	2012	742	81	9	1	1			4					4
Cattle[e]	Intestine	2009	256	11	0	0									
Pigs	Intestine	2017	241	29	9	4			6	2		1			
Pigs	Meat	2017	228	0	0	0									
Pigs	Intestine	2015	303	35	4	1				1		2			1
Pigs	Meat	2015	286	1	1	<1						1			
Pigs	Intestine	2011	184	9	3	2		1		1			1		
Pigs	Meat	2011	100	0	0	0									
Pigs	Intestine	2008	452	9	0	0									
Pigs	Meat	2008	50	0	0	0									
Turkeys	Intestine	2016	86	1	1	1	1								
Turkeys	Intestine	2014	60	12	0	0									
Turkeys	Intestine	2013	55	16	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 isolate sequenced and possessed the gene $bla_{CTX\text{-}M\text{-}1}$. [b] CIT-group, five caecal and three meat isolate 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, 2008-2017.

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

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

Next generation sequencing (NGS) reveals different population-structures of *Escherichia coli* carrying bla_{CMY-2} and *E. coli* carrying $bla_{CTX-M-1}$ in the Swedish broiler production

Using next-generation sequencing (NGS), the 34 ESC-resistant *Escherichia coli* isolates identified to carry transferable genes (Table 4.1) from broilers, were further investigated to identify the specific gene variants encoding ESC-resistance and the relatedness of isolates.

Using the approach "Antimicrobial Resistance Identification By Assembly (ARIBA)" (Hunt et al., 2017) against a local database containing the transferable genes encoding beta-lactam resistance listed in the Resfinder-v3.0-database (https://cge.cbs.dtu.dk/services/ResFinder/) the specific gene variants in the isolates were determined. This approach identified that 20 of the isolates carried the bla_{CMY-2}-gene ($ESBL_M$) and 14 isolates carried the $bla_{CTX-M-1}$-gene ($ESBL_A$). The relatedness of the isolates was then further investigated using the traditional 7-MLST and the core genome MLST (cgMLST) scheme reported by https://enterobase.warwick.ac.uk/ using the SeqSphere+ Software (Ridom, Germany). After identifying the 7-MLST alleles and the presence of cgMLST alleles occurring in all compared isolates, the differences between determined cgMLST profiles were visualized by creating minimum spanning trees.

The analyses revealed that the 20 bla_{CMY-2} isolates belonged to different 7-MLST profiles, but 1 isolate could not be assigned a specific 7-ST due to that the gene *icd* could not be identified in the assembled contigs. Out of the 20 isolates, 16 belonged to the ST2040, with these 16 isolates showing high similarity in the cgMLST-analyse comparing 2453 alleles (Figure 1A). The remaining 4 isolates showed limited relatedness to each other and the ST2040 isolates, differing in at least 379 alleles to ST2040 isolates.

Out of the 14 isolates carrying $bla_{CTX-M-1}$, 13 were shown to belong to 10 different 7-MLST profiles, with three isolates belonging to ST47 and two isolates belonging to ST297 (Figure 1B). One isolate could not be assigned to a specific 7-ST due to that the *icd* gene could not be identified in the assembled contigs. In addition, one isolate was excluded in further comparisons due to poor sequence quality. The cgMLST comparison of the $bla_{CTX-M-1}$ isolates showed high similarity between the three ST57 isolates, while the two ST297 isolates differed in 223 alleles. The limited relatedness between the remaining isolates, as evident by 7-MLST, was further highlighted when comparing them by cgMLST showing differences in >1000 out of the 2431 compared alleles (Figure 1B). Interestingly, one of the $bla_{CTX-M-1}$ isolates belonged to ST2040 dominating among the bla_{CMY-2} isolates, with cgMLST revealing that it differed in 31 alleles to the closest bla_{CMY-2} isolate (Figure 1A).

Using NGS followed by cgMLST comparisons it was revealed that the population structures of *E. coli* carrying bla_{CMY-2} and *E. coli* carrying $bla_{CTX-M-1}$, isolated from the Swedish broiler population in 2017, differed significantly. The spread of *E. coli* with bla_{CMY-2} appears primarily be facilitated by one specific clone belonging to ST2040. In contrast, the $bla_{CTX-M-1}$ isolates showed a high genetic diversity with only three out of 13 analyzed isolates showing high relatedness based on cgMLST. In addition, the *E. coli* ST38 with bla_{CMY-2}, which previously has been shown to dominate in the Swedish broiler population (Myrenås et al., 2018), could not be detected among the bla_{CMY-2} isolates identified in 2017. In addition, the ST38 and ST2040 are not closely related as they differ in 7 out of 7 investigate alleles.

References

Hunt M, Mather AE, et al. 2017, ARIBA: rapid antimicrobial resistance genotyping directly from sequencing reads. *Microb Genom,* 3:e000131.

Myrenås M, Slettemeås JS, et al. 2018, Clonal spread of *Escherichia coli* resistant to cephalosporins and quinolones in the Nordic broiler production. *Vet Microbiol,* 213:123-8.

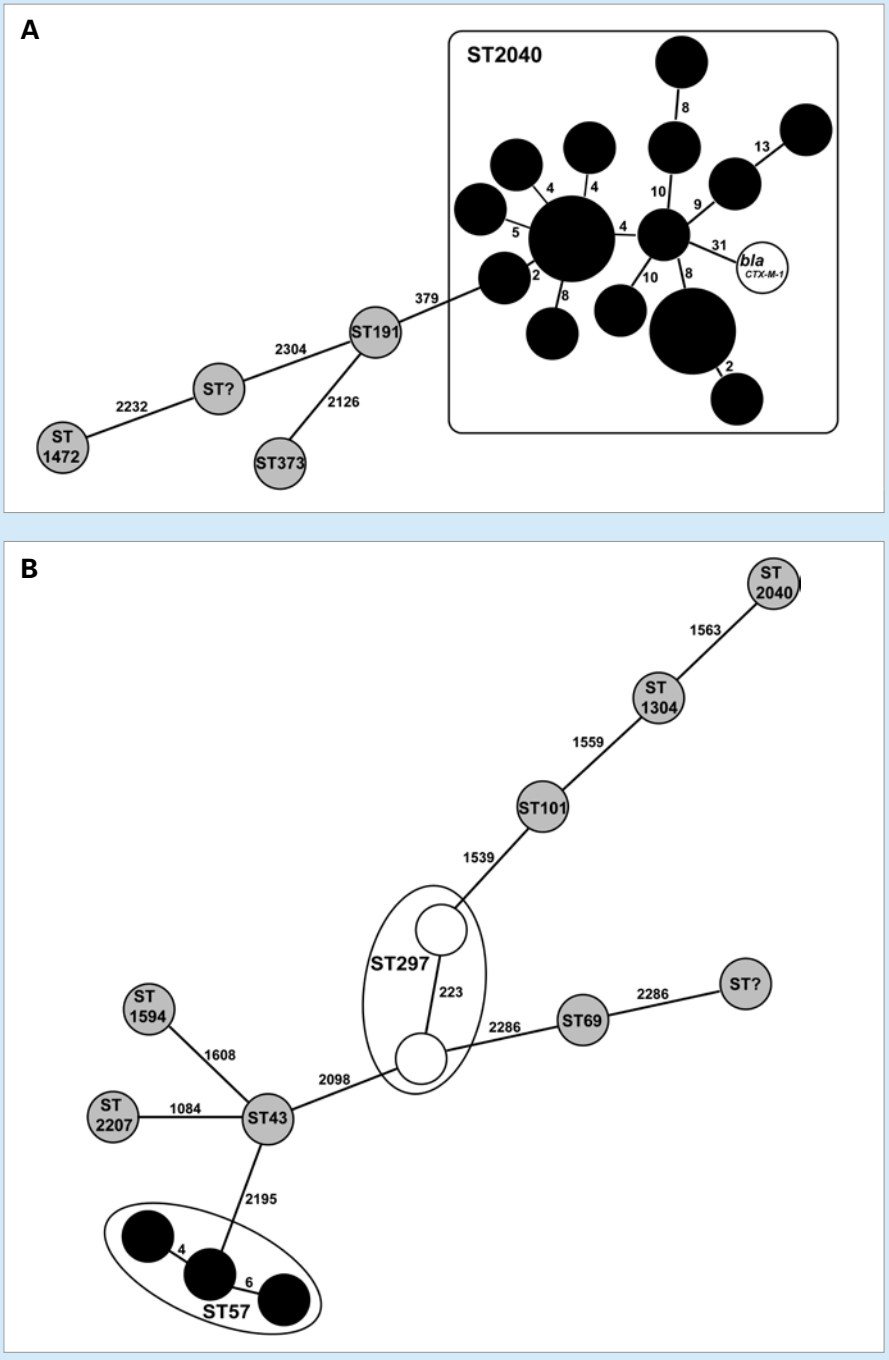


Figure 1. Minimum spanning tree of core genome MLST relationship of *Escherichia coli* from broilers 2017 based on genes present in all compared isolates. Numbers on the lines between isolates indicate differences in alleles between isolates, and the lengths of lines are based on the number of gene differences in a logarithmic scale. The ST-number denotes the multi-locus sequence type as defined by the scheme https://enterobase.warwick.ac.uk/, ST? = the ST could not be determined due to the *icd* gene could not be identified in contigs from assembly.

A. *E. coli* carrying bla_{CMY-2} and an *E. coli* ST2040 isolate carrying $bla_{CTX-M-1}$, based on 2453 alleles.

B. *E. coli* carrying $bla_{CTX-M-1}$ except for the ST2040 isolate, based on 2431 alleles.

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).

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 1100 isolates have been tested up to and including 2017. In this monitoring, PVL-negative MRSA with *mecC* was detected four times in 2010-2011 (Unnerstad et al., 2013), and once in 2013 and 2015, respectively. PVL-positive MRSA with *mecA* was detected in 2012 and PVL-negative MRSA with *mecA* in 2014 and 2017. The monitoring is performed on isolates with anonymized origin. In addition, active monitoring was performed in 40 bovine dairy herds in Kalmar County in 2012. Samples were taken from bulk milk, from five cows and five unweaned calves in each herd. MRSA was not found. In 2012, PVL-positive MRSA with *mecA* was isolated from several animals in a dairy herd.

In 2016 and early 2017 there was an outbreak of MRSA with *mecC* among goats and sheep connected to a zoo. MRSA was found in samples from 20 goats and 6 sheep, both with symtoms of dermatitis around the nostrils and without clinical symtoms. There was an epidemiological link through direct or indirect contact between all positive animals. In addition, MRSA with *mecC* was found in 8 out of 21 sampled goats in a herd in 2017 and in one goat sold from the same herd.

Companion animals and horses

Up to and including 2017, a total of 99 cases of MRSA in companion animals and horses have been confirmed. These include 44 dogs, 15 cats, 1 rabbit and 39 horses. In those species, there was no active monitoring of MRSA during 2017. 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 2017, MRSA was detected in clinical samples, mostly from wound infections, from nine dogs, one cat and one rabbit. Since the first finding of MRSA in companion animals, *spa*-type t032 has been most common, but during the most recent years the *spa*-types have been more varied (Table 4.4). All isolates from dogs in 2017 belonged to different *spa*-types, indicating separate sources.

In 2017, MRSA was isolated from seven horses, five with uterine infection and two with wound infections. In isolates from horses, *spa*-type t011, CC398, has dominated historically. In 2017, MRSA of *spa*-type t011 was isolated from three horses from the same stud farm and transmission within the farm is likely. MRSA of the unusual *spa*-type t1257 was isolated from two horses at the same animal hospital. Transmission within the premises is likely also in this case.

Wild animals

A screening study in hedgehogs was performed in 2015 and MRSA was isolated from 35 out of 55 sampled animals. MRSA has also been detected in four samples from hedgehogs before this study and in one sample during 2016. All isolates from hedgehogs have been MRSA with *mecC*. For more information on MRSA in hedgehogs, see Swedres-Svarm 2016.

TABLE 4.3. Large animals. Isolates of methicillin-resistant *Staphylococcus aureus* (MRSA) in Swedish horses, pigs, cows, goats and sheep up to and including 2017. All isolates were positive for the *mecA* or *mecC* and *nuc* genes. Shaded areas indicate MIC above EUCAST ECOFF.

Animal species	Year	No. of isolates	Antibiotic, MIC (mg/L)												*spa*-type	*mec*-gene
			Fox	Pen	Cet	Cli	Ery	Tet	Fus	Gen	Cip	Tmp	Chl	Lin		
Horse	2007	1	-	>4	1	≤0.25	0.5	64	0.5	>64	1	>32	8		t011	*A*
Horse	2008	1	>16	>4	1	≤0.25	0.5	32	0.5	64	1	>32	8		t011	*A*
Horse	2008	1	>16	>4	2	≤0.25	1	32	1	>64	1	>32	8		t011	*A*
Horse	2008	3	16->16	>4	2	≤0.25	0.5-1	32	0.25-0.5	64->64	0.5	>32	8		t011	*A*
Horse	2008	1	8	>4	2	≤0.25	1	64	1	>64	1	>32	16		t011	*A*
Horse	2008	1	>16	4	4	≤0.25	≤0.25	32	0.12	4	0.25	>32	4		t011	*A*
Horse	2009	1	>16	>4	>8	≤0.25	0.5	64	0.25	16	0.25	>32	8		t011	*A*
Horse	2009	1	>16	4	1	≤0.25	0.5	32	0.25	64	1	>32	8		t011	*A*
Horse	2010	1	>16	>4	8	0.5	2	64	1	>64	1	>32	16		t011	*A*
Horse	2010	2	>16	>4	2-4	≤0.25	1	32	0.5	16->64	0.25-0.5	>32	8		t064	*A*
Horse	2010	3	>16	>4	4-8	≤0.25	0.5	32-64	0.25-0.5	64->64	0.25	>32	8		t011	*A*
Horse	2011	1	>16	>4	1	≤0.25	≤0.25	32	0.12	32	0.25	>32	4		t011	*A*
Horse	2011	1	>16	>4	2	≤0.25	≤0.25	64	0.5	≤0.5	0.25	1	8		t011	*A*
Horse	2012	1	>16	>4	8	1	1	64	0.25	>64	0.5	>32	8		t011	*A*
Horse	2012	1	-	>4	1	≤0.25	0.5	32	0.25	32	0.25	>32	4		t011	*A*
Horse	2013	1	4	>4	>8	≤0.25	1	64	1	>64	1	>32	16		t011	*A*
Horse	2014	1	>16	>4	4	≤0.25	1	64	0.25	64	0.25	>32	8		t011	*A*
Horse	2014	2	>14	>4	1	≤0.25	≤0.25	32	≤0.06-0.12	8-16	0.25	>32	8		t011	*A*
Horse	2014	5	>16	>4	2-4	≤0.25	≤0.25	16-32	≤0.06-0.12	32-64	0.12-0.25	>32	8		t011	*A*
Horse	2014	1	>16	>4	4	≤0.25	≤0.25	32	≤0.06	64	>4	>32	8		t011	*A*
Horse	2015	1	>16	>4	4	≤0.25	≤0.25	32	0.12	16	>4	>32	8		t011	*A*
Horse	2015	1	>16	>4	2	≤0.25	≤0.25	32	0.25	32	0.25	>32	8		t1451	*A*
Horse	2017	2	>8	>4	4	≤0.25	≤0.25	32	≤0.25	16->16	0.5	>8	8	2	t011	*A*
Horse	2017	1	>8	>4	2	≤0.25	≤0.25	32	≤0.25	>16	>4	>8	4	≤1	t011	*A*
Horse	2017	2	>8	>4	4->4	>32	>32	64	≤0.25	>16	>4	>8	8-16	≤1	t011	*A*
Horse	2017	2	>8	>4	2	≤0.25	>32	32	≤0.25	>16	>4	>8	8	≤1-2	t1257	*A*
Pig	2010	1	>16	>4	>8	0.5	1	64	0.5	>64	0.25	>32	16		t011	*A*
Pig	2010	1	>8	2	1	≤0.25	≤0.25	≤0.5	≤0.25	0.5	0.5	0.5	4	2	t373	*C*
Cow	2010	2	16	1-2	1	≤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	>16	>4	4	≤0.25	0.5	≤0.5	0.25	≤0.5	0.5	2	8		t524	*C*
Cow	2011	1	>16	2	2	≤0.25	0.5	≤0.5	0.12	≤0.5	0.25	1	8		t9111	*C*
Cow	2012	2	16->16	2->4	0.5-1	≤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	8	0.5	0.5	≤0.25	1	≤0.5	0.5	≤0.5	0.5	2	8		t843	*C*
Cow	2014	1	>16	>4	2	≤0.25	>32	16	0.25	≤0.5	0.25	2	8		t127	*A*
Cow	2015	1	1	0.25	0.25	≤0.25	≤0.25	≤0.5	0.12	≤0.5	0.25	1	8		t843	*C*
Cow	2017	1	4	1	0.25	≤0.25	≤0.25	≤0.5	4	0.25	0.25	0.5	4	≤1	t008	*A*
Goat	2016	1[a]	>8	2	1	≤0.25	≤0.25	≤0.5	0.12	≤0.5	1	≤0.5	8		t9268	*C*
Goat	2017	1	>8	1	1	≤0.25	≤0.25	≤0.5	≤0.25	0.5	0.25	0.5	8	2	t9268	*C*
Goat	2017	9	8->8	0.5-1	0.5-2	≤0.25	≤0.25	≤0.5	≤0.25	0.25-0.5	0.25	0.5	4-8	≤1-2	t373	*C*
Sheep	2016	3[b]	>8	1-2	1-2	≤0.25	≤0.25	≤0.5	≤0.25	≤0.5	0.25	0.5-1	8		t9268	*C*

[a] One isolate was tested from an outbreak including 19 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 2017. 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 one from a dog in 2017 were not available for further testing and are not included in the table.

Animal species	Year	No. of isolates	Antibiotic, MIC (mg/L)												*spa*-type	*mec*-gene
			Fox	Pen	Cet	Cli	Ery	Tet	Fus	Gen	Cip	Tmp	Chl	Lin		
Dog	2006	3	8->16	>4	8->8	≤0.25	0.5	≤0.5	0.25-0.5	≤0.5-1	>4	1-2	8		t032	*A*
Dog	2007	4	16->16	>4	8->8	≤0.25	0.5	≤0.5	0.25-0.5	≤0.5	>4	1-2	8		t032	*A*
Dog	2007	1	>16	>4	>8	0.5	0.5	2	-	1	>4	2	4		t032	*A*
Dog	2008	3	>16	>4	>8	≤0.25	≤0.25-1	≤0.5	0.25-0.5	1	>4	1-2	8		t032	*A*
Dog	2008	1	>16	>4	>8	0.5	>32	≤0.5	0.5	32	>4	>32	16		t127	*A*
Dog	2009	1	>16	>4	>8	≤0.25	0.5	≤0.5	0.25	≤0.5	>4	2	8		t032	*A*
Dog	2009	1	>16	>4	>8	0.5	1	1	0.5	1	>4	4	16		t032	*A*
Dog	2010	1	>16	>4	>8	>32	>32	≤0.5	0.5	1	>4	2	16		t002	*A*
Dog	2010	1	-	>4	>8	≤0.25	0.5	≤0.5	0.5	≤0.5	>4	1	8		t032	*A*
Dog	2010	1	16	>4	8	≤0.25	>32	≤0.5	0.5	≤0.5	>4	8	4		t020	*A*
Dog	2010	1	16	>4	1	≤0.25	≤0.25	≤0.5	8	1	0.5	2	8		t002	*A*
Dog	2013	1	>16	>4	1	≤0.25	>32	16	0.25	2	0.25	2	8		t127	*A*
Dog	2013	1	>16	>4	2	≤0.25	1	≤0.5	0.5	≤0.5	0.5	4	8		t304	*A*
Dog	2013	1	>16	>4	2	≤0.25	1	≤0.5	0.25	≤0.5	0.5	2	8		t127	*A*
Dog	2013	1	>16	>4	>8	0.5	1	1	1	1	>4	4	8		t032	*A*
Dog	2013	1	>16	>4	2	≤0.25	0.5	≤0.5	0.5	≤0.5	0.5	>32	8		t223	*A*
Dog	2014	1	>16	>4	2	≤0.25	1	16	0.5	1	0.5	4	8		t325	*A*
Dog	2014	1	>16	>4	8	≤0.25	≤0.25	≤0.5	≤0.06	≤0.5	>4	1	8		t032	*A*
Dog	2014	1	>16	>4	1	≤0.25	>32	≤0.5	≤0.06	≤0.5	0.25	1	8		t002	*A*
Dog	2015	1	16	>4	2	0.5	≤0.25	≤0.5	0.5	≤0.5	0.25	≤0.5	8		t373	*C*
Dog	2015	3	>16	>4	2-4	≤0.25	>32	16-32	≤0.06-0.5	≤0.5	0.12-0.25	1-2	4-8		t127	*A*
Dog	2015	1	16	1	0.5	≤0.25	≤0.25	≤0.5	0.12	≤0.5	0.25	1	8		t843	*C*
Dog	2015	1	>16	>4	2	≤0.25	>32	16	0.25	≤0.5	0.5	2	8		t948	*A*
Dog	2015	1	>16	>4	2	≤0.25	>32	16	0.12	≤0.5	0.25	1	4		t177	*A*
Dog	2016	1	16	>4	2	16	≤0.25	32	0.5	16	>4	>32	64		t034	*A*
Dog	2016	1	16	>4	1	≤0.25	>32	8	4	≤0.5	0.5	4	8		t044	*A*
Dog	2017	1	>8	>4	>4	≤0.25	≤0.25	≤0.5	>4	0.25	>4	0.5	8	2	t032	*A*
Dog	2017	1	>8	>4	2	8	≤0.25	64	≤0.25	0.5	>4	>8	4	≤1	t034	*A*
Dog	2017	1	>8	>4	>4	≤0.25	≤0.25	≤0.5	≤0.25	0.25	0.5	1	4	2	t2734	*A*
Dog	2017	1	>8	>4	1	≤0.25	≤0.25	≤0.5	≤0.25	0.5	0.25	>8	8	2	t5634	*A*
Dog	2017	1	>8	>4	2	>32	>32	≤0.5	≤0.25	0.5	1	2	8	≤1	t127	*A*
Dog	2017	1	>8	>4	>4	≤0.25	≤0.25	≤0.5	≤0.25	0.25	>4	0.5	4	2	t022	*A*
Dog	2017	1	>8	>4	2	≤0.25	2	≤0.5	≤0.25	0.25	>4	0.5	4	≤1	t008	*A*
Dog	2017	1	>8	>4	>4	≤0.25	≤0.25	≤0.5	≤0.25	8	>4	>8	8	2	t891	*A*
Cat	2009	1	>16	>4	>8	≤0.25	0.5	≤0.5	0.25	≤0.5	>4	4	4		t032	*A*
Cat	2009	1	>16	>4	>8	≤0.25	0.5	≤0.5	0.5	1	>4	2	8		t032	*A*
Cat	2010	1	-	>4	>8	≤0.25	0.5	≤0.5	1	≤0.5	>4	1	8		t032	*A*
Cat	2010	1	16	>4	>8	≤0.25	≤0.25	≤0.5	0.25	≤0.5	>4	1	8		t032	*A*
Cat	2011	1	>16	>4	>8	≤0.25	≤0.25	≤0.5	0.25	≤0.5	>4	1	8		t022	*A*
Cat	2012	1	>16	>4	>8	≤0.25	≤0.25	≤0.5	0.25	≤0.5	>4	2	8		t032	*A*
Cat	2012	1	>16	>4	>8	0.5	1	1	1	1	>4	2	16		t032	*A*
Cat	2014	1	>16	1	2	≤0.25	≤0.25	≤0.5	0.25	≤0.5	0.25	0.5	8		t978	*C*
Cat	2014	1	>16	2	1	≤0.25	≤0.25	≤0.5	≤0.06	≤0.5	0.25	0.5	8		t978	*C*
Cat	2015	1	16	1	1	≤0.25	≤0.25	≤0.5	≤0.06	≤0.5	0.25	1	8		t843	*C*
Cat	2015	1	16	>4	1	≤0.25	0.5	≤0.5	0.12	≤0.5	0.25	1	8		t933	*A*
Cat	2016	1	16	>4	2	≤0.25	>32	≤0.5	0.5	≤0.5	2	2	8		t008	*A*
Cat	2016	1	>16	>4	2	≤0.25	≤0.25	≤0.5	≤0.06	≤0.5	0.12	≤0.5	4		t304	*A*
Cat	2017	1	>8	>5	1	≤0.25	≤0.25	≤0.5	≤0.25	0.5	0.25	>8	4	≤1	t786	*A*
Rabbit	2017	1	8	>6	1	≤0.25	≤0.25	≤0.5	4	0.5	0.25	0.5	4	≤1	t132	*A*

Methicillin-resistant *Staphylococcus pseudintermedius* (MRSP)

In 2017, there were 47 MRSP cases (all dogs) reported to the Swedish Board of Agriculture (Figure 4.2). This number is about the same level as in 2016. Isolates from 40 cases were available for whole genome sequencing and susceptibility testing, two additional isolates were susceptibility tested only, and five isolates were not available for further typing. Information on the sampling site was available for 44 cases; skin (including external ear canal) 19 cases, wounds (including surgical wounds) 18 cases and the remaining 7 were isolated from various other sites.

The results of the whole genome sequencing could divide the isolates into 23 different multi-locus sequence types, of which ST71 and ST258 were the most common types with 7 isolates each (Table 4.5.). In earlier years, ST71 (a European clone described by Perreten et al. 2010), was dominating among Swedish isolates. Now the picture of MRSP is more diverse with several sequence types occurring. Isolates belonging to ST258 have previously been described as an emerging clone in Europe (Duim et al., 2015; Osland et al., 2012; Damborg et al., 2013).

All but one isolate were defined as multi-resistant. For resistance phenotypes, see Table 4.5.

FIGURE 4.2. Number of cases of methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) in Sweden notified to the Swedish Board of Agriculture 2008-2017. In 2006-2007 the numbers represent the isolates that were sent to SVA and confirmed as *mecA*-positive. The red square for 2017 represents the percent of whole genome sequenced isolates belonging to ST71.

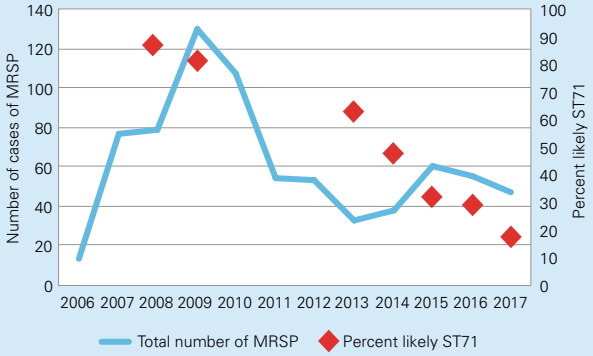


TABLE 4.5 Resistance phenotypes (beta-lactams excluded) and multilocus sequence types of isolates of methicillin resistant *Staphylococcus pseudintermedius* (MRSP) in dogs 2017. All isolates were positive for the *mecA* gene. Shaded MICs indicate resistance.

Antibiotic MIC (mg/L)								MLST (number of isolates)																								
Ery	Cli	Tsu	Tet	Enr	Fus	Gen	Nit	ST71	ST121	ST258	ST261	ST265	ST277	ST419	ST421	ST498	ST551	ST621	ST690	ST728	ST730	ST743	ST812	ST933	ST934	ST935	ST936	ST937	ST938	ST939	Not tested	Sum
>2	>2	>4/76	>4	1->1	≤0.5-1	4->4	≤16	3	1								4							1	1							10
>2	>2	1/19->4/76	≤0.25	>1	≤0.5	4->4	≤16	4																								4
>2	>2	>4/76	>4	≤0.25	≤0.5	>4	≤16					2							1								1					4
>2	>2	1/19->4/76	>4	≤0.25	>2	≤1	≤16			1											1							1				3
>2	1-2	1/19->4/76	>4	1->1	≤0.5	≤1	≤16				1																		1			2
>2	>2	0.5/9.5	>4	>1	≤0.5	4	≤16																								1	1
>2	1->2	1/19->4/76	>4	≤0.25	≤0.5	≤1	≤16			4				1				2		1			1									9
>2	2->2	0.5/9.5	>4	≤0.25-0.5	>2	≤1	≤16						1									1										2
>2	>2	>4/76	≤0.25	≤0.25	>2	≤1	≤16			1																						1
>2	>2	0.5/9.5	≤0.25	>1	≤0.5	≤1	≤16																							1		1
>2	>2	1/9	≤0.25	≤0.25	≤0.5	2	≤16																								1	1
≤0.5	≤0.5	>4/76	>4	≤0.25	>2	≤1	≤16																			1						1
>2	>2	0.5/9.5	≤0.25	≤0.25	≤0.5	≤1	≤16								1																	1
≤0.5	≤0.5	>4/76	>4	≤0.25	≤0.5	≤1	≤16			1																						1
>2	≤0.5	0.5/9.5	0.5	≤0.25	≤0.5	2	≤16									1																1
							Sum	7	1	7	1	2	1	1	1	1	4	2	1	1	1	1	1	1	1	1	1	1	1	1	1	2	42

Zoonotic pathogens

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

Salmonella

Findings of *Salmonella* in animals are notifiable in Sweden. In Svarm, antibiotic susceptibility is determined in one isolate from each notified incident in farm animals or horses each year. Isolates from incidents previously notified but still under restrictions are also included. In incidents involving more than one serovar, one isolate of each serovar is tested. From incidents in companion animals and wild animals a selection of isolates is tested. As from 2014, phage typing is not performed on isolates of *Salmonella* from animals. For details on methodology see Materials and methods, resistance in bacteria from animals.

All animals 2017

Altogether, 63 isolates of *S. enterica* were tested of which 29 were *S.* Typhimurium (Table 4.6). Distributions of MICs and resistance for all isolates are presented in Table 4.7 and for the subset *S.* Typhimurium in Table 4.8. Most isolates (95%) were susceptible to all antibiotics tested, and only three isolates were resistant to one or more substances (Table 4.9). Of these isolates two were multiresistant; one isolate of *S.* Infantis from a dog and one isolate of *S.* Typhimurium from an incident in pigs. Notably, the *S.* Infantis isolate was resistant to quinolones.

In the subset of *S.* Typhimurium, resistance was overall low in 2017 but has varied over the years (Figure 4.3). The variation is largely due to differences in occurrence of multiresistant strains between the years.

Farm animals 2000–2017

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

In the period 2000-2017, isolates from the vast majority of notified incidents in major farm animals were tested in Svarm, in total 713 isolates. About half of the isolates, 342 (48%), were *S.* Typhimurium and of these 37% were from pigs, 32% from cattle, 30% from poultry and 1% from sheep.

The majority (73%) of *S.* Typhimurium isolates from farm animal incidents were susceptible to all antibiotics tested but 38 isolates (11%) were multiresistant (Table 4.10). The most common traits were resistance to ampicillin, streptomycin, tetracycline, sulphonamide, chloramphenicol and florfenicol. Resistance to third generation cephalosporins was not

FIGURE 4.3. Resistance (%) to ampicillin, chloramphenicol, sulphamethoxazole and tetracycline in *Salmonella* Typhimurium from all animals, 2000-2017. The number of isolates each year varies (n=24-85).

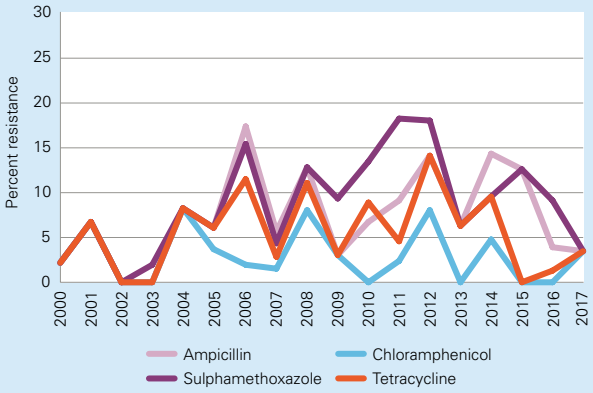


TABLE 4.6 Number of *Salmonella enterica* isolates tested for antibiotic susceptibility, 2017.

Serovar	Cattle	Pigs	Sheep	Poultry	Horse	Dogs	Cats	Wild birds	Wild mammals	Total
S. Agona						1				**1**
S. Derby						1				**1**
S. Dublin	4									**4**
S. Duesseldorf	1									**1**
S. enterica ST-416									1	**1**
S. enterica subsp. *diarizonae* (IIIb)	2		13							**15**
S. enterica subsp. *enterica* (I)				1		1		2		**4**
S. Enteritidis	1									**1**
S. Gallinarum biovar Pullorum				2						**2**
S. Infantis	1				1	2				**4**
S. Typhimurium	2	3		2		2	10	8	1	**28**
S. Typhimurium (monophasic 4,5:i:-)								1		**1**
Total	**11**	**3**	**13**	**5**	**1**	**7**	**10**	**11**	**2**	**63**
Percent of total	17	5	21	8	2	11	16	17	3	

TABLE 4.7. Distribution of MICs and resistance (%) in *Salmonella enterica* (n=63) from all animals, 2017.

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	2							84.1	9.5	3.2	1.6					1.6			
Cefotaxime	0			30.2	52.4	4.8	12.7												
Ceftazidime	0					61.9	22.2	3.2	12.7										
Chloramphenicol	2								39.7	54.0	4.8				1.6				
Ciprofloxacin	2	7.9	71.4	19.0		1.6													
Colistin	0						38.1	47.6	14.3										
Florfenicol	2									90.5	7.9		1.6						
Gentamicin	0						92.1	7.9											
Nalidixic acid	2								20.6	69.8	7.9				1.6				
Streptomycin	3									7.9	54.0	34.9	1.6	1.6					
Sulphamethoxazole	3										1.6	17.5	33.3	17.5	17.5	9.5			3.2
Tetracycline	3							93.7	3.2				3.2						
Trimethoprim	0				7.9	50.8	31.7	9.5											

TABLE 4.8. Distribution of MICs and resistance (%) in *Salmonella* Typhimurium (n=29) from all animals, 2017.

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	3							93.1	3.4							3.4			
Cefotaxime	0			6.9	82.8	6.9	3.4												
Ceftazidime	0					72.4	20.7	3.4	3.4										
Chloramphenicol	3								17.2	79.3					3.4				
Ciprofloxacin	0		62.1	37.9															
Colistin	0						24.1	69.0	6.9										
Florfenicol	3									96.6			3.4						
Gentamicin	0						86.2	13.8											
Nalidixic acid	0								3.4	82.8	13.8								
Streptomycin	3										55.2	41.4		3.4					
Sulphamethoxazole	3											3.4	13.8	24.1	37.9	17.2			3.4
Tetracycline	3							93.1	3.4				3.4						
Trimethoprim	0				6.9	20.7	55.2	17.2											

TABLE 4.9. MICs (mg/L) in the three isolates of *Salmonella enterica* resistant to one or more antibiotic, 2017. Shaded fields indicate resistance.

Source	Serovar	Amp	Ctx	Caz	Cip	Nal	Chl	Flf	Col	Gen	Str	Sul	Tet	Tmp
Cattle	*S. enterica* subsp. *diarizonae* (IIIb)	≤1	≤0.06	≤0.25	≤0.016	≤2	4	≤4	≤0.5	≤0.5	32	64	≤1	0.25
Dog	*S.* Infantis	≤1	0.12	0.5	0.25	>64	4	8	≤0.5	≤0.5	16	>1024	32	0.25
Pig	*S.* Typhimurium	>128	0.5	2	0.03	4	>64	32	≤0.5	≤0.5	64	>1024	32	0.5

found and resistance to ciprofloxacin was found in isolates from only five incidents. Six isolates (2%) of other serovars (*S. enterica* subsp., *enterica* (I), *S.* Duesseldorf, *S.* Yoruba, *S.* Dublin, *S.* Infantis) than Typhimurium were multiresistant. Of these, five isolates were from cattle and one from poultry.

The 38 multiresistant isolates of *S.* Typhimurium in the period 2000-2017 were from 37 separate notified incidents of which 24 involved cattle, 8 pigs, 2 poultry and 1 incident involved both pigs and cattle (Table 4.10). Of the two remaining incidents, one was in sheep and one in ducks in a hobby flock. Three incidents in 2004 and two in 2015 involved cattle and were epidemiologically linked through trade of calves. An epidemiological link was also suspected between four incidents 2007-2008 involving cattle, pigs and sheep. There were no known links between the other incidents.

In 2017 none of the notified incidents in farm animals involved monophasic *S.* Typhimurium I (O 4,5,12:i- /O 4,5:i:- / O 4:i:-). However, since this variant was first found in 2006, eight incidents of monophasic *S.* Typhimurium have been confirmed in farm animals in Sweden. Three incidents involved only cattle, three only pigs, one only ducks, and one incident involved both cattle and poultry. In six of the incidents the isolates were multiresistant (Table 4.10). Monophasic *S.* Typhimurium has also been isolated from four dogs and two wild birds. All four isolates from dogs were multiresistant wheras the isolates from wild birds were susceptible to all antibiotics tested. Epidemiological links were confirmed between some of the incidents of monophasic *Salmonella*.

TABLE 4.10. Resistance phenotypes of *Salmonella* Typhimurium (n=342) from notified incidents in farm animals, 2000-2017. All isolates were tested for susceptibility to ampicillin, florfenicol, gentamicin, chloramphenicol, ciprofloxacin, nalidixic acid, streptomycin, sulphamethoxazole, tetracycline, trimethoprim and to ceftiofur or cefotaxime.

		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
AmpStrSul	**Cattle**													1								1	1	3
StrSulTet	**Cattle**																			1				1
AmpSul	**Cattle**											2												2
AmpSul	**Pigs**											1												1
StrGen	**Cattle**									1														1
StrGen	**Pigs**								1															1
StrGen	**Poultry**									1														1
StrSul	**Pigs**																					2		2
StrSul	**Poultry**						2																	2
SulTm	**Cattle**																1			1			1	3
SulTm	**Pigs**																						1	1
Amp	**Poultry**																			2				2
Gen	**Poultry**																			1				1
Nal	**Pigs**					1																		1
Str	**Cattle**											1		1		1				4			1	8
Str	**Pigs**								4	3		2		1						4	1		2	17
Str	**Poultry**									2										3				5
Tet	**Pigs**																						1	1
Susceptible	**Sheep**	1																					3	4
Susceptible	**Cattle**	4			2		1	1	1	6		2		5	1	1				27	1	1	15	68
Susceptible	**Pigs**	1	1			2			33	5	1	1		8					1	18	2		21	94
Susceptible	**Poultry**	1		1		1			5	1			1	2				1	1	43	4		28	89
Sum		**7**	**1**	**1**	**2**	**4**	**3**	**1**	**44**	**19**	**1**	**22**	**1**	**20**	**1**	**2**	**1**	**1**	**2**	**104**	**11**	**9**	**85**	**342**

Campylobacter

Campylobacter coli was isolated from samples of colon content from healthy 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.

All isolates from pigs were *C. coli* and of 181 cultured samples 137 were positive. Of the 137 isolates, 46 (34%) were susceptible to all the six tested antibiotics. There was no resistance recorded against gentamicin (Table 4.11). The level of quinolone resistance was comparable to previous years (Figure 4.4). Two isolates were resistant to tetracycline and one to erythromycin. Before 2017 macrolide resistance has not been recorded in *Campylobacter* spp. isolated directly from animals in Sweden. Analysis of whole genome sequencing of the macrolide resistant isolate revealed previously described target altering mutations in the 23S rRNA genes (A2059G, *E. coli* numbering) (Bolinger & Katharíou, 2017). No transferable macrolide resistance genes were found.

Neither quinolones nor fluoroquinolones are authorised or used for treatment of groups of pigs via feed or water in Sweden. Additionally, a national 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 lesser extent other age categories (Sjölund et al., 2015). Selection for quinolone resistance in *Campylobacter* therefore probably occurs in younger pigs before they are moved to the finishing stage.

Occurrence of streptomycin resistance in *Campylobacter coli* is remarkably high (53%). 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 substance likely since 62% 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 -2017. In years 1999-2005 enrofloxacin was tested instead of ciprofloxacin. The number of isolates per year has varied (n=83-171).

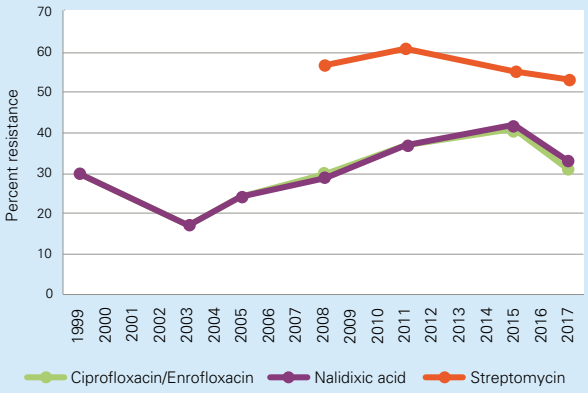


TABLE 4.11. Distribution of MICs and resistance (%) in *Campylobacter coli* from slaughter pigs, 2017.

Antibiotic	Resistance (%) n=137	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	32	64	128	>128
Ciprofloxacin	31	51.8	16.8				3.6	19.7	8.0				
Erythromycin	<1				81.8	16.8	0.7						0.7
Gentamicin	0			57.7	42.3								
Nalidixic acid	33						16.1	40.9	10.2	1.5	6.6	24.8	
Streptomycin	53					14.6	32.8	2.2		6.6	43.8		
Tetracycline	2			98.5							1.5		

TABLE 4.12. Resistance (%) in *Campylobacter coli* from slaughter pigs 2017. Data on *Campylobacter jejuni* from previous Swedres-Svarm reports are given for comparison.

Antibiotic	ECOFF (mg/L) *C. jejuni*	ECOFF (mg/L) *C. coli*	Resistance (%) Broilers *C. jejuni* 2016 (n=170)	Broiler meat *C. jejuni* 2011-2013 (n=111)	Pigs *C. coli* 2017 (n=171)	Cattle *C. jejuni* 2013 (n=109)
Ciprofloxacin	>0.5	>0.5	13	20	31	21
Erythromycin	>4	>8	0	2	<1	0
Gentamicin	>2	>2	0	0	0	2
Nalidixic acid	>16	>16	13	20	33	23
Streptomycin	>4	>4	1	0	53	5
Tetracycline	>1	>2	16	4	2	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 disease. Therefore, data may be biased towards samples from treated animals or from herds where antibiotic treatment is common. Any assessments of trends are based on the assumption that this bias is inherent throughout the observation period. It is likely that in some cases there are more than one animal sampled from the same herd.

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

Pigs

Escherichia coli

Isolates of *E. coli* are from clinical submissions of faecal samples or samples taken post mortem from the gastro-intestinal tract. During the latest years, the number of samples submitted has decreased and the sampling strategy has probably changed to some extent. This may influence the proportion of resistant isolates. Some of the isolates are tested by PCR for genes coding for the virulence factors enterotoxin (LT), heat-stable enterotoxin a and b (STa and STb), verocytotoxin (VT2e) and adhesion factors F4, F5, F6, F18 and F41. However, isolates may be susceptibility tested regardless of presence of virulence factors.

As in previous years, resistance to ampicillin, streptomycin, tetracycline and trimethoprim-sulphamethoxazole were the most common resistance traits (Table 4.13). Resistance to ampicillin and to trimethoprim-sulphamethoxazole has increased considerably over the years but the increase has 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, sampling may be biased towards isolates from herds with therapeutic failure with trimethoprim-sulphonamides, since fluoroquinolones may be an alternative for treatment of *E. coli* diarrhoea. Co-resistance between trimethoprim-sulphonamides and other antibiotics is common.

In order to investigate if biased sampling is contributing to the high resistance to ampicillin and trimethoprim-sulphamethoxazole a project was carried out during 2016-2017. In the project pigs with neonatal diarrhea and weaning diarrhea were sampled in a more randomized way than the routine sampling, without considering therapeutic failure with antibiotics. Distributions and resistance in both isolates from routine sampling and from the project are shown in table 4.13. There were no major differences in resistance between the two materials, indicating that a biased sampling not is the cause of high resistance to ampicillin and trimethoprim-

TABLE 4.13. Distribution of MICs and resistance (%) in *Escherichia coli* from clinical samples from pigs 2017 (routine diagnostic submissions, n=64) and from pigs in a project in 2016-17 (n=158). Clinical isolates from faecal samples (2017 and 2016-17) or from samples taken post mortem from the gastro-intestinal tract (2017).

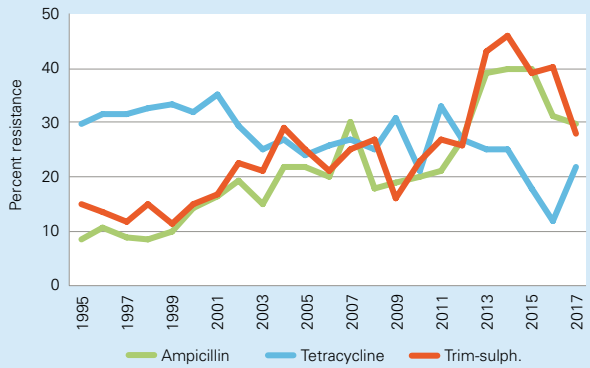
			Distribution (%) of MICs (mg/L)										
Antibiotic	**Source**	**Resistance %**	**≤0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**>64**
Ampicillin	routine	30					60.9	9.4			29.7		
	project	30					67.7	1.9		0.6	29.7		
Cefotaxime	routine	0		100									
	project	0		100									
Colistin	routine	0				93.8	6.2						
	project	3[b]				87.3	10.1	2.5					
Enrofloxacin	routine	6	93.8	1.6		3.1			1.6				
	project	8	91.8	3.8	2.5	1.3			0.6				
Gentamicin	routine	2					98.4	1.6					
	project	2					98.1	1.9					
Neomycin	routine	6						92.2	1.6	1.6	1.6	3.1	
	project	5						94.3	0.6		0.6	4.4	
Nitrofurantoin	routine	0							35.9	56.2	7.8		
	project	0							46.2	51.3	2.5		
Streptomycin	routine	27							65.6	7.8	9.4	3.1	14.1
	project	37							54.4	8.2	5.7	8.2	23.4
Tetracycline	routine	22					76.6	1.6		1.6	20.3		
	project	18					79.7	1.3	0.6		18.4		
Trim-Sulph.[a]	routine	28			71.9				28.1				
	project	32			67.1	1.2			31.6				

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphamethoxazole); [b]Three isolates with MIC 4 mg/L were negative for *mcr-1, mcr-2, mcr-3, mcr-4* and *mcr-5* genes with PCR. One isolate with MIC 4 mg/L was not available for PCR detection of mcr genes.

TABLE 4.14. Phenotypes of multiresistant isolates of *Escherichia coli* from pigs (routine diagnostic submissions 2017, project 2016-17) and cattle (routine diagnostic submissions 2017). Shaded areas with "R" indicate resistance.

Resistance phenotypes									Number of isolates		
Amp	Tsu	Str	Tet	Enr	Neo	Gen	Ctx	Col	Pigs, routine	Pigs, project	Cattle, routine
R	R	R	R	R	R				1		
R	R	R	R	R					1	3	
R	R	R	R		R				1	1	1
R	R	R	R						3	6	2
R	R	R		R						1	1
R	R	R			R				1	2	1
R	R	R				R					1
R	R	R						R		1	
R	R	R							3	14	2
R	R		R		R					1	
R	R		R						2	1	
R	R			R						2	
R		R	R	R					1		
R		R	R		R						1
R		R	R							4	2
R		R					R				1
R			R	R							2
	R	R	R		R					1	
	R	R	R							1	
	R	R			R					1	
	R		R		R						1
								Sum	**13**	**39**	**15**

FIGURE 4.5. Resistance (%) in *Escherichia coli* from pigs 1995-2017. Clinical isolates from faecal samples or from samples taken post mortem from the gastro-intestinal tract. The number of isolates each year varies (n=64-482, 2017 n=64).



sulphamethoxazole in the isolates from routine submissions in 2016 and 2017.

Multiresistance in the routine clinical isolates occurred in 20% (13/64) of the isolates in 2017 and has varied over the years (25% in 2015 and 2016, 42% in 2014 and 38% in 2013). In the project, multiresistance occurred in 25% (39/158) of the isolates. Resistance phenotypes for multiresistant isolates from pigs and cattle are shown in Table 4.14.

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 sus-

TABLE 4.15. Resistance (%) in *Brachyspira hyodysenteriae* from pigs 2005-2017 and distribution of MICs for isolates from 2016-2017. Clinical isolates from faecal samples.

Antibiotic	Resistance (%)					Distribution (%) of MICs (mg/L)												
	2005-06	2007-08	2009-11	2012-15	2016-17	≤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=29[f]	n=26[g]														
Doxycycline	9	3	5	0	0			26.9	65.4	7.7									
Tiamulin	7	18	8	3	31		30.8	11.5	26.9	3.8	7.7		3.8		15.4				
Tylosin	81	76	60	55	27							30.8	30.8	7.7	3.8				26.9
Tylvalosin	NA[b]	93[d]	55	79	42					19.2	38.5	15.4		11.5	11.5		3.8		
Valnemulin	0	18	3	3	46	38.5	15.4		11.5	3.8	11.5		3.8	15.4					

[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; [g]11 isolates 2016,15 isolates 2017.

ceptibility 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 4.15 these cut-off values are used on data from 2005-2017. With the suggested wild type cut-off value >0.25 mg/L for tiamulin, resistance is detected throughout the period. However, during 2016, isolates with MICs above the clinical breakpoint (>2 mg/L) were detected for the first time from Swedish pigs. Therapeutic failure was also observed. Five isolates from 2016 and 2017 are classified as clinically resistant.

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

Brachyspira pilosicoli

Isolates of *Brachyspira pilosicoli* are from clinical submissions of faecal samples. ECOFFs for *B. pilosicoli* are not defined for the antibiotics tested. As guide for the choice of antibiotic for treatment of spirochaetal diarrhoea, a clinical breakpoint for tiamulin of >2 mg/L and for tylosin of >16 mg/L are used at SVA. With these breakpoints, 12% of the isolates were resistant to tiamulin and 55% to tylosin (Table 4.16). If the same wild type cut-off value as for *B. hyodysenteriae* is used, 28% of the isolates were resistant to tiamulin.

Actinobacillus pleuropneumoniae

Isolates of *Actinobacillus pleuropneumoniae* are from post mortem investigations of lungs or from lung samples taken at slaughterhouses within the monitoring programme SvarmPat. For more information on SvarmPat, see In Focus, SvarmPat – monitoring of resistance in pathogens from farm animals. The resistance situation is favourable and almost no resistance was detected (Table 4.17). However, since pneumonia caused by *A. pleuropneumoniae* is an important disease in Swedish pig production, sampling and susceptibility testing is desirable if emerging resistance is to be detected early.

Pasteurella spp.

Most isolates of *Pasteurella* spp. are from post mortem investigations of lungs or from lung samples taken at slaughterhouses within the monitoring programme SvarmPat. Some isolates are also from nasal swabs collected within a control programme for atrophic rhinitis in nucleus and multiplying herds. Isolates from the control programme are likely from healthy pigs, whereas isolates from lung samples are most likely from pigs with respiratory disease. Antibiotic resistance is rare among isolates of *Pasteurella* spp. (Table 4.18).

Isolates from 2013-2017 (n=139) were identified to species level by MALDI-TOF MS and are *Pasteurella multocida*. Isolates from earlier years were identified with biochemical methods. Most of these isolates are *P. multocida*, but species identification of some isolates is uncertain. Cut-off values as given in Table 6.10 for *P. multocida* are used in Table 4.18 for all isolates.

Staphylococcus hyicus

Isolates of *Staphylococcus hyicus* are from skin samples from healthy sows sampled within the SvarmPat programme. ECOFFs for *S. hyicus* are not defined for the antibiotics tested, except for chloramphenicol and erythromycin (table 4.19.). With these ECOFFs no resistance was detected to these two antibiotics. The bimodal distribution for penicillin indicate substantial resistance (69%) to penicillin. This was supported by testing of penicillinase production by the cefinase test. The bimodal distribution for trimethoprim-sulphametoxazole indicates resistance also to this antibiotic.

TABLE 4.16. Distribution of MICs for *Brachyspira pilosicoli* from pigs 2005-2017, n=334. Clinical isolates from faecal samples. The number of isolates each year varies (n=7-67, 2017 n=21).

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			39.8	49.4	3.9	2.4	3.9	0.6						
Tiamulin		36.8	23.7	11.4	9.3	5.7	1.5	0.6	2.1	9.0				
Tylosin							6.9	18.6	16.2	3.6	4.2	4.2	5.7	40.7
Tylvalosin[a]				0.6	12.9	24.6	28.1	6.4	1.8	2.9	11.1	11.7		
Valnemulin	48.2	18.0	5.1	10.5	7.5	4.2	2.1	1.2	3.3					

[a]171 isolates tested.

TABLE 4.17. Distribution of MICs and resistance (%) in *Actinobacillus pleuropneumoniae* from pigs 2011-2017. Clinical isolates from post mortem investigations of lungs. The number of isolates each year varies (n=18-57, 2017 n=23).

Antibiotic	Resistance (%) 2011-2017	Distribution (%) of MICs (mg/L)															
	n=237	≤0.008	0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	>128
Ampicillin	0								100								
Chloramphenicol	0									100							
Ciprofloxacin	0	0.4	17.7	40.9	40.9												
Florfenicol	<1										99.6		0.4				
Gentamicin	0									16.5	73.8	9.7					
Nalidixic acid	0								4.6	72.2	22.8	0.4					
Penicillin	0			0.4	1.7	12.7	43.0	42.2									
Streptomycin	NR[a]											3.8	37.1	57.0	2.1		
Tetracycline	0								100								
Trimethoprim	0					31.6	46.8	19.4	1.3	0.8							

[a]Not relevant since the genus has inherently low susceptibility to streptomycin.

TABLE 4.18. Distribution of MICs and resistance (%) in *Pasteurella* spp. from pigs 2005-2017. Clinical isolates from the respiratory tract, isolated from nasal swabs or from post mortem investigations of lungs. The number of isolates each year varies (n=7-95, 2017 n=10).

Antibiotic	Resistance (%) 2005-2017	Distribution (%) of MICs (mg/L)															
	n=277	≤0.008	0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	>128
Ampicillin	0								100								
Chloramphenicol	0[a]									100							
Ciprofloxacin	0[b]	21.6	58.8	18.6	1.0												
Enrofloxacin	0[c]					98.9	1.1										
Florfenicol	1[d]										98.9	1.1					
Gentamicin	<1									72.9	21.3	5.1	0.4	0.4			
Nalidixic acid	0[b]								50.5	40.2	8.2		1.0				
Penicillin	0					52.7	43.0	4.3									
Streptomycin	NR[e]										2.9	44.0	35.0	12.6	5.4		
Tetracycline	0								98.6	1.4							
Trim-Sulph	1[f]							96.3	0.6	1.2	0.6	1.2					

[a]104 isolates tested; [b]97 isolates tested; [c]180 isolates tested; [d]273 isolates tested; [e]Not relevant since the genus has inherently low susceptibility to streptomycin; [f]163 isolates tested, concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphamethoxazole).

TABLE 4.19. Distribution of MICs and resistance (%) in *Staphylococcus hyicus* from pigs 2017. Isolates from skin of healthy sows.

Antibiotic	Resistance (%) 2017	Distribution (%) of MICs (mg/L)												
	n=65	≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Cefoxitin					16.9	83.1								
Cephalothin				13.8	84.6	1.5								
Chloramphenicol	0								93.8	6.2				
Ciprofloxacin				93.8		4.6	1.5							
Clindamycin					92.3	4.6	3.1							
Enrofloxacin				69.2	27.7		1.5	1.5						
Erythromycin	0				72.3	26.2	1.5							
Fusidic acid					96.9	3.1								
Gentamicin				78.5	20.0					1.5				
Oxacillin					4.6	24.6	64.6	6.2						
Penicillin	69[a]		30.8					1.5	1.5	66.2				
Tetracycline						93.8	3.1				3.1			
Trimethoprim						1.5	15.4	35.4	16.9	1.5	29.2			
Trim-Sulph				55.4	13.8		7.7	12.3	7.7	3.1				

[a]Denotes beta-lactamase production.

TABLE 4.20. Distribution of MICs and resistance (%) in *Streptococcus suis* from pigs 2013-17. Clinical isolates from various organs of pigs (n=36) and isolates from tonsils of healthy slaughter pigs (n=36).

Antibiotic	Resistance (%) 2013-2017 n=72	Distribution (%) of MICs (mg/L) ≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	>8
Cephalothin	1						94.4	4.2	1.4		
Clindamycin	21					79.2	1.4	2.8	16.7		
Enrofloxacin	NR[a]				9.7	62.5	27.8				
Erythromycin	6					94.4		1.4	4.2		
Gentamicin	NR						11.1	54.2	33.3		
Penicillin	0	27.8	61.1	9.7	1.4						
Tetracycline	82				15.3	2.8	2.8	58.3	8.3	12.5	
Trim-Sulph	15				80.6	4.2	4.2		4.2	6.9	

[a]Not relevant since the genus has inherently low susceptibility to the antibiotic

Streptococcus suis

Isolates of *Streptococcus suis* are from post mortem examination of different organs in diseased pigs from 2013-2017 (n=36) or from tonsils of healthy pigs sampled within the SvarmPat programme at slaughter 2017 (n=36). Resistance to penicillin was not detected.

Cattle

Escherichia coli from faecal samples

Isolates of *E. coli* are from the gastro-intestinal tract of calves. Most of the isolates are probably from calves no more than a few weeks old, i.e. during a period when resistance in enteric bacteria often is high in cattle. Resistance was high to ampicillin, streptomycin and tetracycline (Table 4.21 and Figure 4.6), as in previous years. Multiresistance occurred in 48% (15/31) of the isolates from 2017, compared to 32% in 2016, 56% in 2015, 76% in 2014 and 70% in 2013. For resistance phenotypes in multiresistant isolates in 2017, see Table 4.14.

FIGURE 4.6. Resistance (%) in *Escherichia coli* from cattle 2007-2017. 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 n=31).

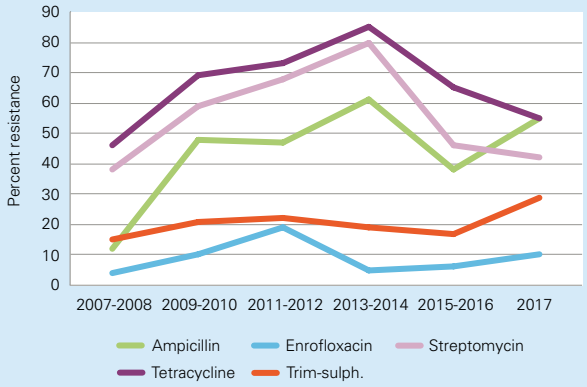


TABLE 4.21. Distributions of MICs and resistance (%) in *Escherichia coli* from cattle 2017. Clinical isolates from faecal samples or from samples taken post mortem from the gastro-intestinal tract.

Antibiotic	Resistance (%) 2017 n=31	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	55					45.2				54.8		
Cefotaxime	3[b]		96.8	3.2								
Colistin	0				93.5	6.5						
Enrofloxacin	10	90.3		9.7								
Gentamicin	3					96.8	3.2					
Neomycin	26						67.7	6.5	3.2	6.5	16.1	
Nitrofurantoin	0							58.1	38.7	3.2		
Streptomycin	42							54.8	3.2		6.5	35.5
Tetracycline	55					45.2				54.8		
Trim-Sulph.[a]	29			71.0				29.0				

[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.

Escherichia coli from milk samples

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

In the material from 2017, 23% (18/79) of the isolates were resistant to at least one antibiotic. Resistance to ampicillin, streptomycin, tetracycline or trimethoprim-sulphamethoxazole was most common as in previous years (Table 4.22). Multiresistance occurred in 10% (8/79) of all isolates.

Three isolates had MICs above the ECOFF for colistin. They were tested with PCR for the presence of the genes *mcr-1*, *mcr-2*, *mcr-3*, *mcr-4* and *mcr-5* and were negative.

Klebsiella pneumoniae from milk samples

Isolates of *Klebsiella pneumoniae* are from clinical submissions of milk samples from dairy cows. Resistance was uncommon and 79% (27/34) of isolates was susceptible to all tested antibiotics, excluding ampicillin. Multiresistance did not occur in isolates from 2017. Three isolates had MICs above the ECOFF for colistin. Two of them were available and tested with PCR for the presence of the genes *mcr-1*, *mcr-2*, *mcr-3*, *mcr-4* and *mcr-5* and were negative.

TABLE 4.22. Resistance (%) in *Escherichia coli* from dairy cows 2013-2017. Distribution of MICs from 2017. Clinical isolates from milk.

Antibiotic	Resistance (%)					Distribution (%) of MICs (mg/L)										
	2013 n=142	2014 n=95	2015 n=113	2016 n=74	2017 n=79	≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	14	20	20	27	15					76.1	17.7			15.2		
Cefotaxime	NA[b]	NA	3[c]	1[e]	0		100									
Ceftiofur	1	0	NA	NA	NA											
Colistin	NA	NA	<1[d]	0	4[f]				92.4	3.8	3.8					
Enrofloxacin	5	6	2	4	3	97.5		2.5								
Gentamicin	0	0	0	1	0					100						
Neomycin	4	1	<1	0	4						96.2			2.5	1.3	
Nitrofurantoin	NA	NA	0	0	0							31.6	68.4			
Streptomycin	16	25	20	26	14							83.5	2.5	1.3		12.7
Tetracycline	9	19	11	16	9					91.1				8.9		
Trim-Sulph.[a]	11	17	12	22	9			91.1				8.9				

[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphamethoxazole); [b]Not analysed; [c]The isolates with MICs 1 and 2 were further tested with PCR but genes genes conferring transferable ESC resistance were not detected. The isolate with MIC 0.5 mg/L was further tested and did not show an ESBL or AmpC phenotype; [d]The isolate was not available for PCR detection of mcr genes; [e]The isolate with MIC 1 mg/L was further tested and had an AmpC phenotype but no genes conferring transferable ESC resistance were detected with PCR; [f]The 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 4.23. Resistance (%) in *Klebsiella pneumoniae* from dairy cows 2013-2017 and distributions of MICs from 2017. Clinical isolates from milk.

Antibiotic	Resistance (%)					Distribution (%) of MICs (mg/L)										
	2013 n=41	2014 n=39	2015 n=41	2016 n=36	2017 n=34	≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	NR[b]	NR	NR	NR	NR					2.9	2.9		8.8	85.3		
Cefotaxime	NA[c]	NA	0	0	0		100									
Ceftiofur	1	0	NA	NA	NA											
Colistin	NA	NA	0	3[d]	9[e]				88.2	2.9	2.9		5.9			
Enrofloxacin	5	6	2	14	3	97.1		2.9								
Gentamicin	0	0	0	0	0					100						
Neomycin	4	1	0	0	0						100					
Nitrofurantoin	NA	NA	NR	NR	NR								2.9	35.3	55.9	5.9
Streptomycin	16	25	15	3	3							94.1	2.9		2.9	
Tetracycline	9	19	10	6	12					82.4	2.9	2.9		11.8		
Trim-Sulph.[a]	11	17	0	6	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]Not analysed; [d]The isolate with MIC 16 mg/L was negative for mcr-1 and mcr-2 genes with PCR; [e]Two isolates with MIC 16 mg/L were negative for *mcr-1, mcr-2, mcr-3, mcr-4* and *mcr-5* genes with PCR. One isolate with MIC 4 mg/L was not available for PCR detection of *mcr* genes.

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 2013-2017 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 as given in Table 6.10 for *P. multocida* are used in Table 4.24 for all isolates.

Antibiotic resistance was generally rare among isolates of *Pasteurella* spp. (Table 4.24), but beta-lactamase producing *P. multocida* has occurred occasionally in samples from calves in 2016 and 2017. In addition, isolates of beta-lactamase producing *P. multocida* have been confirmed in 2003 and beta-lactamase producing *Mannheimia haemolytica* in 2010 and 2015. Penicillin is considered the antibiotic of choice for treatment of pneumonia in cattle in Sweden. Sampling and susceptibility testing is of importance for early detection of resistance, especially if therapeutic failure is seen.

Fusobacterium necrophorum

The isolates of *Fusobacterium necrophorum* are from clinical cases of foot rot in cattle in 12 different herds. For details on methodology see Materials and methods, resistance in bacteria from animals.

If antibiotic treatment is needed in cattle with foot rot in Sweden, penicillin is recommended. For all 24 isolates, MICs of beta-lactams and tetracycline were low and in accordance with results from 2008-2009 (Table 4.25). There are no cut-off values agreed on for *F. necrophorum*, but the unimodal MIC distributions suggest that these isolates are of wild type regarding the antibiotics tested.

TABLE 4.24. Distribution of MICs and resistance (%) in *Pasteurella* spp. from calves 2005-2017. Clinical isolates from the respiratory tract, isolated from nasal swabs or from post mortem investigations of lungs.

Antibiotic	Resistance (%)			Distribution (%) of MICs (mg/L)									
	2005-2015 n=339	2016 n=104	2017 n=86	≤0.06	0.12	0.25	0.5	1	2	4	8	16	>16
Ampicillin	0	13	2				29.1	68.6	1.2		1.2		
Enrofloxacin	0[b]	0	0		98.8	1.2							
Florfenicol	0	0	0						100				
Penicillin	0	13	2	7.0	75.6	14.0	1.2	2.3					
Tetracycline	0	0	0					100					
Trim-Sulph[a]	0	0	1				98.8				1.2		

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

TABLE 4.25. Distribution of MICs (%) for *Fusobacterium necrophorum* from cattle 2008-2009 (n=41) and 2015-2016 (n=24).

Antibiotic	Year	Distribution (%) of MICs (mg/L)													
		≤0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Cephalothin	2008-2009			2.4	14.6	82.9									
	2015-2016				25.0	75.0									
Ciprofloxacin	2008-2009				4.9	14.6	34.1	46.3							
	2015-2016						4.2	95.8							
Erythromycin	2008-2009								14.6	58.5	26.8				
	2015-2016									62.5	37.5				
Penicillin	2008-2009		87.8	12.2											
	2015-2016	4.2	75.0	20.8											
Tetracycline	2008-2009						100								
	2015-2016					87.5	12.5								
Trimethoprim	2008-2009										7.3	26.8	46.3	19.5	
	2015-2016										4.2	29.2	66.7		

Farmed fish

Flavobacterium psycrophilum

Isolates of *Flavobacterium psycrophilum* are from clinical submissions of farmed fish. Data from 2015-2017 are compiled and presented as distributions of MICs in Table 4.26. 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 4.26. Resistance to oxolinic acid and oxytetracycline was high in this material.

In Figure 4.7 resistance to tetracycline and quinolones (nalidixic acid or oxolinic acid) in *F. psycrophilum* 2005-2017 is shown. A three-year moving average is used. There is a marked increase in resistance to these antibiotics over the years. There is a limited therapeutic use of oxolinic acid as well as of tetracycline in aquaculture in Sweden. The antibiotic mostly used is florfenicol (Svarm 2011). The reason for the observed increases in resistance is not known.

FIGURE 4.7. Resistance (%) in *Flavobacterium psycrophilum* from farmed fish 2005-2017 with a three-year moving average. The number of isolates each year varies (n=12-32, 2017 n=26).

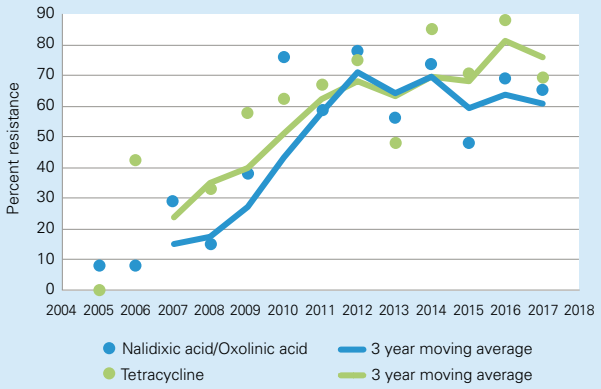


TABLE 4.26. Distributions of MICs and resistance (%) in *Flavobacterium psycrophilum* from farmed fish 2015-2017. The number of isolates each year varies (n=16-31, 2017 n=26).

Antibiotic	Resistance (%) 2015-2017	Distribution (%) of MICs (mg/L)											
	n=73	≤0.008	0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	>8
Florfenicol	0						12.3	52.1	30.1	5.5			
Oxolinic acid	59				5.5	30.1	5.5		1.4	57.5			
Oxytetracycline	75				23.3	1.4	1.4	1.4	15.1	24.7	30.1	2.7	

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 2017

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 2010-2017, about 1100 isolates were tested and MRSA was confirmed in 9 isolates. In addition, about 500 isolates of *S. aureus* without beta-lactamase production were tested in 2013, but MRSA was not detected.

- Continuous monitoring of 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. The most commonly found bacterial species are *S. aureus*, *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 pigs, cattle and sheep

- The important respiratory pathogens *Actinobacillus pleuropneumoniae* and *Pasteurella multocida* from pigs, *P. multocida* and *Mannheimia haemolytica* from cattle and *M. haemolytica* and *Bibersteinia trehalosi* from sheep 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, cattle and sheep.

Samples from pigs

- *Brachyspira hyodysenteriae* and *Brachyspira pilosicoli*

Swine dysentery and spirochaetal diarrhoea in pigs are important diseases in many countries. The resistance situation in the causative agents, *B. hyodysenteriae* and *B. pilosicoli*, in Sweden is favourable compared to other countries, but resistance to tiamulin in *B. hyodysenteriae* was detected for the first time in 2016. Within SvarmPat, isolates from all identified herds with these diseases in Sweden are susceptibility tested.

- *Escherichia coli*

Resistance to ampicillin and trimethoprim-sulphamethoxazole in *Escherichia coli* from pigs with diarrhoea has been increasing over the years. The increase may be due to sampling bias towards herds with therapeutic failure. A set of more representative isolates has been collected in 2016-2017 in a study with randomized sampling from pigs with neonatal diarrhoea and post weaning diarrhoea. There was 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 biased sampling.

- *Streptococcus suis*

Streptococcus suis is globally an important pathogen in pigs causing meningitis, sepsis, pneumonia and arthritis requiring antibiotic treatments. But the bacterium can also occur in healthy pigs. Knowledge on antibiotic susceptibility is scarce. Clinical isolates from routine submissions and isolates from tonsils of healthy slaughtered pigs were susceptibility tested. Acquired resistance to penicillin was not found.

- *Staphylococcus hyicus*

Staphylococcus hyicus occurs on the skin of healthy pigs but may also be involved in infections like exudative epidermitis. Knowledge on antibiotic susceptibility is scarce. Isolates from skin samples from healthy sows were susceptibility tested. Sixty-nine percent of the isolates produced beta-lactamase, which indicate doubtful clinical response to penicillin treatment. This is worrisome since penicillin is often used for treatment of skin infections in pigs in Sweden.

Horses

Escherichia coli

Isolates of *E. coli* are from clinical submissions of samples from the genital tract of mares. As in previous years, resistance to trimethoprim-sulphametoxazole and streptomycin was most common in 2017 (Table 4.27 and Figure 4.8). Resistance to trimethoprim-sulphametoxazole has increased from 10 to 16% between 2013 and 2017 (Figure 4.8). Resistance to gentamicin is continuously low. The proportions of resistance to the tested antibiotics have differed somewhat over the years and trends are difficult to evaluate.

Multiresistance was detected in 7% (16/240) of the isolates, which is less than 2016 (10%) and 2011 (11%) but comparable to the figures in 2012-2015 (4-6%) (see previous Swedres-Svarm reports). Nine of the sixteen multiresistant isolates were resistant to three antibiotics; two to four; four to five and one isolate were resistant to six antibiotics. The most common phenotype was resistance to ampicillin, streptomycin and trimethoprim-sulphametoxazole, representing 88% (14/16) of the multiresistant isolates. Both isolates resistant to four antibiotics had the common phenotype and were in addition resistant to colistin or gentamicin. Also, three of the four isolates resistant to five and the isolate resistant to six antibiotics had the common phenotype and were in addition resistant to cefotaxime and gentamicin, and for the isolate resistant to six antibiotics also neomycin.

Four isolates were resistant to cefotaxime (MIC >0.25mg/L). Genes conferring transferable ESC resistance were detected in all these isolates. Three of the isolates carried the gene bla_{SVH-12} and one carried the gene $bla_{CTX-M-1}$. For more information, see Notifiable diseases, ESBL-producing Enterobacteriaceae.

Eight isolates were resistant to colistin (MIC >2mg/L). Five of the isolates were available for PCR detection of the genes *mcr-1*, *-2*, *-3*, *-4* and *-5*, and all were negative.

FIGURE 4.8. Resistance (%) in *Escherichia coli* from horses, 2004-2017. Clinical isolates from the genital tract of mares. The number of isolates each year varies (n=124-324, 2017 n=240).

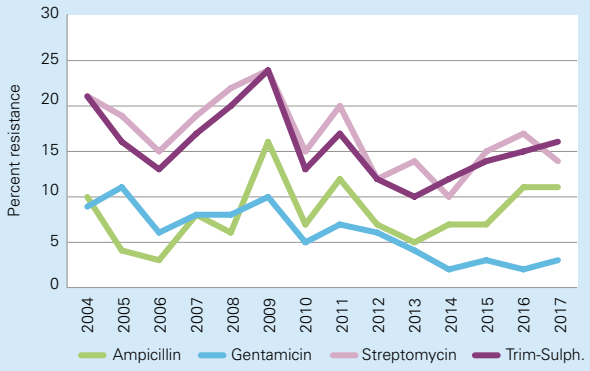


TABLE 4.27. Distributions of MICs and resistance (%) in *Escherichia coli* from horses, 2017. Clinical isolates from the genital tract of mares.

Antibiotic	Resistance (%) 2017 n=240	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	11					70.4	18.3	0.4	0.8	10.0		
Cefotaxime	2		98.3		0.4	0.8	0.4					
Colistin	3				81.2	15.4	2.9		0.4			
Enrofloxacin	<1	99.6		0.4								
Gentamicin	3					97.1	0.4	0.4		2.1		
Neomycin	1						97.9	0.8			1.3	
Nitrofurantoin	0							55.4	42.9	0.4	1.3	
Streptomycin	14							80.8	5.0	2.1	2.5	9.6
Tetracycline	3					96.3	0.8			2.9		
Trim-Sulph.[a]	16			83.3	0.4	0.4		15.8				

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

Streptococcus equi subsp. *zooepidemicus*

Isolates of *Streptococcus equi* subsp. *zooepidemicus* are from clinical submission of samples mainly from the respiratory tract (84%). Over the years studied isolates of *S. equi* subsp. *zooepidemicus* have remained uniformly susceptible to the tested antibiotics apart from trimethoprim-sulphametoxazole, for which the proportion of resistance has varied between 5 to 18% in 2010-2017 (Table 4.28 and previous Swedres-Svarm reports).

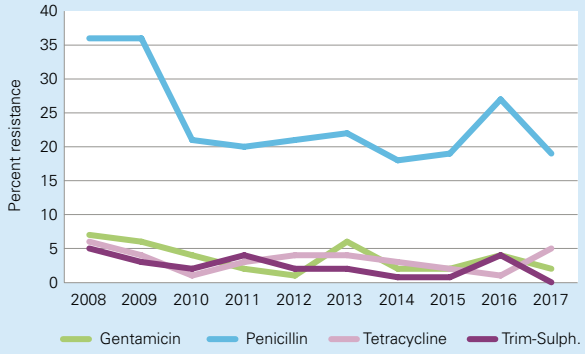
Streptococcus equi subsp. *zooepidemicus* has a low inherent susceptibility to aminoglycosides (e.g. gentamicin) and tetracyclines. The MICs of gentamicin were above concentrations that can be obtained during systemic therapy.

Staphylococcus aureus

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

The proportions of resistance to gentamicin, penicillin, tetracycline and trimethoprim-sulphametoxazole over the last ten years are shown in Figure 4.9. Resistance to penicillin due to penicillinase-production dominates but has declined compared to the figures in 2008-2009 (36%) and was 19% in 2017 (Table 4.29).

FIGURE 4.9. Resistance (%) in *Staphylococcus aureus* from horses, 2008-2017. Clinical isolates from the skin. The number of isolates each year varies (n=75-145, 2017 n=127)



Multiresistance was detected in 3% (4/127) of the isolates. Three of the isolates were resistant to three antibiotics and one to four antibiotics. No common phenotype was seen.

One isolate was resistant to cefoxitin (MIC >4) and analysed with PCR for *mecA/mecC* genes but was negative. For more information on MRSA isolated from horses, see Notifiable diseases, MRSA in animals.

TABLE 4.28. Distribution of MICs and resistance (%) in *Streptococcus equi* subsp. *zooepidemicus* from horses, 2017. Clinical isolates mainly from the respiratory tract.

Antibiotic	Resistance (%) 2017 n=81	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						100							
Clindamycin	4					96.3	3.7							
Erythromycin	1					98.8			1.2					
Gentamicin	NR[b]						1.2		6.2	92.6				
Nitrofurantoin	0										100			
Penicillin	0	97.5	2.5											
Tetracycline	NR				1.2		16.0	61.7	17.3	3.7				
Trim-Sulph.[a]	14				71.6	14.8	9.9			3.7				

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

TABLE 4.29. Distribution of MICs and resistance (%) in *Staphylococcus aureus* from horses, 2017. Clinical isolates from the skin.

Antibiotic	Resistance (%) 2017 n=127	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Cefoxitin	<1			0.8		26.8	71.6		0.8			
Cephalotin	5				95.3	3.9		0.8				
Clindamycin	6			94.5	5.5							
Enrofloxacin	0		96.1	3.9								
Erythromycin	<1			85.0	14.2		0.8					
Fusidic acid	9			91.3	7.9	0.8						
Gentamicin	2				93.7	3.9	0.8	1.6				
Nitrofurantoin	0								99.2	0.8		
Oxacillin	7		35.4	25.2		7.1						
Penicillin[a]	19											
Tetracycline	5		44.1	49.6	1.6	0.8	0.8	3.1				
Trim-Sulph.[b]	0		96.9	3.1								

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

Dogs

Escherichia coli

Isolates of *E. 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 most common in 2017 (Table 4.30 and Figure 4.10). The proportions of resistance to the tested substances have differed somewhat between the years (Figure 4.10).

Multiresistance was detected in 7% (68/1038) of the isolates, a somewhat lower figure compared to 2016 (9%) and the same as in 2015 (see previous Swedres-Svarm reports). Sixty-six percent (45/68) of the multiresistant isolates were resistant to three antibiotics; 28% (19/68) to four; 4% (3/68) to five and 1% (1/68) to six. The most common phenotype, resistance to ampicillin, streptomycin and trimethoprim-sulphametoxazole, was detected in 69% (47/68) of the isolates. The same phenotype was also the most common in *E. coli* from horses (88%) and cats (54%). Of the twenty-two isolates resistant to four or more antibiotics, seventeen were of the common phenotype, and often also resistant to tetracycline (15/22) and/or enrofloxacin (13/22).

Five (<1%) 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. One of the isolates carried the gene $bla_{\text{CTX-M-14}}$ and the other carried the gene $bla_{\text{CTX-M-15}}$. For more information, see Notifiable diseases, ESBL-producing Enterobacteriaceae.

Twenty-five (2%) of the isolates were resistant to colistin (MIC >2 mg/L). Fifteen of these were available for PCR detection of the genes *mcr-1*, - *2*, *-3*, *-4* and *-5*, and all were negative.

FIGURE 4.10. Resistance (%) in *Escherichia coli* from dogs, 2005-2017. Clinical isolates from urine. The number of isolates each year varies (n=304-1162, 2017 n=1038).

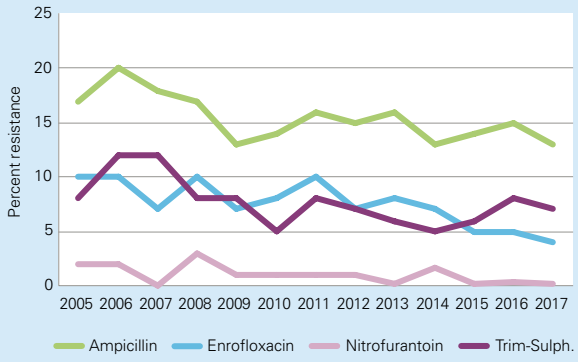


TABLE 4.30. Distribution of MICs and resistance (%) in *Escherichia coli* from dogs, 2017. Clinical isolates from urine.

Antibiotic	Resistance (%) 2017 n=1038	Distribution (%) of MICs (mg/L)										
		≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	13					66.6	19.7	0.6	0.4	12.7		
Cefotaxime	<1		99.5	0.2	0.1		0.2					
Colistin	2				90.0	7.6	2.0	0.2	0.2			
Enrofloxacin	4	95.7	1.4	1.2	0.8	0.3		0.6				
Gentamicin	<1					99.5	0.4			0.1		
Neomycin	<1						99.1	0.6	0.1	0.1	0.1	
Nitrofurantoin	<1							42.2	56.3	0.8	0.5	0.2
Streptomycin	9							85.5	5.9	2.0	1.9	4.7
Tetracycline	4					95.0	0.8		0.3	3.9		
Trim-Sulph.[a]	7			92.8	0.7	0.4	0.3	5.9				

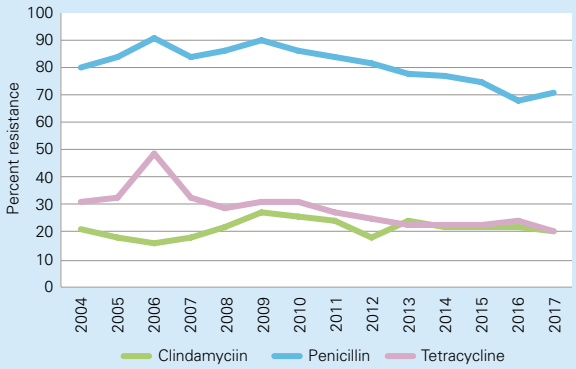
[a]Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphametoxazole).

Staphylococcus pseudintermedius

Three different collections of *Staphylococcus pseudintermedius* from clinical submission are presented (Table 4.31): isolates from skin lesions, excluding wounds and abscesses (S1); isolates from wounds (S2); isolates from the external ear canal (S3). Data S2 and S3 have not been presented previously but data for S1 can be compared to earlier figures (Figure 4.11).

Resistance to penicillin due to penicillinase-production dominates for all sample collections (71-79%, Table 4.31). Resistance to individual antibiotics in S1 has varied somewhat over the years but penicillin resistance appears to have decreased since 2009 (90%) (Figure 4.11). However, resistance to clindamycin and tetracycline remains at approximately the same levels throughout the years presented (Figure 4.11).

FIGURE 4.11. Resistance (%) in *Staphylococcus pseudintermedius* from dogs, 2004-2017. Clinical isolates from skin. The number of isolates each year varies (n=89-566, 2017 n=417).



Multiresistance is common in *S. pseudintermedius*. Between 2009 and 2015 the proportions of multiresistance in sample collection S1 have varied from 26 to 36% (see previous Swedres-Svarm reports). In 2017 the corresponding figure was 26% (109/417). The proportion of multiresistance in collection S1 is about the same as in S2; 25% (208/844) and S3; 25% (163/648). This is high compared to the figures of other staphylococci from animals reported in Swedres-Svarm, e.g. *S. aureus* from horses (3%), *S. schleiferi* from dogs (3%), and *S. felis* from cats (5%).

Twenty-one percent (23/109) of the S1 multiresistant isolates were resistant to five or more antibiotics. This is less compared to 2016 when one-third of the isolates were resistant to five or more antibiotics. The most common phenotype, resistance to penicillin, clindamycin and erythromycin, was the same for the three sample collections, S1; 69% (75/109), S2; 56% (117/208) and S3; 53% (87/163). Eighty-five percent (50/59) of S1 isolates resistant to four or more antibiotics had the common phenotype and most common combined with resistance to tetracycline 53% (31/59), fusidic acid 41% (24/59) and/or trimethoprim/sulphamethoxazole 25% (15/59). The same phenotype (resistance to penicillin, clindamycin and erythromycin) dominated also in isolates of *S. felis* (15/20).

Six (S1), nine (S2) and four (S3) isolates were resistant to oxacillin (MIC >0.5 mg/L) and were analysed with PCR (*mecA/mecC*). Three isolates were found to be MRSP in sample collection S1, 8/9 in S2 and 2/4 in S3. For more information on MRSP isolated from dogs in Sweden, see Notifiable diseases, MRSP in animals.

TABLE 4.31. Distribution of MICs and resistance (%) in *Staphylococcus pseudintermedius* from dogs, 2017. Clinical isolates from skin (S1), wounds (S2) and external ear canals (S3).

Antibiotic	Resistance (%)			Distribution (%) of MICs (mg/L) S1 = skin sample									
	2017 n=648 S3	2017 n=844 S2	2017 n=417 S1	≤0.12	0.25	0.5	1	2	4	8	16	32	64
Cephalothin	3	2	3				97.1	2.6	0.2				
Cefoxitin[a]							68.8	29.7	0.7	0.5	0.2		
Clindamycin	15	15	20			80.3	0.7	0.5	18.5				
Enrofloxacin	1	3	1		95.2	3.4	0.5	1.0					
Erythromycin	16	17	21			79.1	1.2		19.7				
Fusidic acid	21	17	17			79.4	3.8	1.4	15.3				
Gentamicin	3	2	1				97.1	1.4	0.2	1.2			
Nitrofurantoin	0	<1	0								99.8	0.2	
Oxacillin	<1	1	1		90.4	8.2	1.2	0.2					
Penicillin[b]	76	79	71										
Tetracycline	22	24	20		76.0	3.1	0.7			20.1			
Trim-Sulph.[c]	17	17	12		54.7	33.6	8.6	0.5		2.6			

[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 of various locations, but mainly (95%) from the external ear canal, skin or wounds.

The proportion of resistance in isolates of *S. schleiferi* (Table 4.32) was lower or equal compared to isolates of *S. pseudintermedius* (Table 4.31), except for enrofloxacin with 13% resistance for *S. schleiferi* and 1% for *S. pseudintermedius*. In *S. aureus* isolated from horses (Table 4.29) and *S. felis* from cats (Table 4.36) there was no resistance to enrofloxacin. In contrast, the proportion of isolates with penicillinase production was less than 1% in *S. schleiferi* compared to 71-79% in *S. pseudintermedius* (Table 4.31), 19% in *S. aureus* from horses (Table 4.29) and 20% in *S. felis* from cats (Table 4.36).

Multiresistance was detected in 2% (3/175) of the *S. schleiferi* isolates compared to 25-26% in *S. pseudintermedius*, 3% in *S. aureus* from horses and 7% in *S. felis* from cats. Of the three multiresistant *S. schleiferi* isolates, one was resistant to three antibiotics and two to four antibiotics.

Pseudomonas aeruginosa

Isolates of *Pseudomonas aeruginosa* are from clinical submissions of samples from the external ear canal. Notably, *P. aeruginosa* is inherently resistant to trimethoprim-sulphonamides, tetracyclines and aminopenicillins (including combinations with clavulanic acid) and data for these antibiotics are not presented.

The isolates of *P. aeruginosa* were until 2013 tested with polymyxin B and all tested isolates have been sensitive throughout the years (see previous Swedres-Svarm reports). In 2014 polymyxin B was replaced by the equivalent colistin. Since 2014 to 2017, 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 declined from 25% in 2009 to 10% in 2017 and the figures for gentamicin have stabilized at about 1-2% over the recent years (see Table 4.33 and previous Swedres-Svarm reports). None of the isolates were resistant to all three antibiotics, but one isolate was resistant to both enrofloxacin and gentamicin.

TABLE 4.32. Distribution of MICs and resistance (%) in *Staphylococcus schleiferi* from dogs, 2017. Clinical isolates from various locations.

Antibiotic	Resistance (%) 2017 n=175	Distribution (%) of MICs (mg/L)										
		≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Cephalothin	2				97.7	2.3						
Cefoxitin[a]			34.9	62.9	1.7	0.6						
Clindamycin	3			96.6	2.3		1.1					
Enrofloxacin	13		83.4	4.0	10.9	1.7						
Erythromycin	1			98.9			1.1					
Fusidic acid	9			79.4	11.4	3.4	5.7					
Gentamicin	1				96.6	2.3	0.6	0.6				
Nitrofurantoin	0								99.4	0.6		
Oxacillin	0		97.1	2.9								
Penicillin[b]	<1											
Tetracycline	2		89.1	7.4	1.1	0.6		1.7				
Trim-Sulph.[c]	<1		91.4	8.0	0.6							

[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 4.33. Distribution of MICs and resistance (%) in *Pseudomonas aeruginosa* from dogs, 2016. Clinical isolates from the external ear canal.

Antibiotic	Resistance (%) 2017 n=306	Distribution (%) of MICs (mg/L)									
		≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Enrofloxacin	10	1.6	1.3	16.3	42.2	28.4	3.9	6.2			
Colistin[a]	<1				77.1	17.6	4.6	0.7			
Gentamicin	1					88.2	9.8	1.0	0.7	0.3	

[a]Colistin is equivalent to polymyxin B.

TABLE 4.34. Distribution of MICs and resistance (%) in *Pasteurella canis* from dogs, 2017. Clinical isolates from various locations.

Antibiotic	Resistance (%) 2017 n=152	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	0				100						
Enrofloxacin	<1	98.0	1.3	0.7							
Gentamicin	0					96.7	3.3				
Penicillin	0	96.7	2.6	0.7							
Tetracycline	0				100						
Trim-Sulph.[a]	0			100							

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

Pasteurella canis

Isolates of *Pasteurella* spp. are from clinical submissions of samples from various locations, but mainly the ear canal, skin lesions, wounds, abscesses and the respiratory tract. The most commonly detected *Pasteurella* spp. in the material was *P. canis* (n=152). The proportion of resistance in the *P. canis* isolates was low (Table 4.34). *Pasteurella dagmatis* (n=14), *P. multocida* (n=12) and *P. stomatis* (n=12) were less common, and except for one isolate (*P. multocida* resistant to trimethoprim-sulphametoxazole) those isolates were susceptible to all the tested antibiotics (data not shown). The same cut-off values were used for all *Pasteurella* spp.

Cats

Escherichia coli

Isolates are from clinical submission of urine, submitted either as urine or cultures from dip-slides or other agar plates. As in previous years, and as in *E. coli* from dogs (Table 4.30 and Figure 4.10), resistance to ampicillin was most common in 2017 (Table 4.35 and Figure 4.12). In comparison, in *E. coli* from horses, resistance to trimethoprim-sulphametoxazole and streptomycin was most common (Table 4.27 and Figure 4.8). The proportions of resistance in *E. coli* from cats have differed somewhat over the years as shown in Figure 4.12.

Of the *E. coli* isolates tested in 2017, 5% (26/539) were multiresistant, which is comparable to figures between 2010 and 2016 (2-5%) (see previous Swedres-Svarm reports). Thirteen of the isolates were resistant to three antibiotics; eleven to four; one to five and one to six antibiotics. The most common phenotype in the multiresistant isolates was resistance to ampicillin, streptomycin and trimethoprim-sulphametoxazole with 54% (14/26). Eight of these isolates were also resistant to tetracycline.

FIGURE 4.12. Resistance (%) in *Escherichia coli* from cats, 2007-2017. Clinical isolates from urine. The number of isolates each year varies (n=131-539, 2017 n=539).

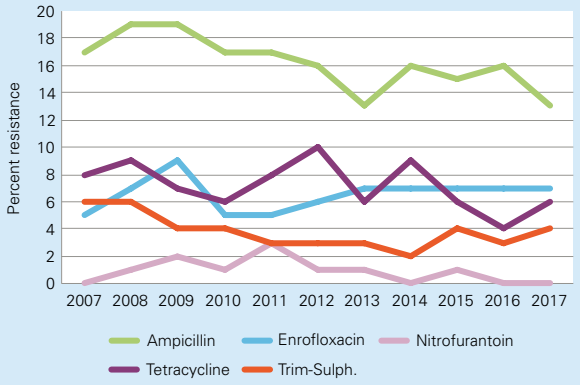


TABLE 4.35. Distribution of MICs and resistance (%) in *Escherichia coli* from cats, 2017. Clinical isolates from urine.

Antibiotic	Resistance (%) 2017 n=539	Distribution (%) of MICs (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ampicillin	13					76.4	10.0	0.6	0.2	12.8		
Cefotaxime	<1		99.4	0.2			0.4					
Colistin	2				89.2	8.5	1.9	0.4				
Enrofloxacin	7	92.9	1.1	4.1	0.4	0.2		1.3				
Gentamicin	1					98.9	0.6		0.2	0.4		
Neomycin	<1						99.3	0.2	0.2	0.4		
Nitrofurantoin	<1							48.2	51.0	0.6	0.2	0.2
Streptomycin	6							90.0	3.5	1.5	1.3	3.7
Tetracycline	6				93.9					6.1		
Trim-Sulph.[a]	4			96.1	0.4	0.4	0.2	3.0				

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

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. One of the isolates carried the gene $bla_{CTX\text{-}M\text{-}15}$ and the other carried both the gene $bla_{CTX\text{-}M\text{-}65}$ and the gene $bla_{CMY\text{-}2}$. For more information, see Notifiable diseases, ESBL-producing Enterobacteriaceae.

Twelve isolates were resistant to colistin (MIC >2mg/L). Seven of the isolates were available for PCR detection of the genes *mcr-1*, *-2*, *-3*, *-4* and *-5*, and all were negative.

Staphylococcus felis

Isolates of *Staphylococcus felis* are from clinical submission of samples from various locations, but mainly external ear canal or other skin locations, abscesses, wounds and urine.

The proportions of resistance to individual antibiotics in *S. felis* from cats (Table 4.36) are less than in *S. pseudintermedius* in dogs (Table 4.31). For example, resistance to penicillin due to penicillinase production was 20% in *S. felis*, but 71-79% in *S. pseudintermedius* (Table 4.31).

Multiresistance was detected in 7% (20/287) of the isolates which is slightly higher compared to the figures in 2015 (4%) and 2016 (5%), as well as figures of *S. aureus* from horses (3%) and *S. schleiferi* from dogs (2%), but less than in *S. pseudintermedius* from dogs (25-26%). Sixteen of the twenty multiresistant isolates were resistant to three antibiotics and four to four antibiotics. The most common phenotype was resistance to penicillin, clindamycin and erythromycin (15/20).

Pasteurella multocida

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

Pasteurella multocida was the most common *Pasteurella* spp. (n=301) found. The proportion of resistance to antibiotics commonly used in pets was low in the tested isolates (Table 4.37). *Pasteurella dagmatis* (n=16), *P. stomatis* (n=7) and *P. canis* (n=3) were also isolated. All those isolates were susceptible to all the tested antibiotics (data not shown). The same cut-off values were used for all *Pasteurella* spp. tested.

TABLE 4.36. Distribution of MICs and resistance (%) in *Staphylococcus felis* from cats, 2017. Clinical isolates from various locations.

Antibiotic	Resistance (%) 2017 n=287	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[c]			93.0	5.2	0.3	1.4						
Clindamycin	7			93.4	1.0		5.6					
Enrofloxacin	0		97.6	2.4								
Erythromycin	15			85.0	5.9		9.1					
Fusidic acid	3			92.3	4.9	1.0	1.7					
Gentamicin	0				97.6	2.4						
Nitrofurantoin	0								99.0	1.0		
Oxacillin	<1		98.6	1.0		0.3						
Penicillin[a]	20											
Tetracycline	1		93.4	5.2	0.3			1.0				
Trim-Sulph.[b]	<1		96.9	2.8	0.3							

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

TABLE 4.37. Distribution of MICs and resistance (%) in *Pasteurella multocida* from cats, 2017. Clinical isolates from various locations.

Antibiotic	Resistance (%) 2017 n=301	Distribution (%) of MICs (mg/L)									
		≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	0				100						
Enrofloxacin	2	96.3	1.3	1.7	0.7						
Gentamicin	<1					38.9	57.5	3.0	0.7		
Penicillin	0	74.1	24.9	1.0							
Tetracycline	0				99.7	0.3					
Trim-Sulph.[a]	2			94.0	2.3	1.3		2.3			

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

Indicator bacteria from animals

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

In 2017, indicator bacteria from pigs were studied. Samples of intestinal contents were collected at slaughter and cultured for *E. coli*. Samples from pigs were also screened for *E. coli* resistant to ESCs by selective culture on media supplemented with cefotaxime. In addition, rectal swabs from

FIGURE 4.13. Percent resistance in *Escherichia coli* from pigs 2000-2017. The number of isolates each year varies (n=140-390, 2017 n=143).

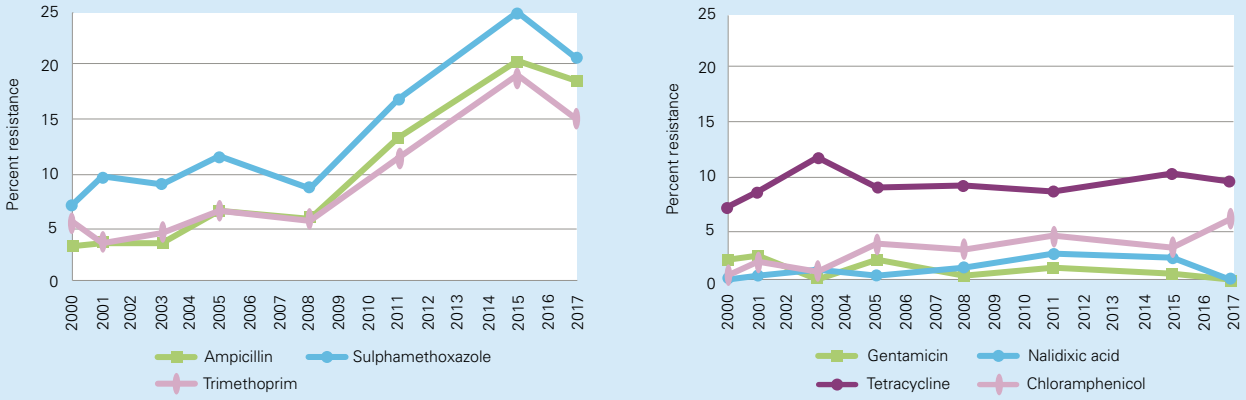


TABLE 4.38. Resistance (%) and multiresistance (%) in indicator *Escherichia coli* from pigs, 2017. Data on indicator *E. coli* from previous Svarm-reports are given for comparison.

Antibiotic	ECOFF (mg/L)	Resistance (%)									
		Broilers	Broiler meat	Cattle	Laying hens	Pigs	Pig meat	Sheep	Turkeys	Dogs	Horses
		2016 n=175	2012 n=92	2015 n=101	2012 n=61	2017 n=143	2011 n=20	2006-09 n=115	2016 n=85	2012 n=74	2010-11 n=274
Ampicillin	>8	13	18	1	3	19	30	2	8	9	2
Azithromycin	>16	0	-	1	-	0	-	-	0	-	-
Cefotaxime	>0.25	3	0	0	2	0	0	0	0	1	0
Ceftazidime	>0.5	3	-	0	-	0	-	-	0	-	-
Chloramphenicol	>16	0	0	0	0	6	0	0	0	0	<1
Ciprofloxacin	>0.06	6	4	0	5	0	10	<1	1	3	<1
Colistin	>2	0	1	1	0	0	0	-	0	0	<1
Gentamicin	>2	1	3	0	2	0	0	3	0	0	<1
Meropenem	>0.12	0	-	0	-	0	-	-	0	-	-
Nalidixic acid	>16	6	4	0	5	0	0	0	1	0	<1
Sulphamethoxazole	>64	13	16	2	8	21	10	7	6	4	15
Tetracycline	>8	11	14	1	13	9	0	<1	16	8	2
Tigecycline	>1	0	-	0	-	0	-	-	0	-	-
Trimethoprim	>2	7	7	0	5	15	10	2	4	1	16
Multiresistance[a]											
Susceptible to all above		71	66	96	80	71	70	89	71	84	83
Resistant to 1		17	18	2	7	9	10	9	24	8	2
Resistant to 2		5	7	2	7	6	5	2	6	7	12
Resistant to 3		4	3		7	7	15	<1			2
Resistant to >3		4	5			6				<1	<1

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

healthy calves (<2 months old) were collected (as a part of an ongoing research project) and cultured for *E. coli*. The calves were sampled on the farm of origin and each sample represents a unique farm. For details on methodology see Material and methods, resistance in bacteria from animals.

Escherichia coli

Pigs

Escherichia coli was isolated from 140 (98%) of 143 samples cultured. The majority of the isolates (71%) was susceptible to all antibiotics tested (Table 4.38 and 4.39). Resistance to sulphonamides (21%), ampicillin (19%) and trimethoprim (15%) were the most common traits. Nineteen isolates (14%) were multiresistant, i.e. resistant to three or more antibiotics. All of these had resistance to sulphonamides in their phenotype. Resistance to ampicillin and/or trimethoprim were also common traits in these isolates.

Levels of resistance in *E. coli* from pigs are low in an international perspective. For some antibiotics, levels of resistance have been stable over the years studied whereas resistance to other substances appears to have increased during the last years (Figure 4.13). More precisely, resistance to ampicillin, sulphonamides and trimethoprim in *E. coli* from pigs has increased considerably since 2008, and even if the figures have decreased from 2015 to 2017, the difference is not statistically significant. The reason(s) for these changes is not known but spread of multiresistant clones and/or plasmids are potential explanations.

When screening for resistance to ESC, *E. coli* resistant to cefotaxime was isolated from 29 (12%) of 241 samples. In nine isolates (4%), transferable genes for resistance to ESC were found. Six had $bla_{\text{CTX-M-14}}$, two $bla_{\text{CTX-M-15}}$, and one $bla_{\text{CTX-M-55}}$. Twenty isolates were of the AmpC type but transferable genes for resistance to ESC were not found. Resistance in these isolates is likely caused by mutational hyperproduction of AmpC beta-lactamases and this has also been confirmed by whole genome sequencing of eight isolates. For more details and comments see section Antibiotic resistance in animals, Notifiable disease.

TABLE 4.39. Distribution of MICs and resistance (%) in *Escherichia coli* from intestinal content from pigs (n=140), 2017.

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							5.7	45.7	30.0			0.7		17.9				
Azithromycin	0								5.7	30.0	56.4	7.9							
Cefotaxime	0					100													
Ceftazidime	0						100												
Chloramphenicol	6										94.3		2.9	2.1	0.7				
Ciprofloxacin	0	95.0	5.0																
Colistin	0							99.3	0.7										
Gentamicin	0						82.1	16.4	1.4										
Meropenem	0		100																
Nalidixic acid	0									100									
Sulphamethoxazole	21										20.0	32.9	23.6	2.9					20.7
Tetracycline	9								90.0	0.7				5.0	4.3				
Tigecycline	0					99.3	0.7												
Trimethoprim	15					37.1	43.6	4.3						15.0					
		≤0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	>1024

Cattle

Escherichia coli was isolated from 85 (100%) of 85 samples cultured. About half of the isolates (51%) were sensitive to all the tested substances and 22% were resistant to one or two substances (Table 4.40). Twenty-three isolates (27%) were multiresistant, i.e. resistant to three or more antibiotics and five isolates (6%) were resistant to five substances or more. Resistance to streptomycin (41%), sulphamethoxazole (31%) tetracyclines (26%), or ampicillin (23%) were the most common traits. No isolate was resistant to cefotaxime, ceftazidime, colistin, florfenicol or gentamicin. Of the multiresistant isolates, the majority (83%) were resistant to sulphonamides and streptomycin and 61% were resistant also to tetracycline. Nine isolates (39%) were resistant to sulphonamides, streptomycin, tetracyclines and ampicillin.

Occurrences of resistance and multiresistance were on a similar level but slightly lower than in *E. coli* from a research project in 2004-05, where calves of the same age were sampled (Table 4.40). The difference could be due to the fact that isolates from 2016-17 were from healthy calves only whereas about two thirds of the isolates in 2004-05 were from calves with diarrhea. Levels of resistance are in general higher among *E. coli* from diarrheic calves (see Antibiotic resistance in animals, Notifiable disease) and it can be assumed that the antibiotic selection pressure is higher on farms that experience problems with diarrheic calves resulting in higher levels of resistance than on farms with mostly healthy calves.

The relatively high levels of resistance in indicator bacteria from healthy young calves are in stark contrast to those from older cattle sampled at slaughter. As an eaxmple, 96% of isolates from healthy cattle between 6-12 months in 2015 were susceptible to all antibiotics tested. Carriage of resistant *E. coli* in calves is inversely related to the age of the animals, but the mechanism behind is not yet known.

TABLE 4.40. Distribution of MICs and resistance (%) in *Escherichia coli* from fecal samples from calves 0-2 months of age (n=85), 2016-2017.

Antibiotic	Resistance %		Distribution (%) of MICs (mg/L)																
	2004-05	2016-17	≤0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	>1024
	n=87	n=85																		
Ampicillin	29	24							12.9	61.2	2.4					2.4	21.2			
Cefotaxime	0[a]	0			85.9	11.8	2.4													
Ceftazidime	0[a]	0					98.8	1.2												
Chloramphenicol	5	2								9.4	76.5	11.8				2.4				
Ciprofloxacin	10[b]	7	56.5	32.9	3.5	2.4	4.7													
Colistin	NA	0						63.5	31.8	4.7										
Florfenicol	0	0									29.4	69.4	1.2							
Gentamicin	0	0						95.3	4.7											
Nalidixic acid	14	8								69.4	22.4			1.2	3.5	3.5				
Streptomycin	48	41									49.4	4.7	4.7	15.3	11.8	14.1				
Sulphamethoxazole	41	31										18.8	42.4	7.1	1.2					30.6
Tetracycline	37	26							61.2	12.9				5.9	11.8	8.2				
Trimethoprim	10	5				4.7	47.1	40	2.4	1.2				4.7						
			≤0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	>1024

[a]Ceftiofur tested, cut-off value defining resistance >2 mg/mL. [b]Enrofloxacin, cut-off value defining resistance >0.25 mg/mL

Comparative analysis

Antibiotic consumption in human and veterinary medicine

Data included and calculations

The figures on the total sales of antibiotics for systemic use in humans (ATC group J01 excluding methenamine, and JA07AA oral glycopeptides; outpatient and hospital sales) were retrieved as defined daily doses and calculated to kg active substance. Data on sales of antibiotics for use in animals (QJ01 and QA07AA, total sales) are also presented in Sales of antibiotics for animals, excluding QJ51. Sales for aquaculture were not included, nor were sales of drugs authorized for human use but sold for animals. The contribution of such sales to the total volume is minor.

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

Comparison of sales in tonnes active substance

In 2017, a total of 61.0 and 10.2 tonnes of antibiotics in included ATC classes were sold in human and veterinary medicine, respectively. Figure 5.1 displays the sales of beta-lactam antibiotics. These substances are by far the most sold antibiotics in both human and veterinary medicine and also represent the largest amounts measured as kilograms. Penicillins (J01C and QJ01C) represent most of the amount in kg active substance of antibiotics for both humans and animals; 70 and 58%, respectively. The substances shown in Figure 5.2 are sold 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 sold in a total quantity exceeding 1 000 kg during 2017 are included. The only group where sales for animals outweighs those for humans is trimethoprim-sulphonamides, of which more than half are products only authorised for use in horses.

FIGURE 5.1. Sales of beta-lactam antibiotics in human and veterinary medicine, kg active substance, 2017. Please note the difference in indexation of the x-axis between Figure 5.1 and 5.2.

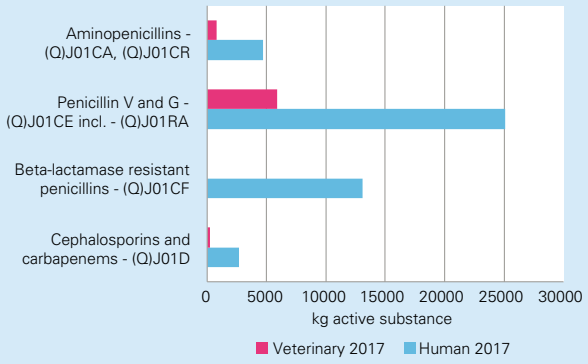
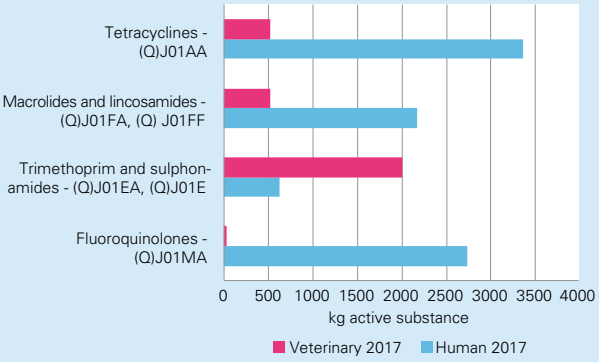


FIGURE 5.2. Sales of fluoroquinolones, macrolides, lincosamides, trimethoprim and sulphonamides, and tetracyclines in human and veterinary medicine, kg active substance, 2017. Please note the difference in indexation of the x-axis between Figure 5.1 and 5.2.

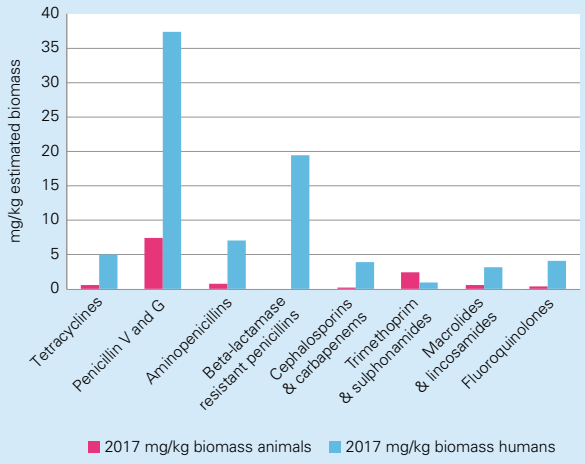


Comparison of sales expressed as mg per kg estimated biomass

In 2017, the sales expressed as mg per kg were 90.9 and 12.8 mg active substance per kg estimated biomass in human and veterinary medicine, respectively. In Figure 5.3 a comparison of sales of antibiotics for use in humans and animals are shown expressed as mg per estimated kg biomass. Data on the total sale do not take the heterogeneity of the likelihood of exposure within the population into account. This is especially true for data on sales of antibiotics 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 betalactamase resistant penicillins where sales for animals is negligible, and for the fluoroquinolones where sales for humans are 126 times higher than in animals.

FIGURE 5.3. Sales of antibiotics in humans and animals expressed as mg active substance per estimated kg biomass in 2017. Only classes where the total sales exceeded 1 000 kg active substance are shown.



Zoonotic aspects on antibiotic resistance

ESBL-producing Enterobacteriaceae

It has been concluded that transmission of Enterobacteriaceae with $ESBL_A$ or $ESBL_M$, and their corresponding genes, between farm animals and humans, can occur (EFSA, 2011, de Been, 2014). The possibility for direct transfer to people handling animals should also be kept in mind.

The available data show that ESBL-producing bacteria are rare in animals and on food in Sweden, except for broilers where *E. coli* with $ESBL_A$ or $ESBL_M$ resistance are found in a large proportion of birds. However, in a majority of the broiler samples, the $ESBL_A$- or $ESBL_M$-producing *E. coli* only constitute a small part of all the *E. coli* in the intestinal flora. Previously, it has been clear that the majority of isolates from humans in Sweden is not of the same types of $ESBL_A$ or $ESBL_M$ as in broilers. Due to an increased occurrence of $bla_{CTX\text{-}M\text{-}1}$ among *E. coli* from broilers in the last years, this difference is now less clear. Still, nothing indicates a need to revise the previous conclusion that food on the Swedish market is a limited source for ESBLs for humans (Börjesson et al., 2016). Nevertheless, continued vigilance towards 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.

LA-MRSA

During more than ten years, the zoonotic aspects on MRSA in farm animals, mostly in pigs but also in veal calves, broilers and dairy cows, has widened due to spread of livestock-associated MRSA (LA-MRSA), mostly of clonal complex (CC) 398 in many countries. In countries with high prevalence of LA-MRSA in pigs, the pig population constitutes a reservoir with continuous transmission to people in close contact with pigs. This transmission can be of importance for the overall human MRSA burden in countries with low prevalence of MRSA in humans (EFSA, 2009).

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

In humans, domestically acquired MRSA CC398 has been detected in 76 cases during 2006 to first half of 2017. The number of cases each year has varied between two and twelve. In the first half of 2017 there were eight cases and the isolates were of *spa*-types t011, t034, t1255 and t2383. The epidemiological information concerning possible animal contacts is scarce. The low number of MRSA CC398 in humans in Sweden may indicate that MRSA is not widespread in Swedish pigs, since high occurrence in pigs would lead to transmission to humans in contact with pigs.

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).

In animals in Sweden, MRSA with *mecC* has been isolated from two dogs (*spa*-types t373 and t843), three cats (*spa*-types t978 and t843), milk samples from six dairy cows (*spa*-types t524, t9111 and t843), 40 hedgehogs (several *spa*-types, t843 most common) and in one sample from pigs (*spa*-type t373). In addition, MRSA with *mecC* has been isolated from goats and sheep (*spa*-type t9268) in an outbreak at a zoo and from goats (*spa*-type t373) in a herd.

In humans in Sweden, domestically acquired MRSA with *mecC* has been isolated from 92 cases during 2011 to first half of 2017, of which 10 were from 2017. Several *spa*-types were seen among the human isolates. The two most common *spa*-types were t843 (29 cases) and t373 (20 cases). Some of the *spa*-types in humans have also been found in animals: t843 (dog, cat, dairy cow, hedgehog), t373 (dog, pig, goat), t3391 (hedgehog), t9111 (dairy cow, hedgehog), t978 (cat, hedgehog), t5771 (hedgehog), t9268 (goat, sheep) and t10893 (hedgehog).

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). After transmission to an animal, the animal may serve as vector for transmission to other humans. The magnitude of companion animals as vectors for spread between humans is however not known. The most common *spa*-type among Swedish dogs and cats has been t032 until 2012, but in recent years the *spa*-types have been more varied. *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. MRSA of *spa*-types t127 and t008 were detected in milk sample with anonymized origin from 2014 and 2017, respectively. Because also these *spa*-types are common among human MRSA-cases, transmission from humans to cows can be suspected. There is, however, no epidemiological information available about these cases.

Conclusions

The MRSA situation in Sweden is still favourable both in humans and in animals. If this situation is preserved in animals, a reservoir of MRSA in animals with risk of spread from animals to humans can be prevented. Biosecurity, with caution in trade of live animals and measures to prevent introduction by indirect routes, is important for preventing introduction and spread of MRSA in animal populations. Measures to prevent transmission from humans to animals are also of importance, since human types of MRSA may be established also in animal populations.

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. Moreover, although the dominating variant of VRE in both broilers and humans is *E. faecium* with the *vanA* gene, genotypically related isolates from broilers and humans have not been found. Hence, there are no indications that the presence of VRE in broilers in Sweden has affected the situation in Swedish healthcare.

Salmonella

Occurrence of *Salmonella* among farm animals, as well as among other animals, is low in Sweden and few incidents involve multiresistant strains. Notably, transferable ESC resistance has never been found and resistance to fluoroquinolones (e.g. ciprofloxacin) is rare. Thus, the overall situation in the veterinary sector is favourable which is largely due to the strategies in the Swedish salmonella control programme initiated in the 1950-ies.

Comparison between isolates from humans and animals is difficult because about two-thirds of the human *Salmonella* infections were aquired abroad. Moreover, of the domestically acquired cases, the origin of the isolates is not known but considering the low occurrence of *Salmonella* in animals in Sweden the majority probably has a foreign source, e.g. imported foodstuffs. Nevertheless, the high occurrence of resistance to fluoroquinolones in isolates from humans (22%) in comparison to the very rare occurrence of such resistance in isolates from animals indicates that fluoroquinolone resistant isolates in human infections have foreign sources.

Campylobacter

Data from feacal isolates of *Campylobacter jejuni* from humans were available 2017 and of these 37% were resistant to fluoroquinolones, 28% to tetracycline and <1% (three isolates) to erythromycin. This year isolates from pigs were tested and of these 137 were *C. coli* and none *C. jejuni*. However, in Svarm 2016, *C. jejuni* from broilers were included (n=170) and the resistance percentages were lower than the data for humans 2017; fluoroquinolones (13%), tetracycline (16%) and erythromycin (0%).

The higher resistance among the human isolates is probably explained by the inclusion of isolates from infections acquired abroad or from imported foodstuffs.

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.

Background data, material, methods and references

Demographics and denominator data

Humans

TABLE 6.1. Number of admissions and patient-days in somatic medical care in Sweden, 2013-2016. Data represent production by acute care hospitals in the counties. Dalarna County is excluded.

Year	Admissions	Patient-days
2013	1 432 175	6 355 463
2014	1 411 121	6 293 096
2015	1 378 806	6 087 579
2016	1 298 939	5 710 715

TABLE 6.2. Number of admissions and patient-days in somatic medical care 2016. Data represent production by acute care hospitals in the counties. Dalarna County is excluded.

County	Admissions	Patient-days
Blekinge	22 544	106 980
Gotland	10 138	42 320
Gävleborg	35 488	155 834
Halland	41 344	165 138
Jämtland	17 823	82 063
Jönköping	51 364	208 411
Kalmar	41 297	153 898
Kronoberg	25 434	116 843
Norrbotten	35 631	171 275
Skåne	175 085	833 583
Stockholm	269 259	1 033 089
Södermanland	34 524	168 452
Uppsala	53 352	270 237
Värmland	39 956	181 517
Västerbotten	44 898	202 866
Västernorrland	33 871	148 880
Västmanland	37 906	173 950
Västra götaland	222 672	1 050 614
Örebro	43 445	191 017
Östergötland	62 908	253 748
Sweden	**1 298 939**	**5 710 715**

TABLE 6.3. Denominator data from the microbiological laboratories 2017.

Laboratory	Number of analyses 2017									Number of positive samples 2017	Number of positive cultures 2017				
	Blood (pair of bottles)	Cerebro-spinal fluid (CFS)	Nasopharynx	Throat	General culture	Screen MRB	Urine	Faeces SSYC	Faeces *Clostridium difficile* (toxin)	Blood (pair of bottles)	*Staphylococcus aureus*	*Streptococcus pneumoniae*	*Streptococcus pyogenes*	*Escherichia coli*	*Clostridium difficile* (toxinpositive)
Aleris Medilab	1 215	0	7 405	2 679	9 227	14 604	39 714	6 100	1 203	155	4 613	328	839	9 638	165
Borås	22 274	200	4 563	1 384	10 451	2 593	22 987	3 952	1 617	3 045	4 001	273	471	6 633	121
Eskilstuna (Unilabs)	16 027	175	7 816	2 311	7 895	4 777	31 589	5 856	1 918	1 799	5 403	684	718	8 701	281
Falun	19 507	282	5 693	1 489	11 640	4 976	35 725	4 378	2 026	3 221	6 504	398	825	10 228	286
Gävle	16 414	175	3 737	894	10 400	6 559	28 067	3 400	2 180	2 558	4 212	377	363	9 215	379
Göteborg[a]	45 631	1 297	2 128	2 621	15 119	25 408	61 347	8 886	3 934	5 594	10 356	646	1 098	14 456	555
Halmstad	16 016	154	3 853	2 287	7 549	16 201	30 653	5 161	1 790	1 971	4 790	606	805	8 714	249
Jönköping	24 110	272	8 252	3 194	17 150	19 309	41 498	6 906	2 979	2 709	9 160	658	1 032	12 901	389
Kalmar	15 466	157	4 101	2 082	8 367	5 012	31 249	4 515	1 297	1 956	4 609	490	630	9 004	117
Karlskrona/ Växjö	25 114	152	8 137	1 663	11 247	5 261	40 312	5 551	3 316	2 962	5 666	797	884	10 832	353
Karlstad	22345b	549	6 306	2 556	14 838	13 175	40 483	4 378	2 492	4052b	6 889	637	823	10 693	176
Karolinska Stockholm	99 207	2 441	32 277	8 576	73 978	149 212	142 327	20 509	11 250	12 598	31 570	2 433	3 295	42 186	700
Linköping	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	80 275	1 816	24 208	11 867	34 963	43 773	170 189	24 118	9 837	10 109	21 989	1 811	3 416	41 535	1 322
Skövde (Unilabs)	15 898	244	4 553	2 099	11 312	6 739	63 312	9 027	2 679	1 620	7 362	328	882	15 935	349
S:t Göran (Unilabs)	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	16 382	184	1 989	1 273	6 829	7 125	30 348	3 642	NP	2 417	4 168	504	477	9 373	NP
NÄL Trollhättan	19 473	185	2 654	1 102	7 785	14 292	27 471	3 181	1 709	2 367	4 348	272	352	7 862	199
Umeå	18 016	526	4 671	2 090	9 479	8 137	33 179	3 824	1 779	1 724	5 441	587	810	10 511	273
Uppsala	24 781[a]	788	7 826	1 592	14 960[a]	9 991	35 580	5 354	3 075	2 992[a]	6 709[a]	585	668	9 022	389[a]
Visby	4 876	31	2 334	454	3 261	NP	7 510	886	466	472	1 641	190	170	2 307	82
Västerås	16 622	172	3 314	1 876	10 398	5 194	29 113	3 978	1 980	2 285	4 445	383	538	8 853	277
Örebro	20 196	483	10 928	2 419	18 763	10 174	36 978	5 812	3 014	2 311	7 295	941	840	9 186	361
Östersund	8 369	162	2 522	995	4 777	3 475	19 015	2 201	1 118	1 918	2 145	274	327	4 231	98
Total	**595 155**	**11 450**	**175 020**	**61 766**	**352 563**	**421 184**	**1 098 096**	**154 876**	**67 026**	**77 016**	**179 458**	**15 618**	**22 045**	**299 544**	**7 966**

[a]2016 års data, [b]not pair; NA, data not available; NP, not performed.

Animals

Agricultural statistics are provided by Statistics Sweden in collaboration with the Board of Agriculture. The Board of Agriculture maintains a statistical database accessible online (www.jordbruksverket.se). The statistics are also published annually as a Yearbook of Agricultural Statistics and continuously as Statistical Messages (SM). Annual figures on number of animals and holdings are given in Table 6.4 & 6.5 and on numbers and volumes of animals slaughtered in Table 6.6. & 6.7. In table 6.8, the average herd size is given.

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 6.4. Number of livestock and horses (in thousands) 1980-2017. From the statistical database of the Board of Agriculture.

Animal Species	1980[a]	1985[a]	1990	1995	2000	2005	2010	2014	2015	2016	2017
Cattle											
Dairy cows	656	646	576	482	428	393	348	344	338	331	322
Beef cows	71	59	75	157	167	177	197	186	184	194	208
Other cattle >1 year	614	570	544	596	589	527	513	490	487	489	500
Calves <1 year	595	563	524	542	500	509	479	472	466	476	472
Total, cattle	1 935	1 837	1 718	1 777	1 684	1 605	1 537	1 492	1 475	1 490	1 502
Sheep											
Ewes and rams	161	173	162	195	198	222	273	287	289	281	301
Lambs	231	252	244	266	234	249	292	301	306	297	304
Total, sheep	392	425	406	462	432	471	565	588	595	578	605
Pigs											
Boars & sows	290	260	230	245	206	188	156	145	142	140	141
Fattening pigs >20 kg[b]	1 254	1 127	1 025	1 300	1 146	1 085	937	857	830	835	836
Piglets <20kg[c]	1 170	1 113	1 009	769	566	539	427	376	384	378	385
Total, pigs	2 714	2 500	2 264	2 313	1 918	1 811	1 520	1 378	1 356	1 354	1 362
Laying hens											
Hens	5 937	6 548	6 392	6 100	5 670	5 065	6 061	6 549	7 571	8 174	7 294
Chickens reared for laying	2 636	2 159	2 176	1 812	1 654	1 697	1 647	1 713	1 842	1 575	1 994
Total, hens	8 573	8 708	8 568	7 912	7 324	6 762	7 707	8 262	9 413	9 750	9 288
Horses											
Total, horses						283[d]	363			356	

[a]For 1980 and 1985 only cattle and sheep at premises with more than 2 ha counted; [b]Before 1995, the figure denotes pigs above 3 months of age; [c]Before 1995, the figure denotes pigs below 3 months of age; [d]Data from 2004.

TABLE 6.5. Number of holdings with animals of different types, 1980-2017. From the statistical database of the Board of Agriculture.

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

TABLE 6.6. Number of animals slaughtered (in thousands) at slaughterhouses, 1980-2017. From the statistical database of the Board of Agriculture.

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

[a]Data supplied by the National Food Administration.

TABLE 6.7. Quantity of livestock slaughtered (in 1 000 tonnes) at slaughterhouses, 1990-2017. From the statistical database of the Board of Agriculture.

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

[a]Data supplied by the National Food Administration.

TABLE 6.8. Average number of animals per holding 1995-2017. From the statistical message JO 20 SM 1702.

Animal Species	1995	2000	2005	2010[a]	2015[a, b]	2016[a]	2017[a, b]
Cattle							
Dairy cows	27.2	33.7	46	61.9	81,5	85,4	89,1
Beef cows	9.2	12.0	13.8	16.2	17.7	18,7	19,8
Sheep	19.5	24.8	29.2	31.7	31.8	32,5	32,7
Boars and sows	31	63	156	156	186	182	165
Fattening pigs	157	294	471	664	845	820	825
Laying hens	640	995	471	1 638	2 587	2 822	2 506

[a]The definition of holdings included changed from 2010; [b]Data for 2015 and 2017 are estimated from a sample and therefore have a larger uncertainty

Materials and methods, sales of antibiotics

Legal framework and distribution of medicines

Marketing of medicines 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 licence prescription for a medical product for a specified pharmacy, prescriber or clinic.

Medicinal products with antibiotics as active substance are, outside of hospitals, only dispensed through pharmacies. The pharmacies in Sweden are supplied by wholesalers and manufacturers with permission to supply medicinal products. In outpatient care, antibiotics (including medicated feed in veterinary use) may only be sold on prescriptions, ApoDos (individually packed doses of drugs often dispensed to elderly) or requisitions. Prescribers (veterinarians or doctors) are not permitted to own a pharmacy or to otherwise sell medicinal products for profit. Veterinarians may provide products to the animal care-taker in relation to examination of a case for self-cost (no profit). In hospital care, both for humans and animals, antibiotics are usually bought on requisitions from pharmacies, but some counties manage drug supplies to human hospitals by themselves.

All pharmacies in Sweden are required to provide statistics on sales of all products on a daily basis to the Swedish eHealth Agency. This agency maintains a national database with sales statistics for all drugs and provides statistics to the competent national and regional authorities and to others on a commercial basis.

Feed mills may only mix antimicrobials in feed if they are controlled and authorised by the Swedish Board of Agriculture (SBA). The feed mills normally acquire the antibiotic products from a pharmacy. All quantities of antibiotic products used by feed mills are reported yearly to the SBA as part of the feed control. Mixing of antibiotics in feed may also take place on farms; provided that the SBA has inspected and authorised the establishment for the purpose. In such cases, the premix is sold by a pharmacy following prescriptions from a veterinarian.

The ATC classification system and defined daily doses (DDD)

Since 1988, the Anatomical Therapeutic Chemical (ATC) and ATCvet classification system recommended by the WHO is used in Sweden for national drug statistics. For drugs sold for use in humans, to facilitate drug utilisation studies from a medical point of view, the concept of defined daily dose (DDD) is used as a unit of comparison in drug statistics. The DDD for a drug is established on the basis of the assumed average dose per day for the drug given to adults for its main indication. If possible, the DDD is given as the amount of active substance. The DDDs are usually equal for all dosage forms of a preparation. The statistical data systems of the Swedish eHealth Agency are upgraded yearly according to the recommendations made by the WHO Collaborating Centre for Drug Statistics methodology in Oslo, Norway. The DDDs used in this report are shown in Table 6.9. The sales of drugs are presented as number of DDDs per 1 000 inhabitants and day (DDD/1 000 and day), which give an estimate of the proportion of the population daily exposed to a particular drug. This figure is a rough estimate and should be interpreted with caution.

Sales of antibiotics for humans

Swedish national statistics on sales of medicines

Since 1975, the National Corporation of Swedish Pharmacies regularly produces sales statistics on medicines, for the country as a whole and for individual counties. The sales are registered as number of DDDs, cash value and number of packages. Out-patient care data include 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 often dispensed to elderly) is also included in the survey. Recorded data are trade name, quantity, patient fee, total cost, sex and year of birth of the patient. Data can be expressed as DDD/1000 inhabitants and day or number of prescriptions/1000 inhabitants.

Hospital care data include drug 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 reregulation 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 activity in the state-owned company Apotekens Service were transferred to the Swedish eHealth Agency (eHälsomyndigheten).

The Swedish eHealth Agency aims to contribute to improved health care and public health and better caring by pursuing development of a national e-health infrastructure. They are responsible for Sweden's national drug statistics.

Completeness of data

In Sweden, pharmacies are required by law to report sales statistics to the Swedish eHealth Authority. Concerns have been raised that after the reregulation of the pharmacy market, the statistics on sales of medical products to hospitals in Sweden is less complete than before. After the reregulation, counties can choose to manage drug supplies to hospitals by themselves. If so, the counties are not required to report data to the national database.

Definitions of DDD 2017

TABLE 6.9. DDD for all antibiotic substances (J01) sold in Sweden in 2017. Substances are sorted according to ATC-code.

	DDD (g)		DDD (g)
J01AA02 - doxycycline	0.1	J01FA01 - erythromycin	1
J01AA04 - lymecycline	0.6	J01FA01- erythromycin erythylsuccinat tablets	2
J01AA06 - oxitetracycline	1	J01FA06 - roxithromycin	0.3
J01AA07 - tetracycline	1	J01FA09 - clarithromycin - oral	0.5
J01AA12 - tigecycline	0.1	J01FA10 - azithromycin - parenteral	0.5
J01BA01 - chloramphenicol	3	J01FA10 - azithromycin - oral	0.3
J01CA01 - ampicillin	2	J01FA15 - telithromycin	0.8
J01CA04 - amoxicillin	1	J01FF01 - clindamycin - parenteral	1.8
J01CA08 - pivmecillinam	0.6	J01FF01 - clindamycin - oral	1.2
J01CE01 - benzylpenicillin	3.6	J01GB01 - tobramycin - parenteral	0.24
J01CE02 - fenoximethylpenicillin	2	J01GB01 - tobramycin - oral inhalation solution	0.3
J01CF02 - cloxacillin	2	J01GB01 - tobramycin - oral inhalation powder	0.112
J01CF05 - flucloxacillin	2	J01GB03 - gentamicin	0.24
J01CR02 - amoxicillin and enzyme inhibitor-oral	1	J01GB06 - amikacin	1
J01CR05 - piperacillin and enzyme inhibitor	14	J01GB07 - netilmicin	0.35
J01DB01 - cefalexin	2	J01MA01 - ofloxacin	0.4
J01DB03 - cefalotin	4	J01MA02 - ciprofloxacin - parenteral	0.5
J01DB05 - cefadroxil	2	J01MA02 - ciprofloxacin - oral	1
J01DC02 - cefuroxime- parenteral	3	J01MA06 - norfloxacin	0.8
J01DC02 - cefuroxime - oral	0.5	J01MA12 - levofloxacin	0.5
J01DC08 - loracarbef	0.6	J01MA14 - moxifloxacin	0.4
J01DD01 - cefotaxime	4	J01XA01 - vancomycin	2
J01DD02 - ceftazidime	4	J01XA02 - teicoplanin	0.4
J01DD04 - ceftriaxon	2	J01XB01 - colistin	3 MU
J01DD08 - cefixime	0.4	J01XB02 - polymyxin B	0.15
J01DD14 - ceftibuten	0.4	J01XC01 - fusidic acid	1.5
J01DE01 - cefepime	2	J01XD01 - metronidazole	1.5
J01DF01 - aztreonam - parenteral	4	J01XE01 - nitrofurantoin	0.2
J01DF01 - aztreonam - inhalation	0.225	J01XX01 - fosfomycin - parenteral	8
J01DH02 - meropenem	2	J01XX01 - fosfomycin - oral	3
J01DH03 - ertapenem	1	J01XX04 - spectinomycin	3
J01DH51 - imipenem and enzyme inhibitor	2	J01XX05 - methenamine - hippurate	2
J01EA01 - trimethoprim	0.4	J01XX05 - methenamine - mandelate	3
J01EC02 - sulfadiazin	0.6	J01XX08 - linezolide	1.2
J01EE01 - sulfamethoxazol and trimethoprim	1.92		

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 counties. During 2017 there were only two counties that did not report data to the Swedish eHealth Agency.

Data sources and inclusion criteria

Data on sales of antibiotics in outpatient and hospital care as well as population data for the calculations regarding antibiotic consumption 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. The substance methenamine is excluded in the data. Measures used are defined daily doses per 1 000 inhabitants and day (DDD/1 000 inhabitants and day) and prescriptions per 1 000 inhabitants and 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. Data on weight of the population in Sweden were obtained from Statistics Sweden, a Swedish authority responsible for official Swedish statistics.

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

Trend analysis

In this year's report, several general regression models were executed in the section "Consumption of antibiotics". Time was used as explanatory variable and the outcome was the sales of antibiotics, adjusted for population size in Sweden and number of patient-days at the given time. The analyses were exectued on a basis of a negative binomial distribution. In outpatient care the analyses were executed on the sales of antibiotics between 2000 and 2017 for different age groups, on sales of antibiotics commonly used to treat respiratory tract infections between 2000 and 2017 and on sales of antibiotics commonly used to treat UTI in men 65 years and older between 2000 and 2017. In hospital care, an analysis was executed on data of antibiotic groups often used within acute care hospitals between 2013 and 2017.

The Swedish Prescribed Drug Register

Since July 2005, the Swedish National Board of Health and Welfare supplies an individually based register on all drugs prescribed and dispensed in outpatient care. Among others this data give 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 and year (Users/1000/year). It is also possible to follow the number of purchases per person.

Number of admissions and patient-days

Each of the 21 county councils in Sweden deliver data once a year 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 2017 are not available until the end of 2018, denominator data from 2016 are therefore used in some figures in this report. The number of admissions and patient-days in Swedish somatic medical care (produced by acute care hospitals) 2013-2016 is shown in Table 6.1. The National Board of Health and Welfare keeps a searchable database at the web, http://www.socialstyrelsen.se/statistik.

Sales of antibiotics for animals

Data sources, inclusion criteria and analysis

As the result of a new interpretation of existing legislation on confidentiality, it has not been possible for SVA to obtain raw data per product for calculation to kg active substance and subsequent analyses from the eHealth Agency. Therefore, the Public Health Agency of Sweden has performed the calculations with methodological support from SVA. To facilitate, a few products with limited sales, sold on special license, were excluded from the material. The data source is the same as before, i.e. information in the database of the eHealth Agency on sales from pharmacies to animal owners (prescriptions dispensed) or to veterinarians (requisition).

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

Data are retrieved as number of packages sold per product. Calculation to kg active substance is done based on information on strength and package size obtained from the national product register of the MPA.

Products sold with special licence

Most antibiotic products sold with special licence (products prescribed and sold on exemption from general Swedish market authorization) 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 are no less complete than for products with general marketing authorisation. For 2017, a few products with limited sales, sold on special license, were excluded from the material.

Materials and methods resistance in bacteria from humans

Antibiotic susceptibility testing

The microbroth dilution method is the internationally accepted reference method for susceptibility testing to which other methods are compared. Clinical microbiology laboratories in Sweden have a long tradition of using disk diffusion antibiotic susceptibility testing (AST). This method is quantitative (diameter of inhibition zones measured in mm) but results are normally interpreted to give a qualitative "recommendation": S (susceptible, sensitive), I (intermediate) and R (resistant).

The disk diffusion method has been successfully standardized by the Swedish clinical microbiology laboratories in collaboration with the former SRGA-M, which since 2011 is replaced by NordicAST, a NordicAST Committee with representatives from Denmark, Norway and Sweden. Until 2009 all laboratories used the methodology based on ISA medium and a semi-confluent bacterial inoculum as recommended by SRGA-M. From 2011 all laboratories have adopted the new European method as described by EUCAST, based on Mueller Hinton agar and an almost confluent inoculum (equivalent to a 0.5 McFarland turbidity standard). The disk diffusion method is still the most commonly used routine method for susceptibility testing. It can also be used as a screening method which in some cases needs to be followed up by methods for gene detection (e.g. MRSA, VRE) and in other instances by MIC-determination (e.g. beta-lactam resistance in pneumococci, chromosomally mediated beta-lactam resistance in *Haemophilus influenzae*), and still in others by methods for enzyme detection (e.g. beta-lactamase detection in *Haemophilus influenzae* and *Neisseria gonorrhoeae*).

Internal and external quality assurance and quality control of susceptibility testing is performed by each laboratory. Internal quality control includes using international QC strains regularly (preferably on a daily basis) and analysing data in relation to national guidelines. Validation of susceptibility testing can also be done by histogram analysis of consecutive clinical isolates (see www.eucast.org). External quality control is often done by participation in UK-NEQAS and/or other international programmes.

National surveillance of antibiotic resistance

Surveillance regulated in the Communicable Disease Act

Statutory notifications of certain communicable diseases are regulated in the Communicable Disease Act (SFS 2004:168, SFS 2004:255). With the exception of certain sexually transmitted infection (STI), and from 2007 ESBL-producing Enterobacteriaceae, both the clinician caring for a patient with a notifiable disease (clinical notification) and the laboratory diagnosing the pathogen causing the disease (laboratory notification) are obliged to notify. This double notification significantly enhances the sensitivity of the surveillance system. Notification shall be done within 24 hours, in duplicate to the County Medical Officer for Communicable Disease Control (smittskyddsläkare) and to the Public Health Agency of Sweden. Notifications, with the exception of STI, are done with full personal identification. The clinical notification shall also include information on the likely source and route of infection, as well as other information of epidemiological importance.

Infections (or colonisation) with different antibiotic resistant pathogens are included in the list of notifiable diseases. *Streptococcus pneumoniae* with benzylpenicillin MIC ≥ 0.5 mg/L (PNSP) have been notifiable since 1996 (MIC > 1 mg/L from 2012). Methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant (*vanA* and *vanB*) *Enterococcus faecalis* and *Enterococcus faecium* (VRE) have been notifiable since 2000.

Since 1st February 2007 ESBL-producing Enterobacteriaceae were made notifiable by laboratory notifications. The definition of an ESBL was extended in 2009 to include not only ESBLs inhibited by clavulanic acid (now referred to as $ESBL_A$) but also plasmid-mediated AmpC enzymes ($ESBL_M$) and carbapenemase enzymes ($ESBL_{CARBA}$).

All notifications are entered into the national computerized surveillance system, SmiNet. At the Public Health Agency of Sweden, the clinical and laboratory notification for each case are merged and checked for errors. If data are missing, contact persons in the counties are asked to supplement the information. As an important complement to the notifications, the $ESBL_{CARBA}$, MRSA (only clinical isolates), VRE and PNSP isolates are sent for epidemiological typing. For MRSA *spa*-typing based on whole genome sequencing (WGS) is the primary typing method, for VRE it is WGS, and for PNSP serotyping.

Tuberculosis (TB) is a notifiable disease, irrespective of drug resistance. On a voluntary basis the TB laboratories are reporting all drug-resistant isolates of Mycobacterium tuberculosis and M. bovis to the Public Health Agency of Sweden. All resistant isolates are sent to the Public Health Agency of Sweden for epidemiological typing, using restriction fragment length polymorphism (RFLP).

The feedback of notification data is done monthly on the webpage (http://www.folkhalsomyndigheten.se) and yearly in this and other reports. Data on drug-resistant TB are also annually published in "the Swedish Tuberculosis Index".

Possible epidemiological links between patients from different counties, as identified from the epidemiological typing results and the notifications, are communicated to the persons in charge of the communicable disease control actions at the county level.

Gonorrhoea and invasive infections caused by *Neisseria meningitidis* are also notifiable. The descriptions of materials and methods for these pathogens are found under their respective result section.

Svebar, the Swedish combined surveillance and QC programme (RSQC surveys), and ResNet

Prior to 2015, ResNet was used to collect data on seven bacterial species. From 2015 and onwards, yearly data based on SIR (susceptibility categories) reported by the clinical microbiological laboratories in an automated system, Svebar, were

used. The RSQC surveys and ResNet are gradually discontinued as more laboraratories are connected to Svebar.

In 1994 a model for the concomitant surveillance of antibiotic resistance and quality assurance of antibiotic susceptibility testing was devised. In Sweden there are at present 26 clinical microbiology laboratories, each covering a county (or part of county) of Sweden. The demographics of the laboratories, their geographic areas and their corresponding populations are well characterized. The antibiotic susceptibility testing methods of the laboratories have been standardized through the combined work of the former SRGA-M (since 2011 replaced by NordicAST) and the microbiology laboratories.

Each year the laboratories were asked to collect quantitative data (zone diameters) for defined antibiotics in 100-200 consecutive clinical isolates of a defined set of bacterial species. Since 1994, *Streptococcus pneumoniae*, *Streptococcus pyogenes* and *Haemophilus influenzae* have been part of this yearly program. Since 2001 *Escherichia coli*, *Klebsiella pneumoniae*, *Staphylococcus aureus* and *Pseudomonas aeruginosa* have been part of these surveys. The number of antibiotics tested for each pathogen has varied between 4 and 6.

In 2002, the web-based software (ResNet) was introduced. It received the aggregated data from the laboratories and, following approval of registered data by one of two web administrators, instantly displayed it in the form of resistance frequencies on the geographical areas on a map of Sweden. Behind each resistance frequency the distribution of zone diameters together with the relevant demographic data are directly accessible. The graphs presenting the data are designed to include all necessary information in order for the graphs to be used on their own (in presentations etc). Laboratories could view their own data and link information to websites of their own local health care system.

Surveillance of blood culture results

Starting 2015 almost all surveillance of blood culture results is using data collected through Svebar, an automated system to which laboratories deliver all their culture results. Deduplication of isolates can not be done with data from Svebar, since personal identities are not allowed in the system. This is mainly expected to influence results for unusual resistance types, where repeated sampling is common.

EARS-Net

The European network of national surveillance systems of antimicrobial resistance (EARSS) is an on-going surveillance of invasive infections of *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Escherichia coli*, and *Enterococcus faecalis/faecium*. Data are reported per country and year. From 2005 invasive isolates of *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* are also part of the scheme. In 2014 *Acinetobacter* species was added to the programme.

During 2009 a transition of the EARSS management from RIVM in the Netherlands to ECDC in Stockholm was prepared, and from 1st January 2010 the network, renamed as EARS-Net, is coordinated from ECDC.

Data collected by EARS-Net should be routinely generated quantitative data (MICs or inhibition zones), but the data presented is in the format of susceptibility categories (SIR). External quality assurance exercises have so far been carried out by EARS-Net in cooperation with UK-NEQAS once every year. Results of those exercises have shown that participating laboratories were capable of delivering good quality susceptibility data, indicating that the overall resistance rates as monitored through EARS-Net are accurate.

The participation from laboratories in Sweden is coordinated through the Public Health Agency of Sweden, where electronic data collection, validation and verification of specific resistance mechanisms are performed. Sweden, because of its well organised network of clinical laboratories and high quality of routine susceptibility testing, is one of the largest contributors of national data to EARS-Net.

Surveillance of invasive isolates not included in EARS-Net

Starting 2015 data for *Streptococcus agalactiae* and *Haemophilus influenza*, as well as data for *Salmonella* and *Campylobacter* were collected through Svebar in the same way as described above for EARS-Net data. Data for *Streptococcus pyogenes* were collected through the microbial surveillance programme at the Public Health Agency of Sweden.

Sentinel surveillance

A national surveillance programme for *Clostridium difficile* was initiated by the Swedish Institute for Communicable Disease Control (now included in the Public Health Agency of Sweden) in 2009. The programme included both a voluntary laboratory reporting system of all new cases of *Clostridium difficile* infection (CDI) through SmiNet and a determination of resistance and epidemiological typing of isolates from the clinical microbiology laboratories. All *C. difficile* strains isolated during week 11 and 39 were sent to SMI for typing by PCR ribotyping and antibiotic susceptibility testing.

Susceptibility testing of gastrointestinal pathogens such as *Salmonella*, *Shigella*, *Campylobacter* spp. and *Helicobacter pylori* is not performed on a regular basis most clinical laboratories. Existing data are derived from selected laboratories, with a higher proportion of tested isolates.

Materials and methods resistance in bacteria from animals

Sampling strategy

Antibiotic resistance as notifiable diseases

ESBL

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

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. Furthermore, screening for $ESBL_A$, $ESBL_M$ and $ESBL_{CARBA}$-producing *Escherichia coli* was performed on caecal samples from healthy broilers.

Samples from 241 pigs were collected at slaughter under the supervision of the National Food Agency (SLV) at six abattoirs that together processed more than 85% of the total number of pigs slaughtered in Sweden 2017. At each abattoir, a proportional number of samples in relation to the 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 March-April and 50 in September. Each sample was from a unique flock but not always from a unique production site. Samples cultured were collected at seven abattoirs that in 2017 accounted for approximately 98% of the total volume of broilers slaughtered. The number of samples from each abattoir was roughly proportional to the annual slaughter volume of the abattoir.

Samples of fresh pork (295) and beef (286) were collected throughout the year at retail stores by municipal environmental departments in fifteen different cities in Sweden. In each city, a proportional number of samples in relation to the human population was collected.

MRSA and MRSP

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

Findings of MRSA and MRSP in animals are notifiable in Sweden and hitherto the majority of isolates from notified incidents has been confirmed using molecular methods at SVA.

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

Zoonotic pathogens

Salmonella

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

Campylobacter

Screening for *Campylobacter coli* in caecum from pigs were performed on the same samples as for ESBL (see above).

Clinical isolates from animals

Clinical isolates included are from routine bacteriological examinations of clinical submissions or post-mortem examinations. Isolates of *Staphylococcus hyicus* and *Streptococcus suis* from pigs, part of the isolates of *Actinobacillus pleuropneumoniae* from pigs and part of the isolates of *Pasteurella* spp. from calves are, however, isolated from samples collected in surveys initiated within the SvarmPat programme. Isolates of *Fusobacterium necrophorum* were collected within a research project financed by The Swedish Farmers' Foundation for Agricultural Research.

In pigs, isolates of *E. coli* are from the gastro-intestinal tract and isolates of *Brachyspira* spp. from faecal samples. Isolates of *Pasteurella* spp. from pigs are isolated from nasal swabs collected within a control programme for atrophic rhinitis in nucleus and multiplying herds or from tissue samples from lungs taken post mortem. Isolates of *A. pleuropneumoniae* in pigs emanate from tissue samples from lungs sampled post mortem. Isolates of *S. hyicus* are from skin samples in healthy sows and isolates of *S. suis* are from post mortem investigation of various organs or from samples from tonsils in healthy slaughtered pigs.

In cattle, isolates of *E. coli* are from samples from the gastro-intestinal tract or from milk samples. Isolates of *Klebsiella pneumoniae* are from milk samples. Isolates of *Pasteurella* spp. are from the respiratory tract. *Fusobacterium necrophorum* isolates are from clinical cases of foot rot.

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

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

In dogs, isolates of *E. coli* are from urine, *Staphylococcus pseudintermedius* is isolated from skin, wounds and external ear canal, *Staphylococcus schleiferi* from various locations (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 organs (mainly external ear canal, other skin locations, abscesses, wounds and urine) and *Pasteurella* spp. from various locations (mainly wounds, skin, abscesses, external ear canal and the respiratory tract).

Indicator bacteria

Culturing for indicator *E. coli* in caecum from pigs were performed on the same samples as for ESBL (see above). However, only 143 of the samples from pigs were cultured for indicator *E. coli* and these samples were evenly distributed over the year.

Rectal swabs from calves (0-2 months of age) on dairy farms across Sweden were collected during the fall 2016 and spring 2017. The samples were collected by the farmers on the farms of origin. These samples were taken as part of a larger research project were six calves on each farm were sampled. To include only a subset of samples where one sample represents one calf on a unique farm, only the most recently collected sample on each farm was selected. All sampled calves were healthy and had not been treated with antimicrobials.

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: Briefly, 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 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 detection. *E. coli* like colonies on CC agar and CO agar were sub-cultured on horse blood agar and then species identified by MALDI-TOF.

Meat samples: Briefly, 25 g of surface meat was homogenized in 225 ml BPW and incubated at 37°C overnight. From the BPW homogenizate 10 µL per agar plate was spread on MacConkey agar with cefotaxime (1 mg/L), CC agar and CO agar and incubated overnight at 44°C (MacConkey agar) or 37°C (CC, CO agar). From MacConkey agar with cefotaxime 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 and further tested for ESBL detection. *E. coli* like colonies on CC agar and CO agar were sub-cultured on horse blood agar and then species identified by MALDI-TOF.

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.

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 identifed by MALDI-TOF.

Clinical isolates from animals

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

Indicator bacteria

Escherichia coli

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

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

Rectal swabs were transferred to isotonic saline and the sample suspensions were plated on Petrifilm Select *E. coli* Count plates and incubated overnight at 42°C. From each

plate, one random colony resembling *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, 2013). 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, 37°C for 16-18 hours, or by dilution in Haemophilus test medium (HTM) followed by incubation in CO2, 37°C for 16-18 hours. Also dilution in CAMHB supplemented with 5-10% horse serum and incubation in CO_2, 37°C for 16-18 hours was used. For testing of *A. pleuropneumoniae* dilution in HTM broth was used followed by incubation in CO_2 at 37°C for 16-18 hours. Also, *S. equi* subsp. *zooepidemicus* was tested using CAMHB supplemented with 5-10% horse serum followed by incubation at 37°C for 16-18 hours. *Fusobacterium necrophorum* was tested in CAMHB. The inoculum was prepared by colony suspension to a concentration of approximately 10^6 CFU/ml and the inoculation volume was 100 µl per well. Incubation was performed in anaerobic jars at 37°C for 48 hours.

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

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

Bacteria from fish are tested for antibiotic susceptibility by broth microdilution adapted for aquatic bacteria according to CLSI (2014a).

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

Genotyping

Suspected isolates of MRSA were confirmed by detection of the *nuc*, *mecA* and *mecC* genes applying real-time PCR as described by Pichon et al. (2012). *Spa*-typing, a single locus sequence typing method using the polymorphic region X of the protein A gene, was performed on all isolates confirmed as MRSA, according to Harmsen et al. (2003) and the specific *spa*-type was determined using BioNumerics® (Applied Maths).

PCR was performed for identification of $ESBL_M$ (Perez-Perez and Hanson, 2002), $ESBL_A$ (Woodford et al., 2006), genes coding OXA-1 group, TEM-groups and SHV-groups (Fang et al., 2008) and $ESBL_{CARBA}$ (Poirel et al., 2011).

DNA from confirmed ESBL-producing Enterobacteriaceae, MRSA and MRSP was extracted from overnight cultures on horse-blood agar using Qiagen EZ1 DNA tissue kit, according to the recommendations of the manufacturer. DNA-concentrations were determined using Qubit HS DNA-kit (Life technologies). DNA was then sent to Sci-life clinical genomics (Solna, Sweden) for library preparation and 100-bp 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 a local database containing the transferable genes encoding beta-lactam resistance listed in the Resfinder-v3.0-database (https://cge.cbs.dtu.dk/services/ResFinder/). The MLST for included isolates was extracted. Reads were then trimmed with Trimmomatic 0.36 and genome assembly was performed with SPAdes v.3.9.1 with the careful parameter and an input average coverage of 40x, followed by Pilon v1.21 with default settings to correct assemblies (Bankevich et al., 2012; Bolger et al., 2014; Walker et al., 2014). Using the assembled contigs the isolates were assigned an MLST when available, using MLST Schemes at http://pubmlst.org/.

The specific gene variants for a collection of isolates for which NGS produced 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 Micobiology is accredited for isolation and identification of animal pathogens and of *Salmonella* according to the same standard.

For susceptibility tests of zoonotic, pathogen and indicator bacteria, *Escherichia coli* ATCC 25922, *Enterococcus faecalis* ATCC 29212, *Staphylococcus aureus* CCUG 15915 (analogue to ATCC 29213), *A. pleuropneumoniae* ATCC 27090 and *Campylobacter jejuni* CCUG 11284 (analogue to *Campylobacter jejuni* ATCC 33560) were included as quality controls.

Relevant control strains were also included and evaluated at least once weekly, when testing, for animal pathogens. For testing of *Brachyspira*, the *B. hyodysenteriae* type strain B78^T ATCC 27164^T was used for quality control.

Dept. of Animal Health and Antimicrobial Strategies participates in two proficiency tests for antibiotic susceptibility testing and one comparative test for isolation and antibiotic susceptibility testing. These are arranged by the European Union Reference Laboratory - Antimicrobial Resistance and as a national ring trial. Likewise, Dept. of Microbiology participates in proficiency tests concerning isolation and identification of *Salmonella* and general clinical veterinary bacteriology and susceptibility tests.

Data handling

Records on *Salmonella* and animal pathogens such as source of cultured sample, identification results, antibiotic susceptibility etc. were registered in a database at SVA. Data for indicator bacteria were recorded in an Access database.

Cut-off values for resistance

For interpretation of MICs from susceptibility testing of zoonotic bacteria (*Salmonella* and *Campylobacter*) and indicator bacteria (*Escherichia coli* and enterococci) epidemiological cut-off values (ECOFF) issued by EUCAST (www.eucast.org) or values suggested by the European Food Safety Authority are used. For some antibiotics, values based on MIC distributions obtained in Svarm are used. This applies e.g. for narasin in *E. faecium* where the ECOFF (>4 mg/L) cuts through the resistant MIC population for some animal categories (e.g. broilers) in a manner not in agreement with the concept of wild-type distributions.

ECOFFs are used when available also for clinical isolates from animals. When ECOFFs are not available, or the range of concentrations tested precludes use of a recommended value, values based on MIC distributions obtained in Svarm are used but clinical breakpoints issued by CLSI (CLSI, 2015a) or epidemiological cut-offs (ECVs) issued by CLSI (CLSI, 2014b) are also taken into consideration.

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

TABLE 6.10. Cut-off values (mg/L) for resistance. Values in red are current (March 2018) 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*	*Enterococcus faecalis*	*Enterococcus faecium*	*Escherichia coli* (indicator)	*Escherichia coli* (pathogen)	*Flavobacterium psychrophilum*	*Klebsiella pneumoniae*	*Pasteurella multocida*	*Pseudomonas aeruginosa*	*Salmonella enterica*	*Staphylococcus pseudintermedius, S. felis, S. schleiferi*	*Staphylococcus aureus*	*Staphylococcus hyicus*	*Streptococcus suis*	*Streptococcus zooepidemicus*
Ampicillin	>1				>4	>4	>8	>8			>1		>8					
Azithromycin							>16											
Bacitracin[a]					>32	>32												
Cefepime							>0.12											
Cefotaxime							>0.25	>0.25		>0.25			>0.5					
Cefoxitin															>4			
Ceftazidime							>0.5						>2					
Ceftiofur								>1		>1								
Cephalothin														>1	>1		>2	>2
Chloramphenicol	>2				>32	>32	>16	>16			>2		>16			>16		
Ciprofloxacin	>0.06		>0.5	>0.5			>0.06				>0.06		>0.06					
Clindamycin														>0.5	>0.5[d]		>0.5	>0.5
Colistin							>2	>2		>2		>4	>2					
Doxycycline		>0.5																
Enrofloxacin							>0.12	>0.12		>0.12	>0.25	>2		>0.5	>0.5			
Ertapenem							>0.06											
Erythromycin			>4	>8	>4	>4								>0.5	>1	>1	>0.5	>0.5
Florfenicol	>4							>16	>2		>4		>16					
Fusidic acid														>1	>0.5			
Gentamicin	>8		>2	>2	>32	>32	>2	>2		>2	>8	>8	>2	>2	>2			
Imipenem							>0.5											
Linezolid					>4	>4												
Meropenem							>0.12											
Nalidixic acid	>16		>16	>16			>16				>16		>16					
Narasin					>2	>2												
Neomycin								>8		>8			>4					
Nitrofurantoin								>64						>32 (UVI)	>32			>32
Oxacillin														>0.5	>1			
Oxolinic acid									>0.25									
Penicillin	>0.5										>0.5			c	c		>0.25	>0.06
Streptomycin			>4	>4	>512	>128		>16		>16			>16					
Sulphametoxazole							>64						>256					
Temocillin							>32											
Tetracycline	>1		>1	>2	>4	>4	>8	>8	>0.12	>8	>2		>8	>1	>1		>0.5	
Tiamulin		>0.25																
Tigecycline							>1											
Trimethoprim	>4						>2						>2					
Trim & sulpha[b]								>1		>1	>4			>0.5	>0.5		>0.5	>0.5
Tylosin		>16																
Tylvalosin		>1																
Valnemulin		>0.12																
Vancomycin					>4	>4												
Virginiamycin					>32	>4												

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

Svarm 2000–2017

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

TABLE 6.11. *Salmonella enterica,* number of isolates 2000-2017.

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

TABLE 6.12. *Campylobacter* spp., number of isolates 2000-2017.

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

TABLE 6.13. Indicator *Escherichia coli,* number of isolates 2000-2017.

Source	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Cattle	293						314			223				197		101		85
Pigs	260	308		303		390		342	349			167				200		140
Pig meat									19			20						
Broilers	274	296	306		300			296			181		194		197		175	
Broiler meat											77		92					
Laying hens													61					
Turkeys														55	59		85	
Horses											274							
Dogs							257						74					
Willow grouse						19												
Wild boars		87																
Sheep									115									

TABLE 6.14. Indicator *Enterococcus faecalis* and *E. faecium*, number of isolates 2000-2017 *E. faecalis/E. faecium*).

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

Animal species & bacterial species	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Cattle																		
Escherichia coli (enteric)			220		87	39	24			40	15	15	58	30	29	36	29	31
Escherichia coli (uterine)														60				
Escherichia coli (udder)				169										142	95	113	74	79
Klebsiella spp. (udder)				44			24							41	39	41	36	34
Pasteurella spp.	254			100				27	32	14	27	80	37	39	39	46	104	86
Staphylococcus aureus (udder)		100	100			96			87						74			
Streptococcus dysgalactiae (udder)			100															
Streptococcus uberis (udder)			100															
Fusobacterium necrophorum										41								24
Pigs																		
Actinobacillus pleuropneumoniae	18							84	39	24	16	57	33	36	37	33	18	23
Brachyspira hyodysenteriae	50	75	109	100		31	26	23	15	24	9	7	7	8	7	7	11	15
Brachyspira pilosicoli				93		57	72	44	31	24	13	16	17	12	13	7	17	21
Escherichia coli (enteric)	399	82	340	340	386	325	298	93	83	102	94	91	74	142	118	84	67	222
Pasteurella spp.		75						38	25	24	10	17	24	95	19	7	8	10
Staphylococcus hyicus					20													65
Streptococcus equisimilis												82						
Streptococcus suis																		72
Poultry (laying hens)																		
Escherichia coli (infection)								70										
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

TABLE 6.16. Clinical isolates from companion animals and horses, number of isolates 2000-2017.

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

References

Bankevich A, Nurk S, et al. 2012, SPAdes: a new genome assembly algorithm and its applications to single-cell sequencing. *J Comput Biol*, 19:455-77.

Bolger AM, Lohse M, et al. 2014, Trimmomatic: a flexible trimmer for Illumina sequence data. *Bioinformatics*, 30:2114-20.

Bolinger H, Kathariou S. 2017, The Current State of Macrolide Resistance in *Campylobacter* spp.: Trends and Impacts of Resistance Mechanisms. *Appl Environ Microbiol*, 83:e00416-17.

Börjesson S, Ny S, et al. 2016, Limited Dissemination of Extended-Spectrum beta-Lactamase- and Plasmid-Encoded AmpC-Producing *Escherichia coli* from Food and Farm Animals, Sweden. *Emerg infect dis*, 22:634-40.

CLSI. Performance Standards for Antimicrobial Disk and Dilution Susceptibility Tests for Bacteria Isolated from Animals; Approved Standard - Fourth Edition VET01-A4. Clinical and Laboratory Standards Institute. Wayne, PA, USA, 2013.

CLSI. Methods for Broth Dilution Susceptibility Testing of Bacteria Isolated From Aquatic Animals; Approved Guideline-Second Edition VET04-A2. Clinical and Laboratory Standards Institute. Wayne, PA, USA, 2014a.

CLSI. Performance Standards for Antimicrobial Susceptibility Testing of Bacteria Isolated From Aquatic Animals; Second Informational Supplement VET03/VET04-S2. Clinical and Laboratory Standards Institute. Wayne, PA, USA, 2014b.

CLSI. Performance Standards for Antimicrobial Disk and Dilution Susceptibility Tests for Bacteria Isolated from Animals; Third Informational Supplement VET01S Ed3. Clinical and Laboratory Standards Institute. Wayne, PA, USA, 2015a.

CLSI. Methods for Antimicrobial Dilution and Susceptibility Testing of Infrequently Isolated or Fastidious Bacteria; Approved Guideline - Third Edition M45 Ed3. Clinical and Laboratory Standards Institute. Wayne, PA, USA, 2015b.

CVMP. Reflection paper on MRSA in food producing and companion animals in the European Union: Epidemiology and control options for human and animal health, European Medicines Agency. 2009. www.ema.europa.eu

Damborg P, Moodley A, et al. High genetic diversity among methicillin-resistant *Staphylococcus pseudintermedius* isolated from canine infection in Denmark. 3rd ASM-ESCMID Conference on Methicillin-resistant Staphylococci in Animals; Copenhagen, Denmark. 2013.

de Been M, Lanza VF, et al. 2014, Dissemination of cephalosporin resistance genes between *Escherichia coli* strains from farm animals and humans by specific plasmid lineages. *PLoS genetics*, 10:e1004776.

Duim B, Verstappen KM, et al. 2016, Changes in the population of methicillin-resistant *Staphylococcus pseudintermedius* and dissemination of antimicrobial-resistant phenotypes in the Netherlands. *J Clin Microbiol*, 54:283-8.

EFSA. 2009, Scientific Opinion of the Panel on Biological Hazards on a request from the European Commission on Assessment of the Public Health significance of meticillin resistant *Staphylococcus aureus* (MRSA) in animals and foods. *The EFSA Journal*, 993:1-73.

EFSA. 2011, Scientific opinion on the public health risks of bacterial strains producing extended-spectrum beta-lactamases and/or AmpC beta-lactamases in food and food-producing animals. *The EFSA Journal*, 9:2322.

EMA. 2017. Sales of veterinary antimicrobial agents in 30 European countries in 2015. Trends from 2010 to 2015, Seventy ESVAC report (EMA/WC5002367750). www.ema.europa.eu

Fang H, Ataker F, et al. 2008, Molecular epidemiology of extended-spectrum beta-lactamases among *Escherichia coli* isolates collected in a Swedish hospital and its associated health care facilities from 2001 to 2006. *J Clin Microbiol*, 46:707-12.

García-Álvarez L, Holden MT, et al. 2011, Meticillin-resistant *Staphylococcus aureus* with a novel mecA homologue in human and bovine populations in the UK and Denmark: a descriptive study. *Lancet Infect Dis*, 11:595-603.

Hanberger H, Skoog G, et al. 2014, Antibiotic consumption and antibiotic stewardship in Swedish hospitals. *Ups J Med Sci*, 119:154-61.

Harmsen D, Claus H, et al. 2003, Typing of methicillin-resistant *Staphylococcus aureus* in a university hospital setting by using novel software for spa repeat determination and database management. *J Clin Microbiol*, 41:5442-8.

Hedin K, Andre M, et al. 2006, A population-based study of different antibiotic prescribing in different areas. *Br J Gen Pract*, 56:680-5.

Hunt M, Mather AE, et al. 2017, ARIBA: rapid antimicrobial resistance genotyping directly from sequencing reads. *Microb Genom*, 3:e000131.

Ito T, Hiramatsu K, et al. 2012, Guidelines for reporting novel mecA gene homologues. *Antimicrob Agents Chemother*, 56:4997-9.

Karlsson M, Fellström C, et al. 2003, Antimicrobial susceptibility testing of porcine *Brachyspira* (*Serpulina*) species isolates. *J Clin Microbiol*, 41:2596-604.

Medical Products Agency. Recommendations for the treatment of lower urinary tract infections in women. In Swedish. 2017. https://lakemedelsverket.se/upload/halso-och-sjukvard/behandlingsrekommendationer/Information-fran-lakemedelsverket-nr-5-2017-behandlingsrekommendation.pdf

Medical Products Agency and Strama. Management of respiratory tract infections. In Swedish. 2008. www.lakemedelsverket.se/upload/halso-och-sjukvard/behandlingsrekommendationer/Rev_NLI-rek_091202.pdf

Medical Products Agency and Strama. Recommendations for treatment of acute otitis media. In Swedish. 2010. www.lakemedelsverket.se/upload/halso-och-sjukvard/behandlingsrekommendationer/20101011_rev_Rek_otit.pdf

Medical Products Agency and Swedish Institute for Communicable Disease Control. Management of pharyngitis. In Swedish. 2012. www.lakemedelsverket.se/upload/halso-och-sjukvard/behandlingsrekommendationer/Rev_130117_Handl%c3%a4ggning%20av%20faryngotonsilliter%20i%20%c3%b6ppen%20v%c3%a5rd%20-%20ny%20rekommendation_webb.pdf

Mölstad S, Andre M, et al. 2009, In common infections: to give or not to give antibiotics. In Swedish. *Läkartidningen*, 106:3162-6.

Neumark T, Brudin L, et al. 2009, Trends in number of consultations and antibiotic prescriptions for respiratory tract infections between 1999 and 2005 in primary healthcare in Kalmar County, Southern Sweden. *Scand J Prim Health Care*, 27:18-24.

Osland AM, Vestby LK, et al. 2012, Clonal diversity and biofilm-forming ability of methicillin-resistant *Staphylococcus pseudintermedius*. *J Antimicrob Chemother*, 67:841-8.

Perez-Perez FJ, Hanson ND, 2002, Detection of plasmid-mediated AmpC beta-lactamase genes in clinical isolates by using multiplex PCR. *J Clin Microbiol*, 40:2153-62.

Perreten V, Kadlec K, et al. 2010, Clonal spread of methicillin-resistant *Staphylococcus pseudintermedius* in Europe and North America: an international multicentre study. *J Antimicrob Chemother*, 65:1145-54.

Pichon B, Hill R, et al. 2012, Development of a real-time quadruplex PCR assay for simultaneous detection of *nuc*, Panton-Valentine leucocidin (PVL), mecA and homologue $mecA_{LGA251}$. *J Antimicrob Chemother*, 67:2338-41.

Poirel L, Walsh TR, et al. 2011, Multiplex PCR for detection of acquired carbapenemase genes. *Diagn Microbiol Infect Dis*, 70:119-23.

Pringle M, Landén A, et al. 2012, Antimicrobial susceptibility of porcine *Brachyspira hyodysenteriae* and *Brachyspira pilosicoli* isolated in Sweden between 1990 and 2010. *Acta Vet Scand*, 54:54.

Public Health Agency of Sweden. Urinvägsinfektioner hos män, expertmöte med redovisning av aktuellt kunskapsläge mot bakgrund av ökad antibiotikaresistens. In Swedish. 2013. www.folkhalsomyndigheten.se/pagefiles/12855/Urinvagsinfektioner-hos-man.pdf

Public Health Agency of Sweden. ESBL-producerande tarmbakterier. In Swedish. 2014. www.folkhalsomyndigheten.se/pagefiles/17838/ESBL-producerande%20tarmbakterier.pdf

Public Health Agency of Sweden. Vad påverkar allmänläkare vid förskrivning av antibiotika? In Swedish. 2014. www.folkhalsomyndigheten.se/documents/om-folkhalsomyndigheten/uppdrag-styrdokument/avslutade/faktorer-som-paverkar-lakare-vid-forskrivning-av-antibiotika.pdf

Public Health Agency of Sweden. RSV-rapport för vecka 52, 2016 - 1, 2017. In Swedish. 2017. https://www.folkhalsomyndigheten.se/documents/statistik-uppfoljning/smittsamma-sjukdomar/veckorapporter-rsv/2016-2017/RSV-rapport_v52-1.pdf

Public Health Agency of Sweden. Influensarapport för vecka 52, 2016 – 1, 2017. In Swedish. 2017. https://www.folkhalsomyndigheten.se/documents/statistik-uppfoljning/smittsamma-sjukdomar/Veckorapporter-influensa/2016-2017/Influensarapport_2017-52-1_version2.pdf

RAF. Minimiurval i resistensbesked. In Swedish. 2014. www.sls.se/Global/RAF/Dokument/Resistens/minimiresistensbesked-med-logga.pdf

Shore AC, Deasy EC, et al. 2011, Detection of staphylococcal cassette chromosome mec type XI carrying highly divergent mecA, mecI, mecR1, blaZ, and ccr genes in human clinical isolates of clonal complex 130 methicillin-resistant *Staphylococcus aureus*. *Antimicrob Agents Chemother*, 55:3765-73.

Smith P, Endris R, et al. 2016, Epidemiological cut-off values for *Flavobacterium psychrophilum* MIC data generated by a standard test protocol. *J Fish Dis*, 39:143-54.

Svarm. Swedish veterinary antimicrobial resistance monitoring. Uppsala, Sweden. ISSN 1650-6332. www.sva.se

Swedish National Board of Health and Welfare. Lägesrapport 2011. In Swedish. 2011. https://www.socialstyrelsen.se/publikationer2011/2011-2-1

Swedres. Report on Swedish antimicrobial utilisation and resistance in human medicine. Solna, Sweden. ISBN 987-91-86723-09-5. www.folkhalsomyndigheten.se/publicerat-material/

Walker BJ, Abeel T, et al. 2014, Pilon: an integrated tool for comprehensive microbial variant detection and genome assembly improvement. *PLoS One*, 9:e112963.

WHO. 2017. Critically important antimicrobials for human medicine, 5th revision. http://www.who.int/foodsafety/areas_work/antimicrobial-resistance/cia/en/

Woodford N, Fagan EJ, et al. 2006, Multiplex PCR for rapid detection of genes encoding CTX-M extended-spectrum (beta)-lactamases. *J Antimicrob Chemother*, 57:154-5.

SWEDRES|SVARM 2017

This annual report describes the monitoring of antibiotic resistance and sales of antibiotics in human and veterinary medicine in Sweden in 2017.

The situation in Sweden regarding antibiotic resistance in bacteria from humans and animals is favourable when seen in an international perspective, and this confirms that Sweden's strategies to promote responsible use of antibiotics and to contain antibiotic resistance are effective. With that said, it is important to stress that this is a never-ending task and that society must keep a long-term perspective on policies and efforts in this area.

The total sales of antibiotics in humans have continued to decrease, and positive trends regarding choices of antibiotics have also continued in 2017. The increasing trend seen in the sales of antibiotics to children in 2016 has not continued in 2017. Sales of antibiotics for animals are also decreasing.

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

This highlights once again that efforts to optimize antibiotic use, prevent infections, and minimize dissemination of antibiotic resistance must be ongoing and must be continually improved based on effective monitoring and best available knowledge.

Focus areas in the 2017 report:
- Availability of antibiotics
- Improved surveillance of AMR/AMC in humans and animals
- Genomic-based surveillance of carbapenem- resistant and/or colistin-resistant Enterobacteriaceae at the EU-level (EURGen-CCRE)
- Next-generation sequencing (NGS) reveals different population-structures of *E. coli* carrying bla_{CMY-2} and *E. coli* carrying $bla_{CTX-M-1}$ in the Swedish broiler production
- SvarmPat – monitoring of resistance in pathogens from farm animals

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