SWEDRES | 2011

A Report on Swedish Antibiotic Utilisation and Resistance in Human Medicine

Smi
SMITTSKYDDSINSTITUTET
Swedish Institute for Communicable Disease Control

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Swedish Institute for Communicable Disease Control, SMI, is a government agency with the mission to monitor the epidemiology of communicable diseases among Swedish citizens and promote control and prevention of these diseases.

Publishers:
Swedish Institute for Communicable Disease Control

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Article number 2012-15-3,
ISBN 978-91-86723-05-7.
This title can be ordered from:
Smittskyddsinstitutets beställningsservice
c/o Strömberg, 120 88 Stockholm.
Or from our webstore:
Fax: 08-779 96 67,
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www.smittskyddsinstitutet.se/publikationer.
The title is also available for downloading from the website of the Swedish Institute for Communicable Disease Control, see www.smittskyddsinstitutet.se/publikationer.

Print:
Edita Västra Aros AB

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1. Preface

THE INTRODUCTION of antimicrobials some 70 years ago was a true paradigm shift with immense impact on the possibility to treat infectious diseases in human medicine. Soon antimicrobials were introduced also in animal healthcare and not the least, these drugs came into use in the breeding of animals for food production.

Unfortunately use and misuse of antimicrobials for humans and animals have undermined the usefulness of the miracle drugs by selecting for antimicrobial resistance. The impact of resistance is vast and goes beyond therapeutic failures in single cases. Virtually the foundation of human healthcare as perceived today is being undermined by emergence of resistance. Likewise, modern companion animal healthcare relies on access to effective therapy of infectious diseases as does food production based on breeding of production animals. Not surprisingly emergence of antimicrobial resistance is often described as one of the greatest current global threats and challenges to man.

To recapture the usefulness of antimicrobials for treatment of man and animals, joint actions on several levels are needed. This is generally recognized and was recently addressed by the European Commission in its "Action plan against the rising threats from antimicrobial resistance" released in November 2011 (COM 2011 748). The plan acknowledges a holistic approach comprising actions in several different sectors such as medicine, veterinary medicine, animal husbandry, agriculture, environment and trade.

Among the 12 urgently needed key actions described in the plan is research and development of new antimicrobials to replace drugs that have become obsolete by emerging resistance. This is easily understood but the plan goes further and proposes actions in several other fields. Among these are measures to prevent infectious diseases in man and animals and measures to promote and ascertain prudent use of antimicrobials in human and veterinary medicine. Also surveillance of antimicrobial use and of resistance in human as well as veterinary medicine are among the key actions proposed. Also it is emphasised that harmonisation of monitoring is vital because it increases the usefulness for risk assessment and management of the data generated.

It is in this context the reports from SWEDRES and SVARM should be perceived. To be effective and relevant, actions against resistance must be based on sound knowledge of the current situation and of trends over time. For more than a decade the reports have yearly documented the national situation with regard to antimicrobials use and prevalence of resistance. The data generated so far, and in future, is urgently needed as guidance for actions and initiatives to mitigate antimicrobial resistance as well as for designing strategies on a national level.

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Contact persons representing Swedish Microbiological laboratories (formerly the Antibiotic Resistance Group (ARG) at SMI) in addition to members already listed above: **Hanna Billström, Sven Hoffner, Olle Aspevall, Eva Melander, Christina Åhrén.**

Acknowledgements

The national surveillance of antibiotic resistance would not have been possible without the 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.

Data on antibiotic use in relation to number of admissions and number of patient days in somatic hospital care during 2006-2011 were kindly provided by pharmacists in local Strama-groups.

Katarina Baatz, The National Board of Health and Welfare, has kindly provided individually based data on the use of antibiotics. **Anders Jacobsson,** The National Board on Health and Welfare, has kindly provided data on admissions and patient-days in Swedish medical care.

The Swedish strategic programme against antibiotic resistance (Strama-rådet) for supporting the work with SWEDRES.

2.1. Summary

Use of antibiotics

The total use of antibiotics increased slightly (0.9 percent) in 2011 as compared with 2010. In outpatient care, the antibiotic use decreased (1.3 percent) when measured as prescriptions per 1000 inhabitants. The decrease was mainly due to a large reduction (11.1 percent) in antibiotic prescribing to children age 0-4 years. In all other age groups the antibiotic use increased. Antibiotic prescribing to children has been the subject of information campaigns for several years and the use in this age group has decreased dramatically during the two last decades. Even though the antibiotic use is high among children, other age groups represent the majority of the antibiotic consumption. About half of the Swedish counties showed a small decrease, but apparently not all, and the differences between counties are still large. Prescriptions per 1000 inhabitants and year ranged from 417 in the county of Stockholm to 310 in the county of Västerbotten.

The decrease encompassed almost all antibiotic groups except the following substances which increased: tetracyclines (6.1 percent), nitrofurantoin (6.9 percent), pivmecillinam (1.3 percent), and lincosamides (0.9 percent). When analyzing the antibiotic use in outpatient care in 2011 month by month, an increased use of tetracyclines and macrolides was seen in all age groups during the first and the last three months compared with 2010. These two antibiotic groups are commonly used to treat *Mycoplasma penumoniae* and during the influenza season 2011 an increased prevalence of *Mycoplasma pneumoniae* was seen in Sweden.

Beta-lactamase sensitive penicillins together with tetracyclines were the most commonly used antibiotics in outpatient care. Penicillin V was the overall most commonly prescribed antibiotic and the use of this compound decreased by 0.6 percent in 2011.

Treatment of lower urinary tract infections in women has also been the subject of information campaigns for several years. Usage of the two first line recommended substances, pivmecillinam and nitrofurantoin, has increased every year and represented 74.3 percent of the total sale of antibiotics commonly used to treat urinary tract infections in this patient group in 2011. Data from 66 health centers in Sweden showed that lower urinary tract infection was the single diagnose that lead to most antibiotic prescriptions.

In hospital care the antibiotic use increased with 4.2 percent in 2011, measured in DDD per 1000 inhabitants and day. In recent years, antibiotic use in hospital care has shown a shift from an extensive use of cephalosporins to an increased use of narrow spectrum penicillins. This trend continued also in 2011. However, there were still large differences between counties in this respect. The regional differences were also evident regarding the use of newer classes of broad spectrum antibiotics such as carbapenems and piperacillin with tazobactam, of which the latter increased by 12.0 percent in 2011.

Use of antifungals

Similar to the previous years there has been a small but steady increase in the use of antimycotic drugs for systemic use. The total use of antifungals was, however, still low. In 2010 there was an increase from the previous year by 10 percent to 61.9 DDD per one million inhabitants and day, and during 2011 the increase was 4 percent, giving a total figure of 64 DDD per one million inhabitants and day. Fluconazole still constituted the absolute majority of the antifungals used, 69 percent or 44 DDD per one million inhabitants and day. The total increase of 4 percent in 2011 was related to an increased use of amphotericin B with 18 percent and caspofungin with 18 percent. All other compounds were stable during the last year. The increased use of amphotericin B was seen already in 2010, but the reason for this trend is unknown. No new national guidelines were issued that could have explained the increased use. Most of the rise was seen in the county of Stockholm, which by far harbors the largest population. Since the overall figures were low the increase might be due to the treatment of only a few patients, but as there have been reports from other countries of increased azole resistance in *Aspergillus fumigatus* we cannot currently rule out that the increase in amphotericin B might be due to clinical failure with azole therapy. It is of great importance to closely monitor the future development.

Antibiotic resistance

Swedish surveillance of antibiotic resistance is based on testing of clinical samples and samples taken according to local screening programmes. Some bacterial species with specific mechanisms of antibiotic resistance are notifiable under the Communicable Disease Act and therefore form an important part of the surveillance programme. The vast amount of data on antibiotic resistance in Sweden is however based on susceptibility testing of clinical samples in local clinical microbiology laboratories. This data is voluntarily reported to one or both of the surveillance systems, RSQC, in which all laboratories take part, and EARS-net, in which three fourths of the laboratories contribute with data on defined invasive isolates. For some bacterial species resistance data are produced and presented by laboratories with referral functions and/or with special interest in certain species (e.g. *Neisseria* spp. in Örebro University Hospital). In the present report the most recent data on antibiotic resistance is presented and analysed together with data from previous years.

Surveillance of antibiotic-resistant bacteria notifiable according to the Communicable Disease Act

Four bacterial species are included in the Swedish Communicable Disease Act by virtue of their specific resistance mechanisms. These are *Staphylococcus aureus* with resistance to methicillin and other beta-lactam antibiotics (MRSA), *Streptococcus pneumoniae* with reduced susceptibility or resistance to peni-

cillin (PNSP), *Enterococcus faecalis* and *E. faecium* with resistance to vancomycin (VRE), and bacteria belonging to the family *Enterobacteriaceae* carrying extended-spectrum beta-lactamases of three different kinds (referred to as ESBLs). As in previous years, the reports of ESBLs have outnumbered the other three species manifold.

The total number of MRSA cases was 1884 in 2011, an increase by 304 cases (20 percent) compared to 2010. According to the systematically reviewed notification reports the infection was acquired in Sweden (41 percent) only slightly more often than abroad (37 percent), but in many cases the country of acquisition could not be defined. Community-acquired infections dominated among domestic cases (68 percent) but were less frequent among imported cases (42 percent). Hospital-acquired infections were comparatively more common in imported cases (33 percent) than among domestic cases (7 percent), indicating continued good compliance to basal hygiene principles among healthcare staff. Only 21 new invasive isolates of MRSA were found in 2011.

Epidemiological typing of all MRSA isolates by *spa*-typing showed that the five most commonly encountered *spa*-types in 2011 were t008, t002, t044, t019 and t223, comprising one third of all isolates. The prevalence of MRSA with PVL toxin had increased to 41 percent.

Streptococcus pneumoniae: In 2011 there were 314 notifications of PNSP (*Streptococcus pneumoniae* with MIC of penicillin $\geq$ 0.5 mg/L) in Sweden, a decrease by 23 percent compared to 2010. As in previous years, most cases were identified through nasopharyngeal cultures, and they were found in the age group 0-4 years. In 21 cases the PNSP were isolated from blood. Multiresistance (resistance to penicillin and at least two more antibiotics) was common among PNSP. The serotype distribution among all PNSP 2011 had changed, and preliminary results for the most common serotypes were, in decreasing order, types 19F, non-typeable (NT), 35B, 14, 19A, 6B, 23F, and 9V.

Enterococcus faecalis and *Enterococcus faecium*: In 2011 a total of 122 VRE-cases were reported, a decrease by 43 percent compared to 2010. Most cases were sporadic cases, but an increase of *vanA*-carrying *Enterococcus faecium* was noted.

The epidemic situation of a healthcare-related spread of *vanB*-carrying *Enterococus faecium* in four counties in Sweden, which started in 2007 and peaked in 2008, was declared over during 2011. The total number of cases in this outbreak was 872. Increased awareness of the problem, intensive infection control efforts, implementation of screening programmes, contact tracing, and also other measures undertaken seem to have contributed to the reduction in numbers of new cases in 2011. In 2010, however, yet another new strain of *Enterococcus faecium* with *vanB* was spread within the healthcare setting in the county of Västernorrland, including two regional hospitals. Cases belonging to this outbreak were also reported during the first half of 2011, but then the outbreak was declared to be over. The number of cases belonging to the outbreak was estimated to 100. No cases of invasive VRE were seen in 2011.

Enterobacteriaceae producing extended spectrum beta-lactamases (ESBL) were made notifiable by laboratories from February 2007. A total of 5666 cases were notified in 2011, an increase with 14 percent compared to 2010. Reports came from all 21 counties of Sweden, corresponding to a national incidence of 60 cases per 100 000 inhabitants. The most commonly reported species was *Escherichia coli* with 87 percent of all cases, followed by *Klebsiella pneumoniae* with 7 percent. Most ESBLs were found in urine samples (63 percent). Isolates with ESBLs of CTX-M-type dominated, but isolates with plasmid-mediated AmpC enzymes were found in 5-8 percent according to point-prevalence studies performed in 2007, 2009 and 2011. ESBL-producing isolates were often multi-resistant, i.e. resistant to several other antibiotics, seriously limiting the options for treatment.

Special focus has been put on carbapenemase-producing *Klebsiella pneumoniae* and other *Enterobcteriaceae* from all types of samples since 2007, when the first isolate of *K. pneumoniae* with a carbapenemase (KPC-2) was detected in Sweden. From 2007 to 2011 a total of 35 cases with $ESBL_{CARBA}$ have been identified. The two most common enzyme types were KPC and NDM-1, but a few cases with VIM or OXA-48 enzymes were also detected. All the cases were healthcare related and with connection to a foreign country.

Surveillance of invasive bacteria through the European network EARS-Net

Invasive isolates of seven defined bacterial species have been reported to EARSS/EARS-Net since 2000.

Twenty-five MRSA isolates accounted for 0.8 percent of all invasive *Staphylococcus aureus* (n=3118) in 2011. Sweden is thus one of the few countries still remaining at a MRSA level of less than 1 percent.

The rates of non-susceptibility to penicillins in *Streptococcus pneumoniae* (referred to as PNSP) among invasive isolates (n=960) was similar to previous years, 3.5 percent.

There were no VRE reported among invasive isolates of *Enterococcus faecalis* and *Enterococcus faecium*, but high-level resistance to aminoglycosides (HLAR) was common with 17 and 22 percent, respectively.

For *Escherichia coli* (n=5066), the most frequent of the invasive bacterial species reported to EARS-Net, the level of resistance to third generation cephalosporins had increased to 4 percent. In the majority of these isolates the resistance was caused by plasmid-mediated ESBLs of CTX-M type. They were often co-resistant to other antibiotic classes such as aminoglycosides and fluoroquinolones, thereby defined as multi-resistant. The level of aminoglycoside resistance in *E. coli* increased to 5.1 percent in 2011, a level that was higher than that of cephalosporin resistance, indicating the existence of different combinations of resistance genes. Fluoroquinolone resistance, which had been stable at 13-14 percent during four years, decreased to 10.4 percent in 2011.

Invasive isolates of *Klebsiella pneumoniae* (n=934) were rarely resistant to the antibiotics surveyed through EARS-Net. The rates of resistance were 2.2 percent to cephalospor-

ins (caused by ESBL-production) and to aminoglycosides, 5 percent resistance to fluoroquinolones, and no resistance detected against carbapenem antibiotics.

Invasive isolates of *Pseudomonas aeruginosa* (n=402) had the same levels of resistance as in previous years. The rates of resistance were 5.2 percent to ceftazidime, 1 percent to aminoglycosides, 7 percent to fluoroquinolones, and 7.2 percent to carbapenems.

National surveillance and quality assurance programme, RSQC displayed in ResNet

Staphylococcus aureus isolated from skin and soft tissue infections (RSQC programme) were susceptible to tested antibiotics in > 95 percent of cases except for fusidic acid where the level of resistance was 6 percent. MRSA were found at an average of 1.2 percent of the tested bacterial isolates of *Staphylococcus aureus* from these infections. This is in concordance with the epidemiological information that MRSA is increasingly found in the community setting.

Streptococcus pneumoniae has been monitored yearly, and in 2011 the level of intermediate susceptibility or resistance to penicillin (I+R) continued to rise and reached 8.3 percent. For all other tested antibiotics (erythromycin, clindamycin, tetracycline, trimethoprim-sulfa and norfloxacin) the levels remained the same as in 2010.

Escherichia coli, mainly derived from urinary tract infections, has been included in the national surveillance program (RSQC) since 1996. Resistance to ampicillin and to trimethoprim continued to increase and reached approximately 32 percent and 20 percent, respectively. Cephalosporin resistance reached 3.7 percent, reflecting the increased prevalence of ESBL-producing strains, and this explanation is probably valid also for mecillinam with resistance level of 5 percent. Fluoroquinolone resistance, calculated from nalidixic acid screening test, reached 13 percent. Nitrofurantoin was the only drug to which the bacteria were almost all susceptible (99 percent).

Klebsiella pneumoniae in the RSQC programme showed the same low rates of resistance to tested antibiotics as in the EARS-Net surveillance.

Pseudomonas aeruginosa in the RSQC programme also showed the same rates of resistance to tested antibiotics as in the EARS-Net surveillance.

With a few exceptions, *Haemophilus influenzae* has been monitored in the RSQC programme since 1994. Data on beta-lactamase-producing isolates of *H. influenzae* was obtained in the RSQC programme in 2011 and was compared to the same kind of data (recalculated to include only the beta-lactamase positive isolates) from the previous three years. Beta-lactamase production was found in approximately 18 percent of isolates, whereas close to 24 percent of isolates were resistant to trimethoprim-sulfamethoxazole.

Surveillance of other bacterial species

Data on invasive isolates of a few bacterial species were extracted from the database of consecutive blood isolates obtained from 10 laboratories covering approximately 55 percent of the population in Sweden.

Streptococcus pyogenes represented 1.1 percent of the total count of invasive isolates, and of those 3.2 percent were resistant to erythromycin and clindamycin and 13.3 percent to tetracycline. *Streptococcus agalactiae* represented 1.2 percent of the invasive isolates, and 6.8 percent were resistant to erythromycin and clindamycin, a figure similar to those from the previous years.

Only 0.5 percent of invasive isolates were *Haemophilus influenzae*. Fourteen of those (18 percent) were ampicillin-resistant and beta-lactamase producing, two isolates were classified as BLNAR, and twelve (16 percent) were resistant to trimethoprim-sulfamethoxazole.

The national surveillance program for *Clostridium difficile* initiated by SMI in 2009 has continued in 2010 and 2011. On all *C. difficile* isolates collected during weeks 11 and 39, susceptibility tests and PCR ribotyping was performed. Resistance rates to moxifloxacin, erythromycin and clindamycin were 14-15 percent, and most of the resistant isolates were associated with PCR ribotypes 012, 017, 046 and 231/SE37. There was an overall positive correlation between the rate of moxifloxacin use and the proportion of moxifloxacin resistant isolates.

Antibiotic resistance in gastrointestinal pathogens has been monitored regularly at the University Hospital MAS, Skåne.

In *Helicobacter pylori* derived from gastric biopsies clarithromycin resistance has shown a steady increase since 1994, but the level of resistance suddenly reached 26.3 percent in 2011. In *Campylobacter* spp. high levels of resistance were seen for fluoroquinolones (> 65 percent), tetracyclines (> 35 percent) and low but variable for erythromycin (1-8 percent) during the last ten years. In *Salmonella* spp. and *Shigella* spp. the levels of fluoroquinolone resistance is high although these species are not monitored as regularly as others. Twenty-one *Salmonella* isolates were reported as ESBL-producing in 2011. The majority of those were acquired abroad with Thailand as the most frequently reported country.

Neisseria spp*:* Gonorrhoea is a notifiable disease, and in 2011 951 cases of the disease were reported. Isolates from 805 of those were completely characterised at the Swedish Reference Laboratory for Pathogenic Neisseria, Örebro University Hospital, at Karolinska University Hospital Huddinge, Stockholm, or at University Hospital MAS, Skåne. In 2011 23 percent of the isolates were beta-lactamase producing and ampicillin resistant, 55 percent were resistant to ciprofloxacin, 11 percent were resistant to azithromycin, but alarmingly also 2 percent were resistant to ceftriaxone.

Among *Neisseria meningitidis* 11 percent had reduced susceptibility to penicillin.

Mycobacterium tuberculosis: The total number of new cases of tuberculosis diagnosed in Sweden 2011 was 595, a 13 percent decrease compared to 2010. The cases diagnosed with isoniazid resistant tuberculosis in 2011 represented 12 percent and with multi-drug resistant tuberculosis 3.6 percent. Genetic typing with RFLP (restriction fragment length polymorphism) was performed on resistant strains, and 36 isolates belonged to 31 different clusters with two or more patients in each cluster.

2.2. Sammanfattning

Antibiotikaförbrukning

Den totala antibiotikaanvändningen ökade något (0,9 procent) under 2011 jämfört med 2010. I öppenvården sågs en minskning med 1,3 procent mätt i antal recept per 1000 invånare. Minskningen orsakades till stora delar av en kraftig nedgång (11,1 procent) i antibiotikaförskrivning till barn i åldern 0-4 år. I alla andra åldersgrupper ökade användningen av antibiotika. Antibiotikaförskrivning till barn har varit i fokus för flera informationskampanjer under de gångna åren och användningen i denna åldersgrupp har minskat kraftigt de senaste två decennierna. Även om antibiotikaförbrukningen är hög i barngruppen så står övriga åldersgrupper för merparten av all antibiotikaförbrukning.

Minskningen sågs i dryga hälften av alla län men det finns fortfarande stora skillnader inom landet. Antibiotikaförbrukningen varierade från 417 i Stockholms län till 310 i Västerbottens län, mätt i recept per 1000 invånare och år.

Minskningen som skedde under 2011 omfattar nästan alla antibiotikagrupper utom följande substanser som ökade: tetracykliner (6,1 procent), nitrofurantoin (6,9 procent), pivmecillinam (1,3 procent) och linkosamider (0,9 procent). Vid analys av antibiotikaanvändning i öppenvård månad för månad, ses en ökad användning av tetracykliner och makrolider i alla åldersgrupper under den första och de sista tre månaderna jämfört med 2010. Dessa två antibiotikagrupper används ofta vid behandling av *Mycoplasma penumoniae* och under influensasäsongen 2011 sågs en ökad förekomst av *Mycoplasma pneumoniae* i Sverige.

Beta-laktamaskänsliga penicilliner tillsammans med tetracykliner är de antibiotika som oftast förskrivs på recept. Bland de förstnämnda är penicillin V den substans som förskrivs mest och under 2011 minskade användningen av penicillin V med 0,6 procent.

Behandling av nedre urinvägsinfektion hos kvinnor ser ut att följa nationella rekommendationer. De två rekommenderade förstahandspreparaten, pivmecillinam och nitrofurantoin, har successivt ökat och utgjorde 2011 74,3 procent av den totala försäljningen av antibiotika som ofta används mot urinvägsinfektioner. Data från 66 vårdcentraler i Sverige visade att nedre urinvägsinfektion är den enskilda diagnosen som leder till flest antibiotikarecept.

I slutenvården ökade den totala antibiotikaanvändningen med 4,2 procent under 2011, mätt i DDD per 1000 invånare och dag. De senaste åren har antibiotikaanvändningen på sjukhus skiftat från en hög användning av cefalosporiner till en ökad användning av smalspektrumpenicilliner. Denna trend fortsatte även under 2011. Det finns dock fortfarande stora skillnader mellan länen i detta avseende. De regionala skillnaderna är också tydliga när det gäller användningen av nyare klasser av bredspektrumantibiotika, såsom karbapenemer och piperacillin med tazobaktam. Användningen av den senare ökade med 12,0 procent under 2011.

Förbrukning av antimykotika

Användningen av läkemedel för systemiskt bruk mot svampinfektioner har ökat successivt under de senaste åren. Under 2011 ökade den totala användningen med 4 procent till 64 DDD per miljon invånare och dag. Denna ökning ses framförallt för amfotericin B som ökade med 18 procent och som nu är det vanligaste bredspektrumpreparatet. Caspofungin har också ökat med 18 procent. Därmed fortsätter trenden mot att smalspektrumantimykotika, d.v.s. flukonazol, minskar och att bredspektrumantimykotika tar motsvarande marknadsandel. Denna utveckling ses än tydligare om man inkluderar receptförsäljning av vorikonazol och posakonazol i statistiken över preparat använda på sjukhus, eftersom dessa läkemedel så gott som alltid förskrivs av sjukhusspecialister. Flukonazol utgör dock fortfarande den absolut största delen av antimykotika på sjukhus med 69 procent av DDD.

Den totala mängden av antimykotika på sjukhus är fortsatt låg med 64 DDD per miljon invånare och dag. Det är dock viktigt att noga följa både resistens och konsumtionsdata på både lokal och nationell nivå för att tidigt upptäcka förändringar i resistensmönster eller i artfördelning.

Antibiotikaresistens

Antibiotikaresistens hos vissa bakteriearter anmäls enligt smittskyddslagen (MRSA, VRE, PNSP och ESBL), men den frivilliga rapporteringen av resistensdata från de svenska kliniskt mikrobiologiska laboratorierna utgör basen för resistensövervakningen. Alla laboratorier deltar sålunda i den årliga insamlingen av data till ResNet (RSQC), och tre fjärdedelar av laboratorierna bidrar med data avseende invasiva isolat av sju bakteriearter som definierats av EARS-Net. För vissa mikroorganismer sammanställs data av laboratorier med referensfunktion och/eller specialkunskap (till exempel referenslaboratoriet för *Neisseria*-arter i Örebro). I denna rapport presenteras aktuella svenska resistensdata från 2011 och kommenteras i förhållande till föregående års data.

Övervakning av resistenta bakterier enligt Smittskyddslagen

Fyra bakteriearter är inkluderade i Smittskyddslagen på grund av deras specifika resistensmekanismer. Det gäller *Staphylococcus aureus* med resistens mot meticillin och alla andra betalaktamantibiotika (MRSA), *Streptococcus pneumoniae* med nedsatt känslighet för penicillin (PNSP), *Enterococcus faecalis* och *E. faecium* med resistens mot vankomycin (VRE), och bakterier tillhörande familjen *Enterobacteriaceae* med ESBL av olika typer (kallas ofta enbart ESBL). Liksom tidigare år var rapporteringen av ESBL flerfaldigt högre än för de övriga tre.

Totalt 1884 fall av MRSA anmäldes 2011, en ökning med 304 fall (20 procent) från 2010. Enligt den noggrant genomgångna rapporteringen kring fallen var det nästan lika vanligt med smitta i Sverige (41 procent) som smitta utomlands (37 procent), men i många fall kunde man inte säkert säga var smit-

tan ägt rum. Samhällsförvärvad smitta var vanligare bland de inhemskt smittade fallen (68 procent) än bland de utomlands smittade (42 procent). Sjukhusförvärvad smitta var däremot vanligare bland importerade fall (33 procent) än bland inhemska (7 procent). Endast 21 nya fall av MRSA i blod upptäcktes 2011. Epidemiologisk typning av alla MRSA-isolat med *spa*-typning visade att de fem vanligaste *spa*-typerna fortfarande var t008, t002, t044, t019 och t223. De utgjorde tillsammans en tredjedel av alla isolat. Förekomsten av MRSA med PVL-toxin hade ökat till 41 procent.

Streptococcus pneumoniae: Under 2011 noterades 314 fall av PNSP (isolat med MIC av penicillin > 0,5 mg/L), en minskning med 23 procent. Liksom tidigare år fanns majoriteten av PNSP-fallen i åldersgruppen 0-4 år. I 21 fall påvisades PNSP från blod. Multiresistens (resistens mot penicillin och minst två andra antibiotika) var vanlig hos PNSP. De vanligast förekommande serotyperna var 19F, ej typbara (NT), 35B, 14, 19A, 6B, 23F och 9V.

Enterococcus faecalis och *Enterococcus faecium*: Under 2011 rapporterades 122 fall av VRE, en minskning med 43 procent jämfört med 2010. De flesta fallen bedömdes som sporadiska, men en ökning av *vanA*-bärande *Enterococcus faecium* kunde konstateras. Det stora utbrottet med en *vanB*-innehållande *Enterococcus faecium* som pågått i Stockholms, Hallands, Uppsala och Västmanlands län med start 2007 och en topp 2008, förklarades under 2011 avslutat av respektive län. Det hade då totalt omfattat 872 fall. Under 2010 drabbade en ny *vanB*-innehållande *Enterococcus faecium* stam två sjukhus i Västernorrland. Nya fall upptäcktes även 2011, varefter även det utbrottet förklarades avslutat. Det hade då totalt omfattat 100 fall.

Enterobacteriaceae som producerar betalaktamaser med utvidgat spektrum, så kallade ESBL, blev anmälningspliktiga i februari 2007. Totalt 5666 fall rapporterades under 2011, en ökning med 14 procent. Samtliga landsting rapporterade, och den genomsnittliga incidensen i Sverige var 60 fall per 100 000 invånare. De flesta isolaten återfanns i urinprover och vanligast var *Escherichia coli* (87 procent) följt av *Klebsiella pneumoniae* (7 procent). ESBL av CTX-M-typ dominerade, men fynd av plasmidmedierat AmpC (så kallad $ESBL_M$) utgjorde 5-8 procent i punktprevalensstudier från 2007, 2009 och 2011. Multiresistens var ett vanligt fynd hos isolaten med ESBL.

Särskild uppmärksamhet har ägnats karbapenemas-producerande *Klebsiella pneumoniae* och även andra *Enterobacteriaceae* sedan 2007, då det första *K. pneumoniae* isolatet med karbapenemas av KPC-typ upptäcktes i Sverige. Från 2007 till 2011 har totalt 35 fall med så kallad $ESBL_{CARBA}$ identifierats. De två vanligaste enzymtyperna har varit KPC och NDM-1, men enstaka fall med VIM respektive OXA-48 har också upptäckts. I samtliga dessa fall fanns en bakomliggande historia med sjukvård utomlands.

Övervakning av blodisolat genom EARS-Net

Invasiva isolat av sju definierade bakteriearter ingår i det europeiska nätverket för resistensövervakning, EARS-Net. Från Sverige medverkar 20 laboratorier, vilket ger en täckning av ca 80 procent av befolkningen, och följande har rapporterats under 2011:

Tjugofem MRSA identifierades av totalt 3118 *Staphylococcus aureus* från blododlingar, vilket utgjorde 0,8 procent. Sverige är därmed fortfarande ett av få länder i Europa som ännu ej nått nivån 1 procent.

Frekvensen PNSP hos totalt 960 invasiva isolat av *Streptococcus pneumoniae* var fortsatt låg, 3,5 procent.

Inga fynd av VRE gjordes bland invasiva *Enterococcus faecalis* och *E. faecium* 2011, men höggradig aminoglykosidresistens (HLAR) var vanlig hos båda enterokock-arterna med 17 respektive 22 procent av isolaten.

Escherichia coli är den vanligaste av de bakteriearter som rapporteras till EARS-Net, och 5066 isolat från blod ingick 2011. Resistens mot 3:e generationens cefalosporiner hade ökat till 4 procent, och hos majoriteten av dessa var resistensen orsakad av plasmidmedierade ESBL av CTX-M-typ. De cefalosporin-resistenta stammarna var ofta resistenta även mot andra antibiotikagrupper som aminoglykosider och kinoloner. Den totala resistensen mot aminoglykosider hade ökat till 5,1 procent, medan däremot kinolonresistensen, som de senaste åren legat på 13-14 procent, nu hade sjunkit till 10,4 procent.

Invasiva isolat av *Klebsiella pneumoniae* (n=934) var oftast känsliga för de antibiotika som rapporteras till EARS-Net. Resistensen låg på 2,2 procent mot cefalosporiner (på grund av ESBL-produktion) och aminoglykosider, 5 procent mot kinoloner, men däremot ingen resistens mot karbapenemer.

Invasiva isolat av *Pseudomonas aeruginosa* (n=402) hade samma resistensnivåer som tidigare år. De låg på 5,2 procent mot ceftazidim, 1 procent mot aminoglykosider, 7 procent mot kinoloner och 7,2 procent mot karbapenemer.

ResNet för kvalitetssäkring och övervakning av resistens

Staphylococcus aureus i sårinfektioner var i mer än 95 procent av fallen känsliga för antibiotika med undantag för fusidinsyra, där resistensnivån var 6 procent. Andelen MRSA hade för första gången sedan mätningarna startade överstigit 1 procent. Detta har sannolikt samband med att MRSA allt oftare är en samhällsförvärvad infektion.

Streptococcus pneumoniae i odlingsprov från luftvägar har ingått i övervakningen sedan 1994. Vid mätningar 2011 hade andelen isolat med nedsatt känslighet för penicillin ökat till 8,3 procent, medan resistensen mot övriga testade antibiotika (erytromycin, klindamycin, tetracyklin, trimetoprim-sulfa och norfloxacin) var densamma som 2010.

Escherichia coli huvudsakligen från urinvägsinfektioner, har ingått i övervakningen sedan 1996. Resistens mot ampicillin och trimetoprim hade fortsatt att öka och uppgick till 32 respektive 20 procent 2011. Cefalosporin-resistensen var 3,7 procent, till stor del orsakad av ESBL-producerande isolat, och den

resistensmekanismen ledde också till resistens mot mecillinam på cirka 5 procent. Resistens mot kinoloner (testat med nalidixinsyra) var 13 procent. Nitrofurantoin var det enda urinvägsantibiotikum mot vilket nästan alla isolat (99 procent) var känsliga.

Klebsiella pneumoniae och *Pseudomonas aeruginosa* hade resistensnivåer vid mätningar i ResNet som var desamma som de i övervakningen av blodisolat via EARS-Net.

Haemophilus influenzae: Data från övervakningen i ResNet 2008-2011 visade att cirka 18 procent av isolaten var betalaktamas-producerande (och alltså ampicillin-resistenta). Från 2010 har testmetoden för *H. influenzae* ändrats, och frågan om den nya testen med penicillin 1 unit-lappen ger en sann bild av andelen BLNAR är ännu inte helt besvarad. Tidigare år har förekomsten av BLNAR varit 2-4 procent medan de nu ser ut att utgöra cirka 14 procent. Resistensen mot trimetoprim-sulfa hade ökat till nästan 24 procent.

Antibiotikaresistens hos andra bakteriearter

Data rörande invasiva isolat av vissa arter har hämtats ur databasen över samtliga positiva blododlingar från 10 laboratorier, vilka tillsammans täcker cirka 55 procent av befolkningen.

Streptococcus pyogenes utgjorde 1,1 procent av de invasiva isolaten. Av dessa var 3,2 procent resistenta mot erytromycin och klindamycin, och 13,3 procent var tetracyklinresistenta. *Streptococcus agalactiae* utgjorde 1,2 procent av de invasiva isolaten. Av dessa var 6,8 procent makrolidresistenta, vilket var i samma storleksordning som 2007-2010. *Haemophilus influenzae* var ett sällsynt fynd bland invasiva isolat, endast 0,5 procent av fallen. Fjorton (18 procent) var betalaktamas-producerande och tolv (16 procent) var resistenta mot trimetoprim-sulfa.

Den nationella övervakningen av *Clostridium difficile*, som initierades av Smittskyddsinstitutet 2009, har fortsatt 2010 och 2011. Isolat från alla laboratorier samlades in under veckorna 11 och 39, och resistensbestämning och PCR ribotypning utfördes på samtliga isolat. Resistensen mot moxifloxacin, erytromycin och klindamycin var 14-15 procent. Flertalet resistenta isolat var associerade med PCR-ribotyperna 012, 017, 046 och 231/SE37. Det fanns en positiv korrelation mellan användningen av moxifloxacin och frekvensen moxifloxacin-resistenta isolat.

Antibiotikaresistens hos gastrointestinala patogener har övervakats regelbundet vid Universitetssjukhuset MAS, Skåne. Hos *Helicobacter pylori* från biopsier har resistensen mot klaritromycin ökat stadigt under många år, men 2011 var den plötsligt uppe på nivån 26 procent. Hos *Campylobacter* spp. 2011 var kinolonresistensen > 65 procent, tetracyklinresistensen > 35 procent, och erytromycinresistensen cirka 7 procent. Hos *Salmonella* och *Shigella* var kinolonresistensen fortsatt hög, men dessa båda arter övervakas inte lika regelbundet som andra. Tjugoen isolat av *Salmonella* rapporterades 2011 som ESBL-producerande enligt Smittskyddslagen, och flertalet av dessa fall hade Thailand som troligt smittland.

Neisseria species: Gonorré är en anmälningspliktig sjukdom och 2011 rapporterades 951 kliniska fall. Isolat av *N. gonorrhoeae* från 805 av dessa har undersökts vid det svenska referenslaboratoriet i Örebro, vid Karolinska Universitetssjukhuset Huddinge, Stockholm, eller vid Universitetssjukhuset MAS, Skåne. 2011 var 23 procent av isolaten beta-laktamasproducerande och därmed ampicillinresistenta, 55 procent resistenta mot ciprofloxacin, 11 procent resistenta mot azitromycin, och alarmerande var att 2 procent även var resistenta mot ceftriaxon.

Bland *N. meningitidis* hade 11 procent nedsatt känslighet för penicillin.

Mycobacterium tuberculosis: Antalet anmälda nya fall av tuberkulos var 595 under 2011, en minskning med 13 procent från 2010. *M. tuberculosis* med resistens mot isoniazid var 12 procent, och resistens mot minst två antibiotika (MDR-TB) rapporterades hos 3,6 procent. Epidemiologisk typning med RFLP av de resistenta isolaten visade att 36 stycken tillhörde 31 olika kluster med två eller fler patienter i varje.

3. Use of antimicrobials

3.1. Use of antibiotics

Interpretation of data

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

Comparison of use of antibiotics between 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 this consumption is 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 consumption is 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 is displayed (children 0-6 years, women 18-79 years, inhabitants in a county), the denominator is the number of individuals in the same group.

In this report the term outpatient care includes primary care, open specialist surgeries and parts of nursing homes. Hospital care includes antibiotic sales to hospitals and parts of nursing homes. Since national data on sales of antibiotics to hospitals in Sweden is 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 hospitals has 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 the comparisons based on the statistics.

Total sales of antibiotics

The total use of antibiotics in Sweden increased slightly (0.9%) during 2011 compared with 2010 measured as DDD per 1000 inhabitants and day, Figure 3.1.1. Eighty-nine percent of all antibiotics used in Sweden 2011 were sold in outpatient care. Even though the majority of all antibiotics is prescribed in outpatient care, studies have shown that the antibiotic pressure in Swedish hospitals is high. One of three inpatients are treated with antibiotics.

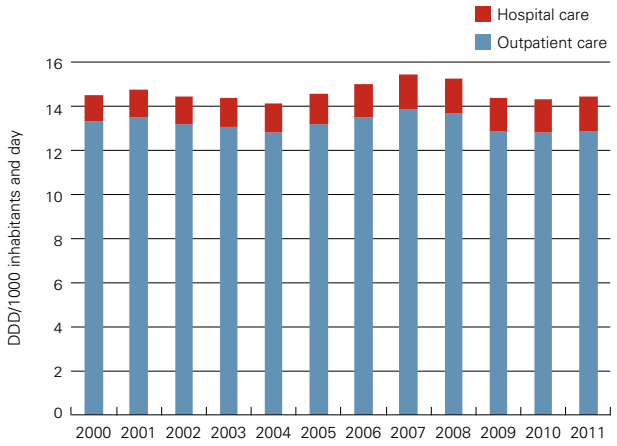


FIGURE 3.1.1. Sales of antibiotics in outpatient and hospital care 2000-2011, DDD/1000 inhabitants and day.

Beta-lactamase sensitive penicillins and tetracyclines are the two antibiotics that were used in greatest amount in Sweden in 2011, Figure 3.1.2.

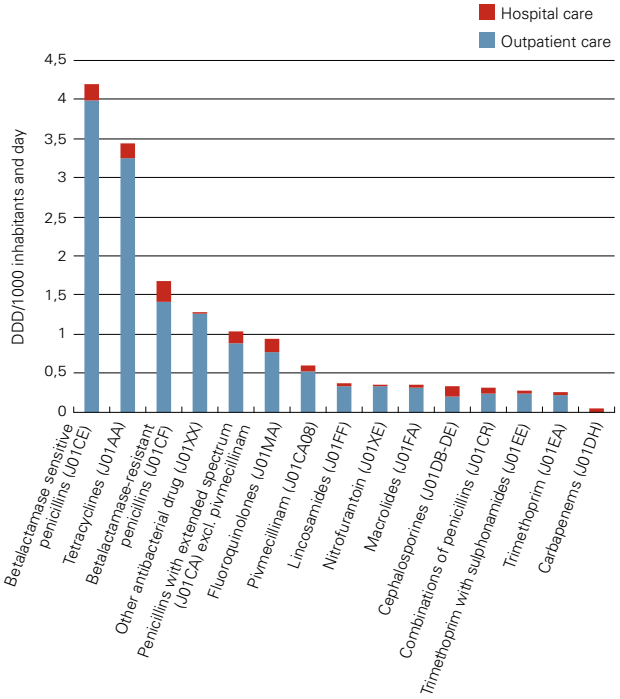


FIGURE 3.1.2. Antibiotics in outpatient and hospital care 2011, DDD/1000 inhabitants and day.

Outpatient care

Sales of antibiotics in outpatient care decreased by 1.3% in 2011, from 390.3 to 385.3 prescriptions per 1000 inhabitants and year. The decrease was related to a great reduction in antibiotic prescribing to the youngest children aged 0-4 years. In this age group the number of prescriptions decreased by 11.1% in 2011, from 542.4 to 482.2 prescriptions per 1000 inhabitants and year. The sale of antibiotics to children aged 0-4 years has decreased with 63.7% since 1992.

In all other age groups the antibiotic use expressed as prescriptions per 1000 inhabitants increased in 2011, Figure 3.1.3.

Since 2009 the age group 65-99 years has the highest use of antibiotics in Sweden measured as prescriptions per 1000 inhabitants and year, Figure 3.1.3. As mentioned earlier in the chapter Interpretation of data, some of the antibiotic use among elderly people is not included in the statistics and possible under-reporting in the age group 65-99 years must be taken into account.

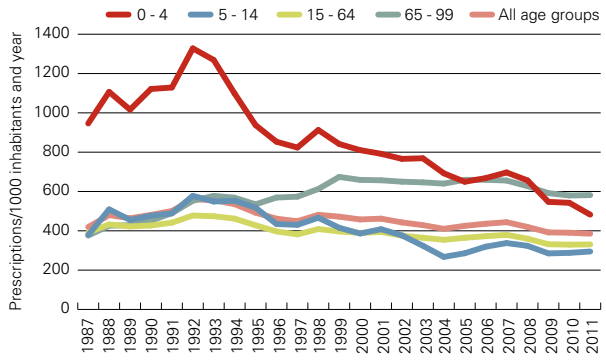


FIGURE 3.1.3. The sales of antibacterial drug for systemic use in outpatient care 1987- 2011, prescriptions/1000 inhabitants and year, both sexes, different age groups.

The slight decrease in antibiotic prescription during 2011 encompasses a majority of all antibiotic groups, Table 3.1.1. Trimethoprim (J01EA), cephalosporines (J01DB-DE) and combinations of penicillins (J01CR) are the antibiotic groups with the greatest decrease expressed in percentage (-14.1%, -9.3% and -9.3% respectively), Figure 3.1.4. The reduction of these substances is seen in most age groups but in varying magnitude, Table 3.1.1.

Beta-lactamase sensitive penicillins (J01CE) and tetracyclines (J01AA) were the most commonly prescribed antibiotics in outpatient care 2011, Figure 3.1.4. Doxycycline (J01AA02) is the most frequently used tetracycline and represents 77% of the sales in this group of substances. Tetracyclines (J01AA) together with nitrofurantoin (J01XE) are also the antibiotic groups that increased most in 2011 expressed as percentage (6.1% and 6.9% respective), Figure 3.1.4.

When analyzing the antibiotic use in 2011 month by month, an increased use is seen during the first and the last three months (January-February and October-December) compared with 2010. During these months, a great increase of tetracyclines (J01AA) and macrolides (J01FA) are seen. The high use of tetracyclines and macrolides during the first and last quarters of 2011 can partly explain why the total antibiotic use in Sweden during 2011 did not decrease more than 1.3% despite strong incentives for restrictive prescribing in outpatient care. Read more about the use of tetracyclines (J01AA) and macrolides in the chapter Antibiotics commonly used to treat respiratory tract infections.

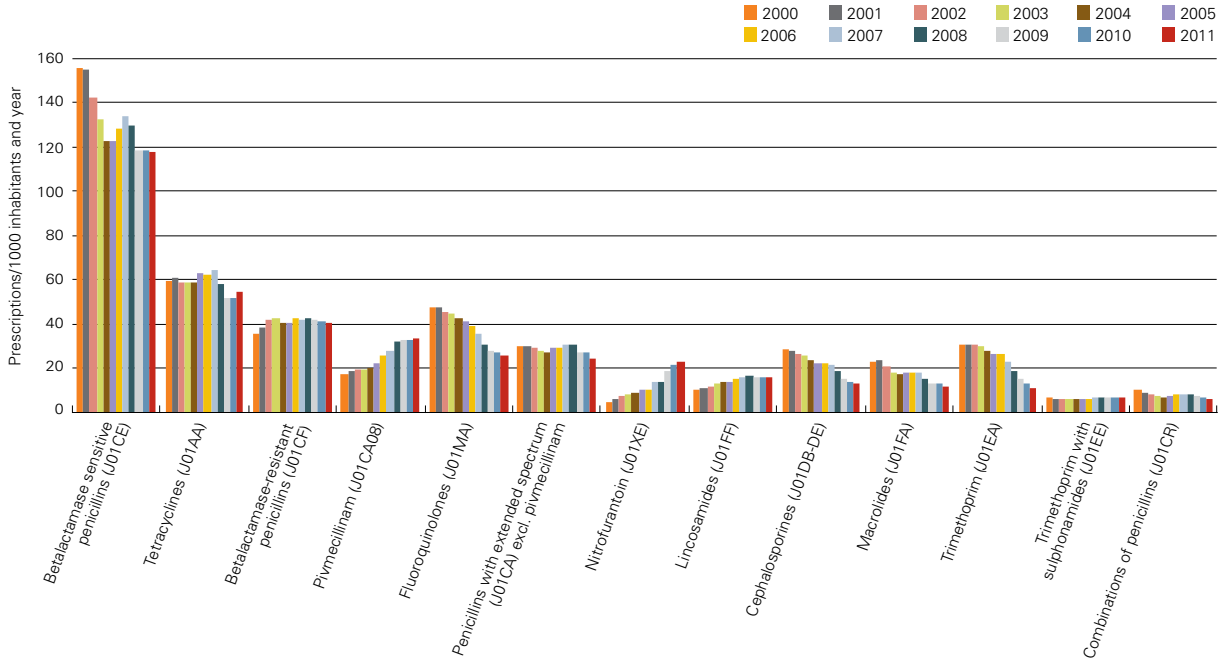


FIGURE 3.1.4. Antibiotics in outpatient care 2000-2011, prescriptions/1000 inhabitants and year, both sexes, all ages. The data are sorted according to the use in 2011.

Gender differences

59.5% of all antibioitcs prescribed in Sweden 2011 were to females and 40.5% to males. This proportion has almost been constant over time and the decrease in antibiotic use that has been seen during the last years has included both genders, Figure 3.1.5.

Among the youngest children, boys get more antibiotic prescriptions per 1000 inhabitants and year. In all other age groups the opposite is seen. The largest differences between genders occur during age 15-39 years and in this age group the main differences is among antibiotics commonly used to treat urinary tract infections, Figure 3.1.6.

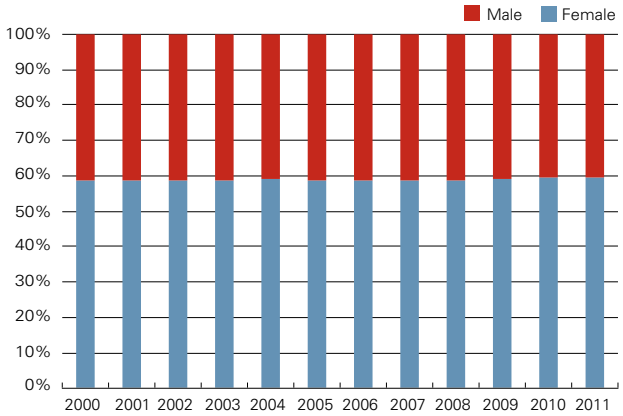


FIGURE 3.1.5. The proportion of antibiotics (J01 excl. methenamine) prescribed to males and females in Sweden 2000-2011, percents of prescriptions.

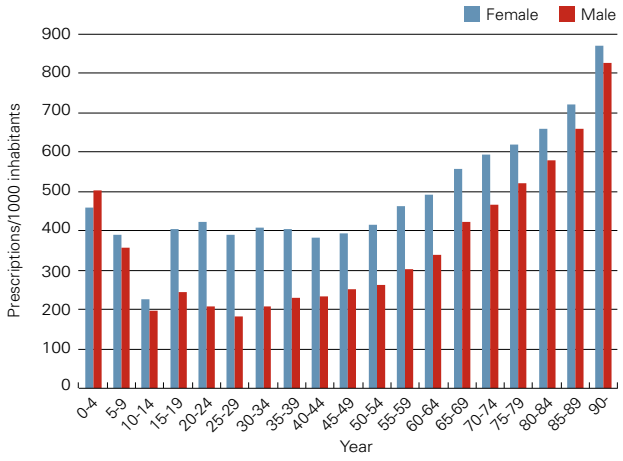


FIGURE 3.1.6. Sale of antibiotic (J01 excl. methenamine) to males and females, different age groups, prescriptions/1000 inhabitants in 2011.

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

Antibiotics commonly used to treat respiratory tract infections are 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 1000 inhabitants and year. In 2011 antibiotics commonly used to treat respiratory tract infections decreased from 217.8 to 215.0 prescriptions per 1000 inhabitants.

Figures 3.1.7 and 8 clearly illustrate the consumption of different antibiotics in different age groups. Even though the antibiotic use is high among children, other age groups represent a great share of the total antibiotic consumption.

When measuring the antibiotic use during 2011 in DDD, the use is greatest in the age groups 15-19, 60-64 and 65-69 years. In the age group 15-19 years, antibiotics commonly used to treat acne represent the largest proportion of all antibiotics and the prescribing of these antibiotics has increased over the recent years.

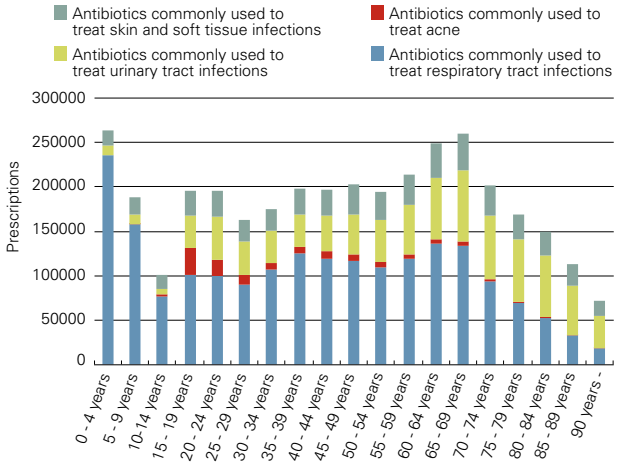


FIGURE 3.1.7. Antibiotics commonly used to treat: respiratory tract infections (J01AA02, J01CE02, J01CA04, J01CR02, J01DB-DE and J01FA), urinary tract infections (J01CA08, J01EA01, J01MA02, J01MA06 and J01XE01), skin and soft tissue infections (J01FF01 and J01CF05), acne (J01AA04, J01AA06 and J01AA07), both sexes, different age groups, prescriptions in 2011.

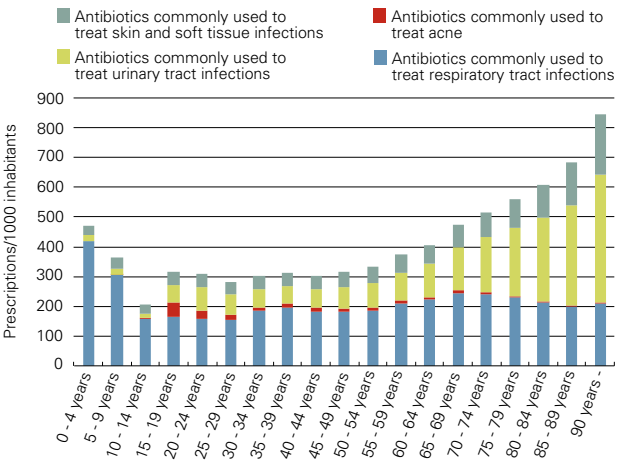


FIGURE 3.1.8. Antibiotics commonly used to treat: respiratory tract infections (J01AA02, J01CE02, J01CA04, J01CR02, J01DB-DE and J01FA), urinary tract infections (J01CA08, J01EA01, J01MA02, J01MA06 and J01XE01), skin and soft tissue infections (J01FF01 and J01CF05), acne (J01AA04, J01AA06 and J01AA07), both sexes, different age groups, prescriptions/1000 inhabitants in 2011.

Antibiotics commonly used to treat respiratory tract infections

Narrow spectrum penicillin, penicillin V, is the recommended first line antibiotic for treatment of common community acquired respiratory tract infections in Sweden and is the most prescribed antibiotic in outpatient care. In the age group 0-6 years, the use of penicillin V decreased with a great amount during 2011, from 290.6 to 271.1 prescriptions per 1000 inhabitants and year. In all other age groups the use of penicillin V actually increased, Table 3.1.1.

Doxycycline is the second most prescribed antibiotic substance in outpatient care. This substance is mainly used to treat respiratory tract infections, which can be one explanation to the great seasonal variation, Figure 3.1.9.

Doxycycline and macrolides, which are commonly used to treat *Mycoplasma pneumoniae*, increased with 20.4% and 2.6% respectively during the fourth quarter in 2011 compared with the same period in 2010, Figure 3.1.9. During the influenza season 2011 an increased prevalence of *Mycoplasma pneumoniae* was seen in Sweden which probably can explain the increased use of doxycyclin and macrolides seen in the latest month of 2011. The greatest increase of these substances was seen in the age group 7-19 years, Table 3.1.1. Read more about the increased number of *Mycoplasma pneumoniae* cases at the website of the Swedish Institute for Communicable Disease Control.

There was a shortage of erythromycin (J01FA01) during the summer and autumn 2011 which can explain the drop in use during these months showing in figure 3.1.9. During this period the prescribing of other types of macrolides (azitromycin and chlarithromycin) increased.

Antibiotics commonly used to treat urinary tract infections

Recommendations for the treatment of lower urinary tract infections in women over 18 years, launched by Strama and the Swedish Medical Products Agency in 2007, recommend pivmecillinam and nitrofurantoin over trimethoprim, and prescribers are also encouraged to minimize the use of fluoroquinolones. The two first-line drugs account for 74.3% of antibiotics commonly prescribed to treat this condition in women in 2011. This is a greater proportion than in 2010 and according to treatment recommendations. Taken together, the total prescribing of antibiotics commonly used to treat urinary tract infections in women in 2011 decreased with 0.5% expressed as prescriptions per 1000 women and with 2.8% expressed as DDD per 1000 women, Figure 3.1.10

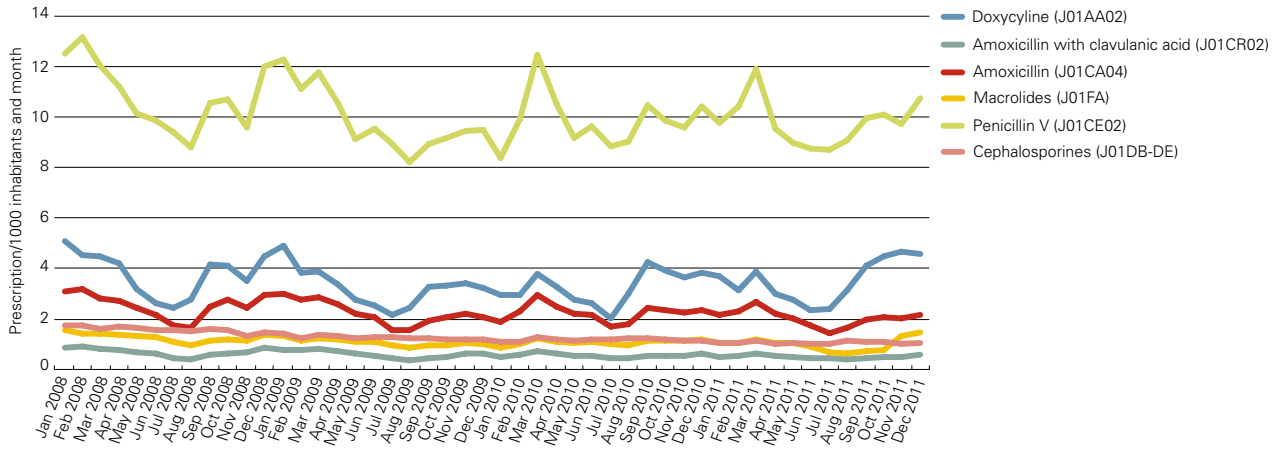


FIGURE 3.1.9. Seasonal variation of antibiotics commonly used to treat respiratory tract infections in outpatient care, 2008-2011, prescriptions/1000 inhabitants and month, both sexes, all ages.

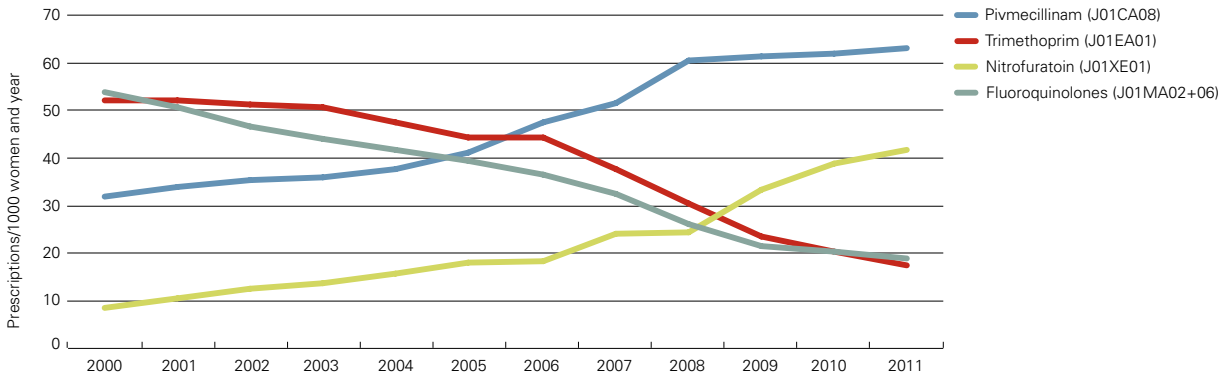


FIGURE 3.1.10. Antibiotics commonly used to treat lower urinary tract infections in women, 2000-2011, prescriptions/1000 women and year.

Antibiotic consumption in children

Antibiotic prescribing to children aged 0-6 years decreased by 9.2% in 2011, from 515.0 to 467.6 prescriptions per 1000 children. The great fall concerns all antibiotic groups except lincosamides (J01FF) and nitrofurantoin (J01XE). The greatest decrease was seen in the use of amoxicillin with clavulanic acid (J01CR02) and amoxicillin (J01CA04) (29.6% and 19.4%) measured as prescriptions per 1000 children in 2011, Table 3.1.1. New recommendations for treatment of acute otitis media were launched by Strama and the Swedish Medical Products Agency in 2010. The new recommendations have been attracting attention from professionals and the public in 2010 and 2011 which may have influenced the antibiotic use to young children.

Different kinds of penicillins are the most commonly prescribed antibiotics to this age group and penicillin V (J01CE02), amoxicillin (J01CA04) and flukloxacillin (J01CF05) represents 76.6%.

Data from the Swedish Prescribed Drug Register (appendix 3) shows that the share of children treated with at least one course of any kind of antibiotic decreased in all counties in 2011. The share ranges within the country from 316.0 users per 1000 children in Skåne County to 154.7 users per 1000 children in Jämtland County, Figure 3.1.11. Taken together, in Sweden the share of children treated with at least one course of antibiotics was 273.3 users per 1000 children, which is 9.3% lower than in 2010, Table 3.1.1.

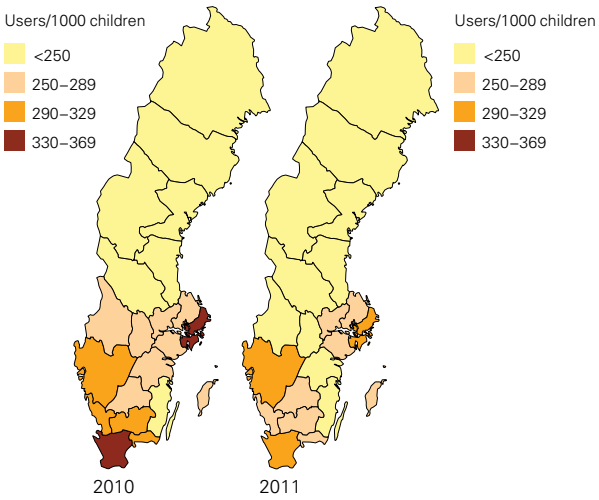


FIGURE 3.1.11. Share of children age 0-6 years treated with at least one course of antibiotics (J01 excl. methenamine) in 2010 and 2011 (users/1000 children and year).

Antibiotic use in children has been in focus of both local and national information activities the last years. The great reduction in sales of antibiotics to children the last years may have several explanations; information about hand hygiene being one and new treatment recommendations for acute otitis media being another.

County data

The share of people treated with at least one course of any kind of antibiotic was 226.3 users per 1000 inhabitants, which is almost the same as in 2010, Table 3.1.1. However, the share of people treated with antibiotics varies within Sweden, from 246.2 users per 1000 inhabitants in Stockholm County to 180.9 users per 1000 inhabitants in Västerbotten County. The antibiotic use is greatest in big cities and their surroundings. In total, the share decreased in 13 out of 21 counties, in 2011, Figure 3.1.12.

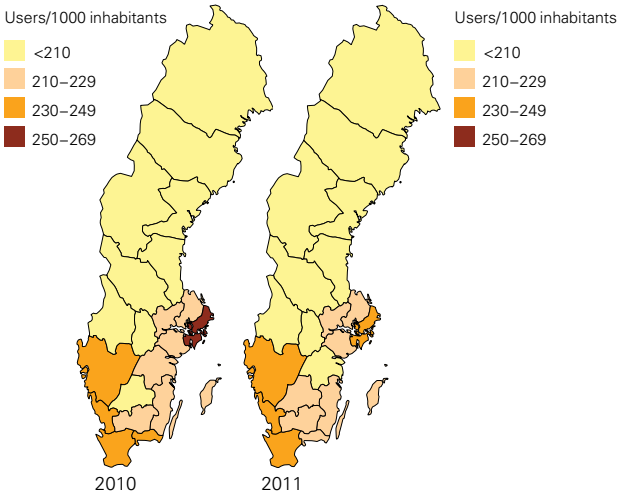


FIGURE 3.1.12. Share of people treated with at least one course of antibiotics (J01 excl. methenamine) in 2010 and 2011 (users/1000 inhabitants and year).

In 2011 the average use of antibiotics in outpatient care measured as prescriptions per 1000 inhabitants in Sweden was 385.3. To reach the Swedish long term target of at most 250 prescriptions per 1000 inhabitants and year the antibiotic use in Sweden must decrease with 35%. Read more about the Swedish target for antibiotic use in chapter *Agreement concerning improved patient safety*. In 2011, a decreased number of prescriptions per 1000 inhabitants is seen in 12 out of 21 counties. There are great regional differences within the country and prescriptions per 1000 inhabitants range from 416.6 in Stockholm County to 310.0 in Västerbotten County, Figure 3.1.13.

TABLE 3.1.1. Antibiotics in outpatient care, classes of antibiotics and age groups. DDD/1000 inhabitants and day, prescriptions/1000 inhabitants and year and users/1000 inhabitants and year, 2006-2011.

	DDD/1000 and day						Prescriptions/1000 and year						Users/1000 and year					
Age group (years)	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**
Tetracyclines (J01AA)																		
0-6	0.00	0.00	0.00	0.00	0.00	0.00	0.1	0.0	0.0	0.0	0.0	0.1	0.1	0.0	0.0	0.0	0.0	0.1
7-19	3.12	3.23	3.26	3.31	3.40	3.48	32.7	33.9	32.0	31.6	32.5	35.1	20.4	21.5	19.6	19.2	20.1	22.9
20-59	3.56	3.68	3.50	3.26	3.32	3.52	66.3	68.3	61.3	53.7	53.9	58.2	51.8	53.4	47.6	41.7	42.0	45.7
60-79	4.11	4.29	4.05	3.64	3.60	3.75	96.3	99.3	90.1	78.3	77.0	79.6	71.6	74.4	67.2	60.1	59.4	61.3
80 -	2.89	2.93	2.78	2.43	2.32	2.35	76.4	77.8	71.7	62.2	58.6	58.8	60.1	62.0	56.8	49.7	46.8	47.2
All age groups	3.33	3.44	3.29	3.08	3.11	3.25	62.6	64.3	58.3	51.7	51.6	54.7	46.9	48.6	43.7	38.8	38.9	41.7
Penicillins with extended spectrum (J01CA) excl. pivmecillinam																		
0-6	1.59	1.74	1.71	1.52	1.62	1.35	86.9	95.2	90.8	72.7	73.3	59.1	64.6	70.5	66.7	56.3	57.6	45.3
7-19	0.45	0.46	0.43	0.39	0.43	0.43	14.1	14.5	13.6	11.8	12.4	12.0	12.4	12.8	11.5	10.1	10.6	10.1
20-59	0.72	0.77	0.75	0.66	0.66	0.63	18.4	19.4	18.7	16.5	16.4	15.4	16.0	16.7	15.1	14.2	14.1	13.0
60-79	1.59	1.62	1.63	1.52	1.49	1.45	41.4	42.0	41.3	37.9	36.9	35.4	32.3	32.9	29.9	30.1	29.4	28.0
80 -	1.81	1.79	1.83	1.76	1.74	1.75	47.3	46.8	46.5	44.0	42.1	41.0	38.3	38.0	32.9	35.4	34.1	33.2
All age groups	0.98	1.02	1.02	0.93	0.94	0.89	29.6	31.0	30.5	26.9	26.9	24.4	23.4	24.5	22.5	21.1	21.2	19.3
Pivmecillinam (J01CA08)																		
0-6	0.01	0.01	0.01	0.01	0.02	0.01	0.5	0.5	0.7	0.8	1.1	1.0	0.4	0.5	0.6	0.7	1.0	1.0
7-19	0.17	0.19	0.24	0.24	0.24	0.22	10.7	12.4	15.5	16.1	15.9	15.7	9.6	11.0	13.6	13.9	13.9	13.5
20-59	0.34	0.36	0.43	0.44	0.44	0.43	20.1	22.2	26.9	27.3	27.7	28.3	17.3	19.0	22.5	23.0	23.4	23.8
60-79	0.71	0.74	0.84	0.85	0.84	0.83	40.3	43.0	49.5	49.9	49.8	51.3	31.2	33.1	37.3	38.1	38.1	38.9
80 -	1.84	1.84	1.95	1.92	1.90	1.79	106.7	109.3	116.6	115.8	115.0	112.6	80.1	81.8	85.1	83.9	83.1	81.4
All age groups	0.43	0.46	0.53	0.54	0.53	0.52	25.5	27.6	32.2	32.8	33.0	33.5	20.7	22.3	25.6	25.9	26.2	26.4
Beta-lactamase sensitive penicillins (J01CE)																		
0-6	3.59	4.03	4.14	3.56	3.71	3.52	327.3	350.7	343.7	287.4	290.6	271.1	230.8	244.3	235.9	210.7	219.3	198.7
7-19	3.38	3.68	3.64	3.46	3.52	3.61	135.0	142.5	135.0	123.3	124.6	127.5	113.1	117.3	110.2	100.7	102.3	103.5
20-59	4.28	4.49	4.42	4.00	3.96	4.07	107.9	112.8	108.4	97.7	96.6	98.4	91.6	95.2	90.9	83.8	83.4	84.9
60-79	4.46	4.57	4.51	4.25	4.09	4.22	107.0	109.0	106.1	99.6	95.8	99.1	88.0	89.4	87.0	84.5	82.1	84.7
80 -	3.33	3.36	3.51	3.38	3.29	3.33	84.2	84.2	85.7	81.7	79.5	80.4	71.4	72.2	72.4	69.9	68.2	69.5
All age groups	4.09	4.30	4.26	3.96	3.93	3.99	128.1	134.3	130.0	118.6	118.4	117.7	104.0	108.1	103.7	96.0	96.3	96.2
Beta-lactamase resistant penicillins (J01CF)																		
0-6	0.35	0.33	0.33	0.31	0.30	0.28	35.6	32.9	32.8	30.8	29.4	28.0	26.7	25.2	24.8	24.2	23.5	22.0
7-19	0.70	0.69	0.80	0.79	0.77	0.76	33.6	31.9	31.9	31.2	31.0	30.0	27.5	26.4	26.2	25.4	25.6	24.6
20-59	0.95	0.96	1.14	1.13	1.11	1.12	33.5	33.3	33.2	32.6	31.9	32.8	26.9	26.7	26.5	26.2	26.9	26.6
60-79	2.04	2.04	2.37	2.29	2.26	2.24	57.4	56.3	56.9	55.0	54.7	53.2	37.7	37.1	37.3	37.1	37.5	36.6
80 -	4.44	4.40	5.01	4.92	4.92	4.69	123.4	122.6	122.1	119.4	113.2	106.2	68.7	67.9	66.8	65.5	66.8	64.8
All age groups	1.25	1.25	1.46	1.45	1.43	1.42	42.9	42.2	42.3	41.7	41.3	40.3	31.2	30.7	30.5	30.1	30.6	29.9
Combinations of penicillins (J01CR)																		
0-6	0.73	0.75	0.67	0.52	0.39	0.28	51.2	52.7	46.4	33.7	25.3	17.8	34.4	35.2	30.9	24.0	18.0	12.3
7-19	0.22	0.21	0.20	0.18	0.17	0.16	6.4	6.4	6.0	5.4	4.9	4.7	5.1	4.9	4.5	4.1	3.8	3.6
20-59	0.18	0.20	0.21	0.20	0.21	0.21	3.9	4.4	4.6	4.3	4.5	4.5	3.5	3.9	4.0	3.7	3.9	3.9
60-79	0.22	0.25	0.27	0.28	0.30	0.31	4.5	5.1	5.5	5.7	6.1	6.2	3.6	4.1	4.4	4.1	4.8	4.9
80 -	0.15	0.17	0.20	0.22	0.24	0.27	3.0	3.4	4.1	4.3	4.8	5.2	2.3	2.7	3.2	3.4	3.9	4.1
All age groups	0.24	0.26	0.26	0.24	0.24	0.24	8.0	8.5	8.3	7.2	6.7	6.1	6.1	6.5	6.3	5.5	5.2	4.7
Cephalosporins (J01DB-DE)																		
0-6	0.52	0.52	0.46	0.36	0.34	0.32	49.0	49.7	43.6	34.1	33.2	31.6	37.6	38.0	33.9	28.1	27.7	25.6
7-19	0.30	0.29	0.27	0.21	0.20	0.18	20.6	20.2	18.4	14.9	13.8	12.8	17.4	17.2	15.7	12.6	11.6	10.7
20-59	0.29	0.28	0.25	0.20	0.18	0.15	16.8	16.2	14.5	11.4	10.3	9.2	14.2	13.7	12.2	9.8	8.8	7.8
60-79	0.46	0.40	0.36	0.29	0.26	0.21	22.6	20.2	17.7	13.8	12.7	11.3	17.1	15.5	13.5	10.7	9.8	8.7
80 -	0.73	0.65	0.54	0.41	0.38	0.34	40.5	35.4	29.4	22.7	21.6	19.9	30.9	27.4	22.9	17.9	16.6	15.5
All age groups	0.37	0.35	0.31	0.25	0.23	0.20	22.5	21.5	19.0	15.2	14.1	12.8	17.9	17.2	15.3	12.3	11.4	10.3

Age group (years)	DDD/1000 and day						Prescriptions/1000 and year						Users/1000 and year					
	2006	2007	2008	2009	2010	2011	2006	2007	2008	2009	2010	2011	2006	2007	2008	2009	2010	2011
Trimethoprim (J01EA)																		
0-6	0.12	0.12	0.10	0.09	0.09	0.08	16.0	15.4	14.0	12.6	12.2	11.3	11.1	10.6	9.8	9.7	9.6	8.8
7-19	0.21	0.18	0.15	0.11	0.10	0.08	12.4	10.9	8.9	7.0	5.9	4.8	10.8	9.5	7.8	6.0	5.1	4.1
20-59	0.33	0.29	0.24	0.18	0.16	0.13	17.4	14.6	11.8	8.7	7.2	5.9	14.7	12.4	9.9	7.2	6.0	4.8
60-79	0.84	0.76	0.64	0.52	0.47	0.42	40.7	35.2	29.2	23.1	20.4	17.7	29.7	25.6	21.0	16.7	14.7	12.5
80 -	2.19	1.91	1.58	1.30	1.23	1.08	120.1	104.5	84.7	69.6	63.3	56.4	73.3	61.6	49.1	38.6	34.5	29.4
All age groups	0.49	0.43	0.39	0.29	0.26	0.23	26.3	22.8	18.8	14.9	13.1	11.2	19.8	16.9	13.8	10.7	9.3	7.9
Trimetoprim with sulphonamides (J01EE)																		
0-6	0.16	0.16	0.14	0.13	0.12	0.10	18.1	18.8	16.7	14.8	13.7	11.8	13.2	13.5	12.0	10.7	10.1	8.2
7-19	0.10	0.10	0.11	0.11	0.10	0.10	4.0	4.1	4.2	4.3	4.0	4.1	2.7	2.6	2.7	2.6	2.4	2.5
20-59	0.13	0.14	0.14	0.15	0.16	0.17	2.9	3.0	3.1	3.3	3.4	3.7	1.9	1.9	2.0	2.1	2.2	2.3
60-79	0.36	0.39	0.44	0.47	0.48	0.49	8.8	9.2	10.1	10.4	10.8	11.0	5.8	6.1	6.8	7.1	7.4	7.5
80 -	0.36	0.39	0.43	0.43	0.46	0.46	11.7	12.2	13.1	12.5	13.1	12.5	8.8	9.1	9.9	9.7	10.1	9.8
All age groups	0.19	0.20	0.21	0.22	0.23	0.24	6.3	6.4	6.5	6.6	6.8	6.7	4.0	4.1	4.3	4.2	4.3	4.2
Macrolides (J01FA)																		
0-6	0.80	0.85	0.68	0.51	0.53	0.51	37.3	38.1	29.9	22.4	23.1	22.2	29.6	30.4	23.3	18.1	18.8	18.3
7-19	0.76	0.74	0.54	0.31	0.33	0.40	22.1	21.7	15.4	12.7	13.8	15.4	17.9	17.2	11.8	9.7	10.7	12.1
20-59	0.54	0.55	0.49	0.28	0.28	0.27	16.3	16.5	14.3	12.1	11.9	10.4	13.0	13.2	11.3	9.6	9.6	8.4
60-79	0.50	0.50	0.47	0.32	0.30	0.31	14.5	14.6	13.0	11.3	10.7	9.6	11.0	11.0	9.6	8.4	8.0	6.9
80 -	0.34	0.32	0.30	0.23	0.21	0.20	9.3	8.7	8.4	7.4	6.9	6.0	7.2	6.8	6.4	5.5	5.2	4.4
All age groups	0.58	0.59	0.50	0.31	0.31	0.32	18.2	18.4	15.3	12.8	12.8	11.9	14.4	14.4	11.7	9.9	10.0	9.3
Lincosamides (J01FF)																		
0-6	0.02	0.03	0.02	0.02	0.02	0.02	5.0	5.3	5.0	5.2	5.0	5.3	3.6	3.9	3.7	3.8	3.9	4.0
7-19	0.11	0.12	0.12	0.12	0.12	0.12	7.8	8.3	8.4	8.2	8.1	8.0	6.2	6.7	6.9	6.6	6.5	6.5
20-59	0.28	0.29	0.30	0.29	0.29	0.30	14.3	15.6	15.6	15.0	14.9	15.5	11.1	12.2	12.2	12.0	12.0	12.4
60-79	0.55	0.55	0.57	0.57	0.55	0.5	23.7	24.4	24.6	23.8	23.6	23.1	15.3	15.9	16.3	16.4	16.2	16.1
80 -	0.75	0.74	0.76	0.72	0.73	0.71	32.6	32.8	33.2	31.0	31.7	30.8	18.1	18.6	19.2	18.8	19.2	19.0
All age groups	0.31	0.32	0.33	0.32	0.32	0.33	15.4	16.3	16.4	15.9	15.9	16.0	10.9	11.7	11.9	11.7	11.7	11.9
Fluoroquinolones (J01MA)																		
0-6	0.01	0.01	0.01	0.01	0.01	0.01	0.8	0.8	0.7	0.7	0.8	0.7	0.4	0.4	0.4	0.4	0.5	0.4
7-19	0.12	0.13	0.12	0.12	0.12	0.12	5.5	5.5	4.8	4.3	4.3	4.3	4.7	4.4	3.9	3.5	3.5	3.4
20-59	0.80	0.76	0.69	0.63	0.61	0.61	30.2	27.8	23.8	20.9	20.2	19.4	22.0	20.3	17.3	15.4	14.9	14.3
60-79	2.05	1.93	1.75	1.67	1.62	1.61	80.2	73.7	63.9	58.6	56.8	54.8	52.7	48.7	42.7	40.2	39.3	37.6
80 -	3.00	2.74	2.41	2.25	2.26	2.18	136.8	119.7	98.5	88.2	87.3	82.0	92.5	81.5	68.1	61.4	60.9	57.8
All age groups	0.98	0.93	0.84	0.80	0.78	0.77	39.0	35.7	30.6	27.8	27.1	26.1	27.0	24.9	21.5	19.6	19.2	18.4
Nitrofurantoin (J01XE)																		
0-6	0.07	0.07	0.06	0.06	0.06	0.06	6.3	6.3	6.2	6.9	7.2	7.3	4.2	4.2	4.2	4.9	5.1	5.1
7-19	0.12	0.14	0.13	0.15	0.14	0.14	5.2	6.7	6.6	9.2	10.6	10.8	4.4	5.8	5.8	7.9	9.0	9.2
20-59	0.20	0.24	0.23	0.26	0.25	0.26	8.5	11.0	10.6	14.7	17.2	18.4	7.0	9.1	8.8	12.2	14.2	15.2
60-79	0.36	0.46	0.47	0.53	0.53	0.56	14.6	19.4	20.6	28.1	32.5	34.9	10.7	14.3	15.2	20.8	24.1	25.8
80 -	0.78	0.97	0.95	1.05	1.06	1.12	37.2	46.7	47.7	61.7	70.6	76.0	24.0	30.3	31.2	40.3	45.6	47.8
All age groups	0.24	0.30	0.29	0.32	0.32	0.34	10.5	16.5	13.6	18.5	21.3	22.8	8.0	10.3	10.4	14.1	16.3	17.3
All agents (J01 excl. methenamine)																		
0-6	7.98	8.62	8.34	7.11	7.21	6.55	634.7	666.8	630.8	522.4	515.0	467.6	333.5	348.5	330.3	298.0	301.4	273.3
7-19	9.79	10.18	10.02	9.52	9.65	9.83	311.1	319.8	301.8	280.8	282.5	286.1	204.5	208.1	195.8	182.1	184.1	185.5
20-59	12.63	13.04	12.82	11.70	11.64	11.89	357.6	366.1	348.0	318.9	318.1	320.9	223.9	228.7	217.8	204.1	203.8	205.1
60-79	18.34	18.58	18.46	17.26	16.86	17.03	554.5	553.7	531.0	497.7	489.6	489.0	288.8	289.6	279.0	269.6	265.8	265.6
80 -	22.74	22.33	22.37	21.13	20.85	20.38	833.3	807.9	765.1	723.5	710.9	690.7	379.4	372.5	356.2	340.1	336.0	330.8
All age groups	13.51	13.87	13.70	12.76	12.68	12.76	436.1	443.8	423.1	391.9	390.3	385.3	249.8	254.1	242.5	228.0	227.8	226.3

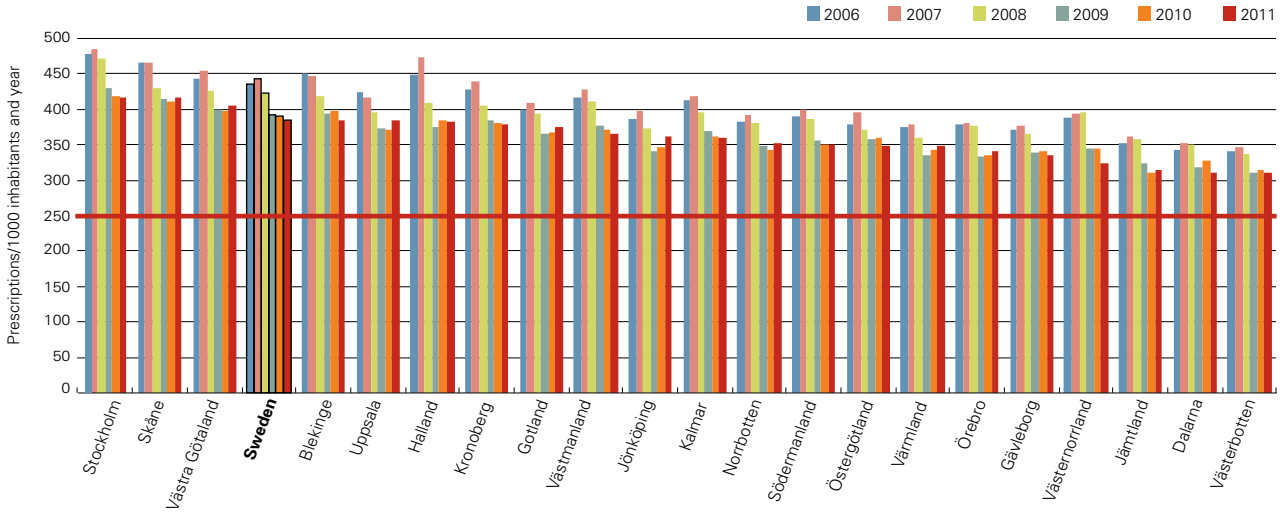


FIGURE 3.1.13. Sales of antibiotics in outpatient care 2006-2011, prescriptions/1000 inhabitants and year. The red line indicates the Swedish long term target of at most 250 prescriptions / 1000 inhabitants and year. The data are sorted according to the use in 2011.

As mentioned in earlier editions of SWEDRES, Strama has proposed two qualitative goals for antibiotic prescribing in outpatient care.

1. 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). This quality indicator is also used by The National Board of Health and Welfare and the Swedish Association of Local Authorities and Regions in their annual benchmarking of medical treatments and procedures.

   In 2011 the proportion of penicillin V of antibiotics commonly used to treat respiratory tract infections in children aged 0-6 years was 67.5% on the national level and the proportion of penicillin V increased in the majority of all counties. Värmland County had the greatest proportion, 77.9%, and Stockholm County the lowest, 63.5%, Figure 3.1.14.

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).

   In Sweden the average proportion of fluoroquinolones prescribed to women aged 18-79 was 14.2% in 2011. Kronoberg was the county with the highest proportion (17.3%) and Dalarna was the county with lowest proportion (11.6%), Figure 3.1.15.

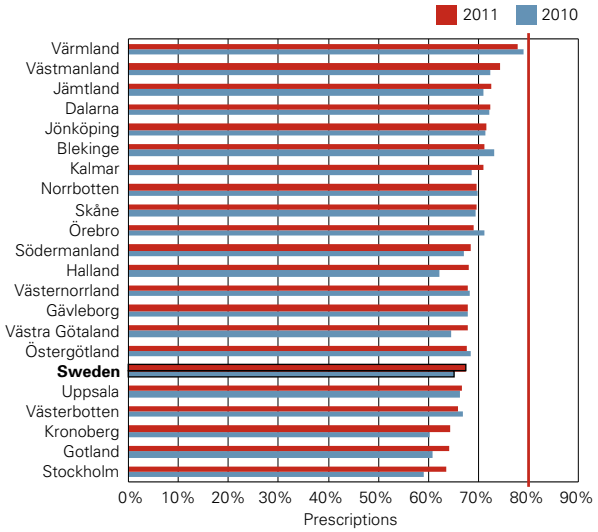


FIGURE 3.1.14. Proportion penicillin V of antibiotics commonly used to treat respiratory tract infections* in children 0-6 years, per county. The red line indicates Strama´s goal at minimum 80% penicillin V. *Amoxicillin (J01CA04), penicillin V (J01CE02), amoxicillin-clavulate (J01CR02), macrolides (J01FA) and cephalosporins (J01DB-DE). The data are sorted according to the use in 2011.

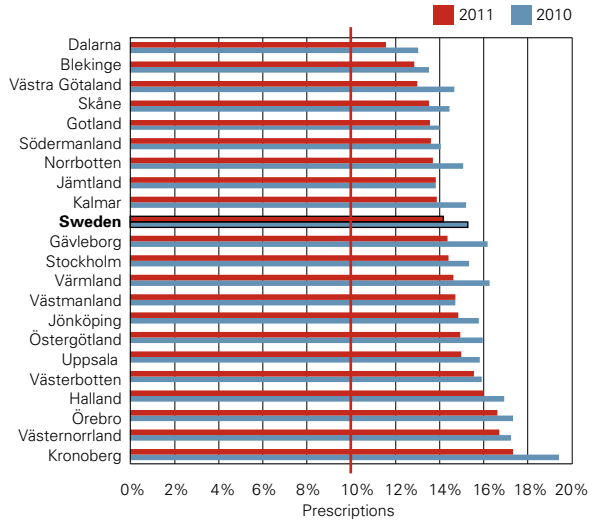


FIGURE 3.1.15. Proportion of fluoroquinolones of commonly used antibiotics in treatment of urinary tract infections* in women 18-79 years, per county. The red line indicates Strama´s goal of maximum 10% fluoroquinolones. * Fluoroquinolones (J01MA02+06), pivmecillinam (J01CA08), nitrofurantoin (J01XE01), trimethoprim (J01EA01). The data are sorted according to the use in 2011.

Agreement concerning improved patient safety

The Government and the Swedish Association of Local Authorities and Regions (SKL) agreed in late 2010 on a performance-based reimbursement for the patient safety efforts in the county councils. SEK 100 million was allocated for the period October 1 2010 - September 31 2011 to improvements of rational use of antibiotics. A prerequisite for receiving compensation was that the county councils must have met a number of basic requirements. One important requirement, based on the work with antibiotic use, was the establishment of a local strategic program against antibiotic resistance (Strama) with a clear mission and adequate financing. All the county councils met this requirement. Those county councils who also worked for an increased compliance to local treatment recommendations concerning common infections in outpatient care, and also decreased the number of antibiotic prescriptions by ten percent of the difference between the number of prescriptions per 1000 inhabitants per year for the period October 1 2009 – September 31 2010, and the long term target of at most 250 prescriptions per 1000 inhabitants and year were entitled to the compensation. An assessment from The Swedish Institute for Communicable Disease Control (SMI) showed that all the county met the requirement regarding compliance to local treatment guidelines. Five county decreased the antibiotic prescriptions, including Stockholm, the largest county in Sweden. The county of Dalarna, Västernorrland and Jämtland furthermore reached the target regarding antibiotic prescriptions and shared SEK 75 million.

The patient safety drive will continue in 2012 and the quantitative antibiotic target with compensation to county councils reaching the target has not changed. The qualitative target is also similar to previous measurement period.

PRIS

Prescribing data from primary care

Data regarding visits at health centers for infectious diseases have been collected since 2007 into a record called PRIS (Primary care Record of Infections in Sweden). Data is collected into PRIS through the search engine RAVE (usually used with the electronic medical record called Medidoc or Profdoc). PRIS includes items on patient age, gender, diagnose, ATC-code for the antibiotic that has been prescribed, results of rapid antigen detection test Strep-A, C-reactive protein (CRP) test and information about whether a microbiologic sample has been taken. Each included patient has an encrypted identification number in PRIS. The purpose of the record is to study how common infections in outpatient care are handled and treated.

PRIS consists of data from 1 200 000 visits for infections during the years 2007-2011. PRIS is administrated by primary care R&D center in Jönköping County and is financed by the Swedish Institute for Communicable Disease Control and the R&D unit in Jönköping County.

In 2011, 66 health centers participated in PRIS and the population was 686 000 patients listed at the participating health centers. During the year, 255 000 visits for infections were registered which represent 22% of all visits in this population, excluding visits during weekends. In total 371 visits per 1000 listed patient were registered whereof 150 received a prescription for an antibiotic.

Ten infection diagnoses represented 89% of all antibiotics prescribed in 2011. Urinary tract infection followed by throat infection and ear infection led to most antibiotic prescriptions, Table 1.

TABLE 1. The 10 diagnoses that represented 89 %of all antibiotic prescribing in 2011 in participating health centers.

Diagnose	% of total antibiotic prescribing	Prescriptions/1000 listed patients
Cystitis	22	32
Tonsillitis	17	25
Acute otitis media	12	18
Skin infection	7	10
Sinusitis	6	10
Pneumonia	6	10
Acute bronchitis	6	9
Upper respiratory tract infection	6	9
Lyme disease	5	7
Impetigo	2	4

According to treatment recommendations a Strep A test or a positive culture shall have been taken on most patients diagnosed with throat infections (tonsillitis and pharyngitis) before antibiotic treatment. In 2011, 54% of those who received antibiotics for throat infections had a positive Strep A test and 12% had a negative Strep A test, while in 34% no test had been taken at all. The corresponding figures for 2010 were 43%, 11% and 47%, Table 2.

TABLE 2. Number of patient with diagnose tonsillitis or pharyngitis and treated with antibiotic in relation to strep A test.

	2010		2011	
	Number	%	Number	%
Positive strep-A test	7306	43	9847	54
Negative strep-A test	1861	11	2199	12
No strep-A test	8037	47	6232	34

The proportion of positive Strep A tests of all taken was 30%. In 2011, 86% of those diagnosed with tonsillitis or pharyngitis and with a positive Strep A test were treated with penicillin V (J01CE02), 5% with cephalosporins (J01DB-DE) and 3% with macrolides (J01FA) and lincosamides (J01FF), respectively.

In 2010, 84% of all children aged 1-12 years that were diagnosed with acute otitis media were treated with antibiotics. The corresponding figure for 2011 was 77%.

In 2007, 60% of all patients diagnosed with acute bronchitis were treated with antibiotics and the corresponding figure for 2011 was 42%. When antibiotics were prescribed for acute bronchitis, 54% of the patients were treated with tetracyclines, 25% with penicillin V and 13% with amoxicillin. The proportion of all patients diagnosed with acute bronchitis and receiving antibiotic treatment varied between the participating health centers, from 12 to 78%, Figure 1. Such variation was noted for the majority of all diagnoses registered in PRIS.

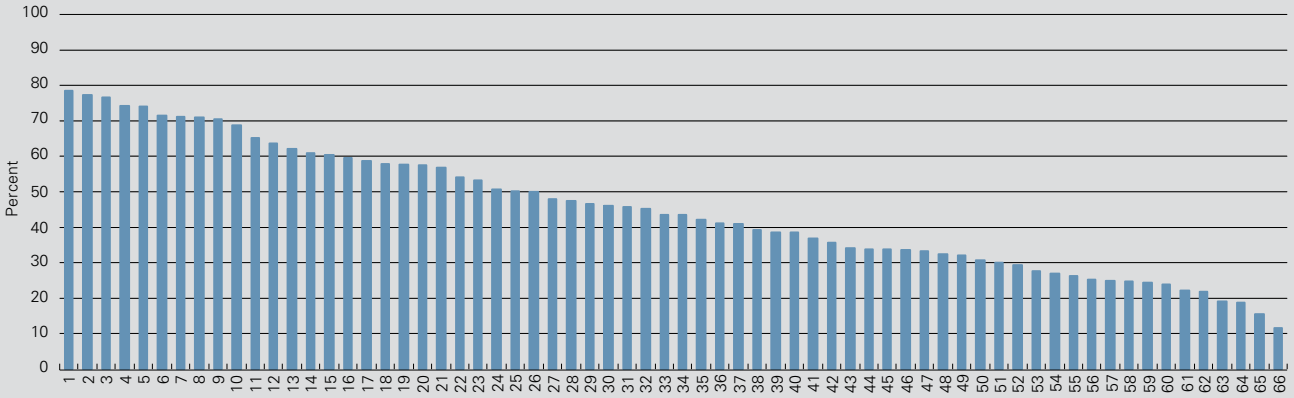


FIGURE 1. The proportion of all patients diagnosed with acute bronchitis and received antibiotic treatment per participating health centers (1-66) in 2011.

The indication for antibiotic treatment in women with urinary tract infections cannot be analyzed by this kind of record. But the choice of antibiotic substance prescribed at the diagnose urinary tract infection can be analyzed and has changed over time. In 2007, the proportion of women diagnosed with a urinary tract infection and treated with the two first line substances, pivmecillinam or nitrofurantoin, was 55% and the proportion treated with trimethoprim or fluoroquionolones was 40%. In 2011, pivmecillinam was prescribed in 50% of all women diagnosed with a urinary tract infection, nitrofurantoin in 34%, trimethoprim in 10% and fluoroquinolones in less than 5%. The proportion of women with urinary tract infections and treated with fluoroquinolones in PRIS can be compared with the goal launched by Strama in 2009; the proportion of fluoroquinolones should not exceed 10% of antibiotics commonly prescribed to treat urinary tract infections in women. When using sales data from pharmacies for the assessment of adherence to treatment recommendations less specific targets need to be applied, as prescribing for other diagnoses cannot be excluded effectively. This illustrates the value of registries like PRIS that approves for an accurate investigation of prescribing for a certain diagnosis.

Conclusion

PRIS is a valuable database for monitoring of the treatment of infections in primary care. All participating health centers receive a summary of their data in comparison with other units' data. There are several possible sources of error in this type of registry, but it can clearly illustrate trends over time and highlight differences in treatment between different units. It is quite clear that the management of especially respiratory tract infections can be improved. Anyone with a concrete question, for example for a student thesis, can access data from the record.

Antibiotics in dentistry

Dentists account for approximately 7% of all antibiotic prescribing in outpatient care in Sweden. The prescribing of antibiotics by dentists increased by 0.5% in 2011. Penicillin V (J01CE02) is the most commonly prescribed antibiotic followed by amoxicillin (J01CA04) and clindamycin (J01FF01). These antibiotic substances represent 75.0%, 11.7% and 10.2% respectively of all antibiotics prescribed by dentists.

Hospital care

Hospital care includes data from all Swedish hospitals as well as data from those nursing homes and other caregivers that order their antibiotics through requisitions. On the national level, about 75% of the antibiotics ordered on hospital requisition are ordered by hospitals and the other 25% by other caregivers. In some counties almost 100% of all antibiotics bought on hospital requisitions is actually used by hospitals but in other counties this proportion is as low as 55%.

The total sales of antibiotics to hospital care increased with 4.2% during 2011, from 1.52 DDD per 1000 inhabitants and day in 2010 to 1.59 DDD per 1000 inhabitants and day in 2011, Table 3.1.2.

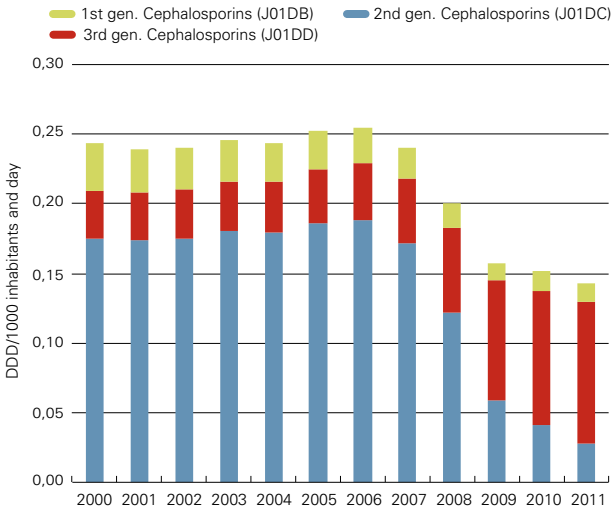


FIGURE 3.1.16. Cephalosporins in hospital care, DDD/1000 inhabitants and day, 2000-2011.

TABLE 3.1.2. Antibiotic use in hospital care 2000-2011, DDD/1000 inhabitants and day.

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
J01 excl methenamine	1.18	1.22	1.25	1.33	1.36	1.43	1.49	1.55	1.52	1.49	1.52	1.59
Total J01	1.21	1.25	1.27	1.37	1.43	1.50	1.56	1.62	1.57	1.53	1.55	1.61
Methenamine (J01XX05)	0.03	0.03	0.03	0.05	0.07	0.07	0.07	0.07	0.05	0.03	0.03	0.02

As reported in earlier issues of SWEDRES, a change towards less broad spectrum and more narrow spectrum antibiotics is desirable and has been promoted for a long time. Penicillin V (J01CE02) is recommended by The Swedish Society of Infectious Diseases as first hand choice in community-acquired pneumonia and the use of cephalosporins should be reduced. Stramas Point Prevalence Survey, performed in 2003, 2004, 2006, 2008 and 2010 confirm that the use of cephalosporins for treatment of uncomplicated community-acquired pneumonia has decreased considerably.

The decrease in the use of cephalosporins seen the latest years continues in 2011, Figure 3.1.16. From 2006 to 2011 the sales of second generation cephalosporins, of which more than 90% was cefuroxime, decreased by 85.0%, from 0.25 to 0.14 DDD per 1000 inhabitants and day. Sales of third generation cephalosporins, mainly cefotaxime and ceftazidime, increased by 151.9% during the same period. The decrease in DDD is partly explained by a shift from cefuroxime to cefotaxime since the prescribed daily dose, PDD, in Sweden of cefuroxime and cefotaxime do not correspond to the WHO definition of DDD. Cefuroxime has often a higher PDD and cefotaxime a lower PDD as compared with WHO's DDD. Considering this the actual decrease is not that large. Taken together, the overall decrease in DDDs for cephalosporins indicates that these substances are actually replaced by other antibiotics.

Figure 3.1.17 shows the use of some antibiotic groups in hospital care 2011 over time measured as DDD per 1000 inhabitants and day. Different kinds of penicillins are the most commonly used antibiotics in hospital care. Beta-lactamase resistant penicillins (J01CF), pencillins with extended spectrum (J01CA) and beta-lactamase sensitive penicillins (J01CE) represent 45.1% of all antibiotics used in hospital care in 2011. The most pronounced increase in use during 2011 is seen among tetracyclines (J01AA) and combinations of penicillins (J01CR), 12.7% and 13.3% respectively. In the later group piperacillin with tazobactam stands for 78%. Piperacillin with tazobactam still represents a small proportion (3.8%) of antibiotic use in hospital care, but the use is increasing rapidly. In 2011 piperacillin with tazobactam increased with 12.0% measured as DDD per 1000 inhabitants and day. The Swedish Point Prevalence Surveys indicate that the increase in piperacillin with tazobactam includes several diagnosis groups. The increased use of piperacillin with tazobactam may be due to increased incidence of ESBL, as well as it is used as an alternative to cephalosporins with the motive that it may not cause resistance in the same way.

Due to the recent rapid decrease (43.9% between 2006 and 2011) in use of cephalosporins, the betalactamase-resistant penicillins (J01CF) are now the largest group of antibiotics in hospital care. This substance is largely used as prophylaxis

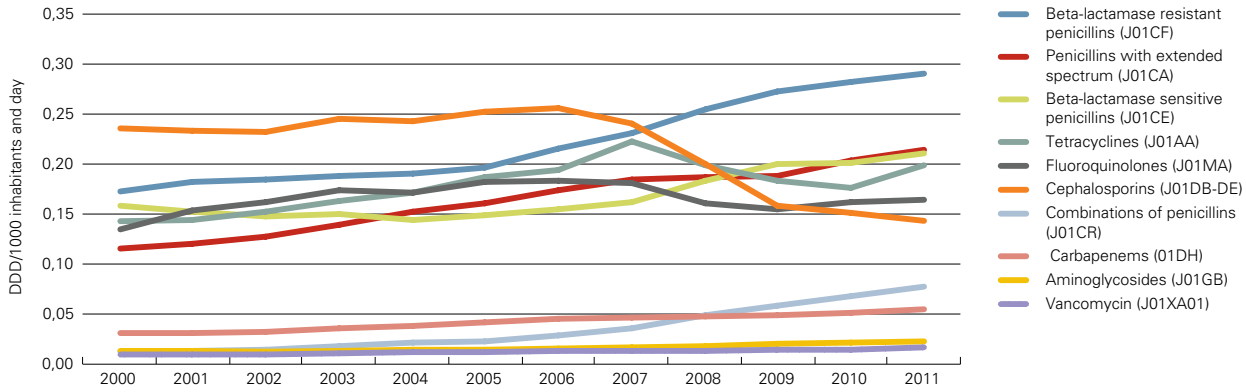


FIGURE 3.1.17. Use of some antibiotic groups in hospital care 2000-2011, DDD/1000 inhabitants and day.

before surgery. In Sweden, a single dose is recommended in nearly all kinds of surgical procedures for which antibiotic prophylaxis is indicated, or at most one-day prophylaxis. Even though communication about dosage regime of antibiotic prophylaxis before surgery has been in focus during the last years, the use of betalactamase-resistant penicillins continues to increase. The use increased with 2.9% in 2011 measured in DDD/1000 inhabitants and day, Figure 3.1.17.

After several years with decreasing use of fluoroquinolones (J01MA) in accordance with recommendations, the use in 2011 increased with 1.5% measured as DDD per 1000 inhabitants and day, Figure 3.1.17.

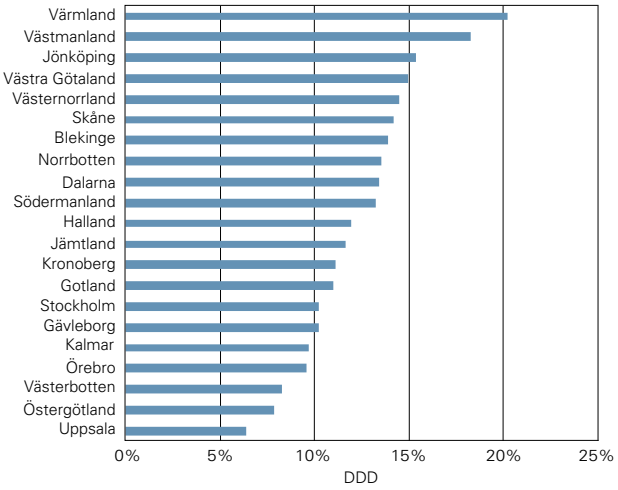


FIGURE 3.1.18. Percentage of narrow spectrum penicillins (penicillin V and G, J01CE) of all antibiotics in Swedish hospitals 2011, per county.

Sales data exclusively to hospitals provided by local Strama groups in all counties

The choice of denominator is crucial when comparing data on antibiotics to inpatients. In the following sections, sales data is related to the number of patient-days and admissions to hospitals in somatic care.

Sales of all kinds of penicillins have increased every year since 2006. The group penicillins with enzyme inhibitors (J01CR), has increased the most during these years and the use has more than doubled, Table 3.1.3 and 4.

Taken together, the amount of antibiotics used per 100 patient-days or admissions to hospital remains quite stable since 2006 – the former increase by 10% and the latter decrease by 2% during these years, Table 3.1.3 and 4. The major changes in antibiotic use in hospital care seem to lie in the shifts between substances.

The proportion of broad and narrow spectrum antibiotics used in hospitals varies greatly between counties, as seen in Figures 3.1.18 and 19. Only 6.4% of systemic antibacterials in hospitals in Uppsala County are penicillins V or G, whereas in Värmland County these substances represent 20.2%. Less variation is seen in sales of one of the most common broad spectrum substances, the fluoroquinolones, which constitute between 8.8% of all antibiotics in Skåne County and 13.4% in Västernorrland County. After several years of decreasing use, the cephalosporins make up only 4.1% of antibiotics in Södermanland County. In Östergötland Counties the proportion is almost four times higher.

As seen in figure 3.1.17 newer broad spectrum antibiotics such as carbapenems and piperacillin with tazobactam, represent a small but steadily growing proportion of the total use of antibiotics in hospitals. There are also great geographical differences; from just a few percent in some counties to nearly 10% percent in others, Figure 3.1.20. The proportion of carbapenems of all antibiotics in hospitals varies threefold, from 2.5% in Värmland County to 7.7% in Östergötland County. Concerning piperacillin with tazobactam, sales vary from 3.5% in Halland County to 7.7% in Uppsala County, Figure 3.1.20.

TABLE 3.1.3. DDD/100 patient-days in somatic medical care in Swedish hospitals 2006-2011.

DDD/100 patient-days	2006	2007	2008	2009	2010	2011*
Tetracyclines (J01AA)	5.49	5.75	5.48	4.71	4.63	5.16
Penicillins with extended spectrum (J01CA)	5.01	5.21	5.84	5.93	6.03	6.56
Betalactamase sensitive penicillins (J01CE)	4.62	4.85	6.21	7.01	6.80	7.27
Betalactamase resistant penicillins (J01CF)	7.70	8.04	9.61	10.44	10.96	10.96**
Combinations of penicillins (J01CR)	1.28	1.57	2.28	2.83	3.36	3.84
Cephalosporins (J01DB-DE)	10.92	10.35	9.48	7.40	7.20	6.89
Carbapenems (J01DH)	2.02	2.08	2.33	2.42	2.59	2.81
Trimethoprim (J01EA)	1.29	1.22	1.19	1.01	0.87	0.79
Trimethoprim with sulphonamides (J01EE)	1.47	1.60	1.88	2.03	2.11	2.28
Macrolides (J01FA)	1.02	1.01	0.98	0.99	0.90	1.09
Lincosamides (J01FF)	1.48	1.53	1.70	1.67	1.70	1.74
Aminoglycosides (J01GB)	0.72	0.74	0.88	1.02	1.08	1.17
Fluoroquinolones (J01MA)	6.48	6.25	6.08	5.94	6.08	6.28
Glycopeptides (J01XA)	0.65	0.64	0.70	0.76	0.71	0.89
Imidazole derivatives (J01XD)	1.60	1.52	1.54	1.36	1.28	1.19
Methenamine (J01XX05)	0.90	0.86	0.79	0.66	0.60	0.55
Linezolid (J01XX08)	0.05	0.05	0.06	0.06	0.08	0.07
All agens (J01)	53.17	53.77	57.57	56.77	57.66	58.67

*Denominator data from 2010.
**Because of errors in the sale database, data for 2010 is showing for this antibiotic group.

TABLE 3.1.4. DDD/100 admissions in somatic medical care in Swedish hospitals 2006-2011.

DDD/100 admissions	2006	2007	2008	2009	2010	2011*
Tetracyclines (J01AA)	28.77	29.91	26.46	22.30	21.45	23.93
Penicillins with extended spectrum (J01CA)	26.22	27.13	28.18	28.09	27.95	30.41
Betalactamase sensitive penicillins (J01CE)	24.20	25.21	29.99	33.17	31.49	33.71
Betalactamase resistant penicillins (J01CF)	40.31	41.82	46.41	49.43	50.77	50.77**
Combinations of penicillins (J01CR)	6.71	8.18	10.99	13.42	15.56	17.80
Cephalosporins (J01DB-DE)	57.17	53.86	45.76	35.01	33.36	31.93
Carbapenems (J01DH)	10.60	10.83	11.27	11.46	11.98	13.01
Trimethoprim (J01EA)	6.74	6.33	5.76	4.78	4.05	3.65
Trimethoprim with sulphonamides (J01EE)	7.71	8.34	9.08	9.59	9.80	10.55
Macrolides (J01FA)	5.36	5.26	4.73	4.69	4.15	5.07
Lincosamides (J01FF)	7.77	7.96	8.20	7.90	7.87	8.05
Aminoglycosides (J01GB)	3.77	3.84	4.24	4.81	4.99	5.40
Fluoroquinolones (J01MA)	33.91	32.52	29.37	28.10	28.19	29.08
Glycopeptides (J01XA)	3.39	3.35	3.40	3.62	3.30	4.11
Imidazole derivatives (J01XD)	8.37	7.93	7.44	6.42	5.95	5.53
Methenamine (J01XX05)	4.73	4.46	3.80	3.13	2.78	2.55
Linezolid (J01XX08)	0.27	0.27	0.30	0.27	0.36	0.31
All agens (J01)	278.38	279.76	278.02	268.70	267.15	271.83

*Denominator data from 2010.
**Because of errors in the sale database, data for 2010 is showing for this antibiotic group.

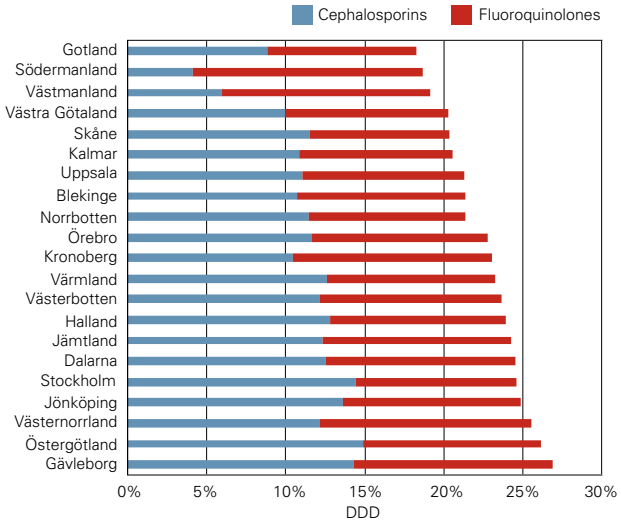


FIGURE 3.1.19. Percentage of broad spectrum antibiotics (cephalosporins, J01DB-DE, and fluoroquinolones, J01MA) of all antibiotics in Swedish hospitals 2011, per county.

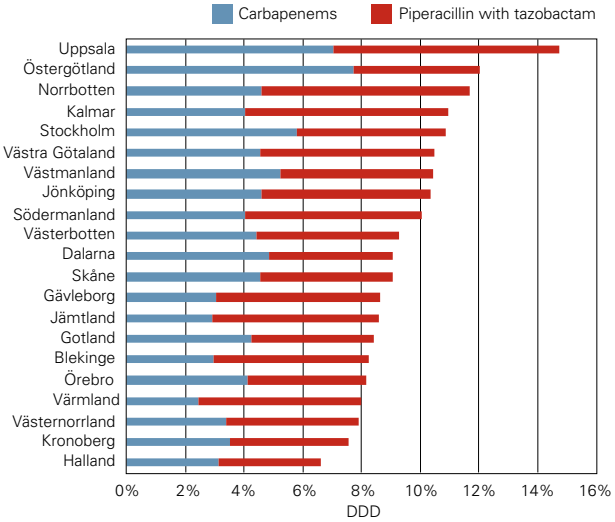


FIGURE 3.1.20. Percentage of carbapenems (J01DH) and piperacillin with tazobactam (J01CR05) of all antibiotics in Swedish hospitals 2011, per county.

The Anti-Infection Tool

IT-tool for automatic registration of healthcare-associated infections

In the spring of 2010 the county councils in Sweden decided to provide funding to a national project for the development of an IT-tool for continuous registration of healthcare-associated infections (HAI) and surveillance of antibiotic use linked to diagnosis. The IT-tool, named The Anti-Infection Tool ("Infektionsverktyget"), aims to support healthcare providers' preventive efforts against HAI and to decrease and optimize the use of antibiotics. The project is managed by the national centre for collaborative e-health. Two counties are involved in the development phase; Västra Götaland and Uppsala.

Initially, the basic requirements for the project were to create a tool that would allow data to be collected automatically at a suitable point of the daily care routine; to make the tool easily applied with a minimal effort from the user; and to integrate the opportunity for flexible extraction of data so that users can generate reports based on reported data at their own convenience. The project has necessitated development of the piloting counties' electronic medical records as well as establishment of a national interface for communication, preparation for a database to hold information retrospectively, and creation of web-based software for generation of reports.

Experiences from Västra Götaland County

One of the piloting counties, Västra Götaland, decided to involve the general surgery units at its major university hospital in the project. Development of the tool has therefore been done in the Melior system for electronic medical records and the Baktlis laboratory data system. Preparations, development, and testing on both local and national levels took little more than a year and active collection and transfer of data from the units started in the end of 2011. Information regarding every prescribed antibiotic is linked to a reason for prescribing by the issuing doctor and continuously transferred to the national database. In the background, data is collected regarding number of admissions to the clinic, surgical procedures, and diagnosis according to ICD-10 for all patients in the clinic, to allow for calculation of overall incidence of HAI. After a few weeks the first reports on which antibiotics were prescribed for which indications were generated and presented back to prescribers in the participating clinics. Figure 1 shows an example of a report from The Anti-Infection Tool, displaying prescribed antibiotics and number of prescribing events for acute community-acquired abdominal infections/peritonitis in the two participating clinics from January to May 2012. The example shows that for the mentioned diagnose antibiotic from the group Combinations of penicillins, incl. Betalactamase inhibitors (J01CR) was prescribed in 34% and fluoroquinolones (J01MA) in 24% of the 961 cases.

The added feature in the medical record is considered simple, self-instructing, and easily used by the surgeons and imposes a minimum of extra work. However, it has become evident that more development is needed to ensure reliable transfer of denominator data on admissions, procedures, and diagnoses. This is approximated to be achieved by September 2012.

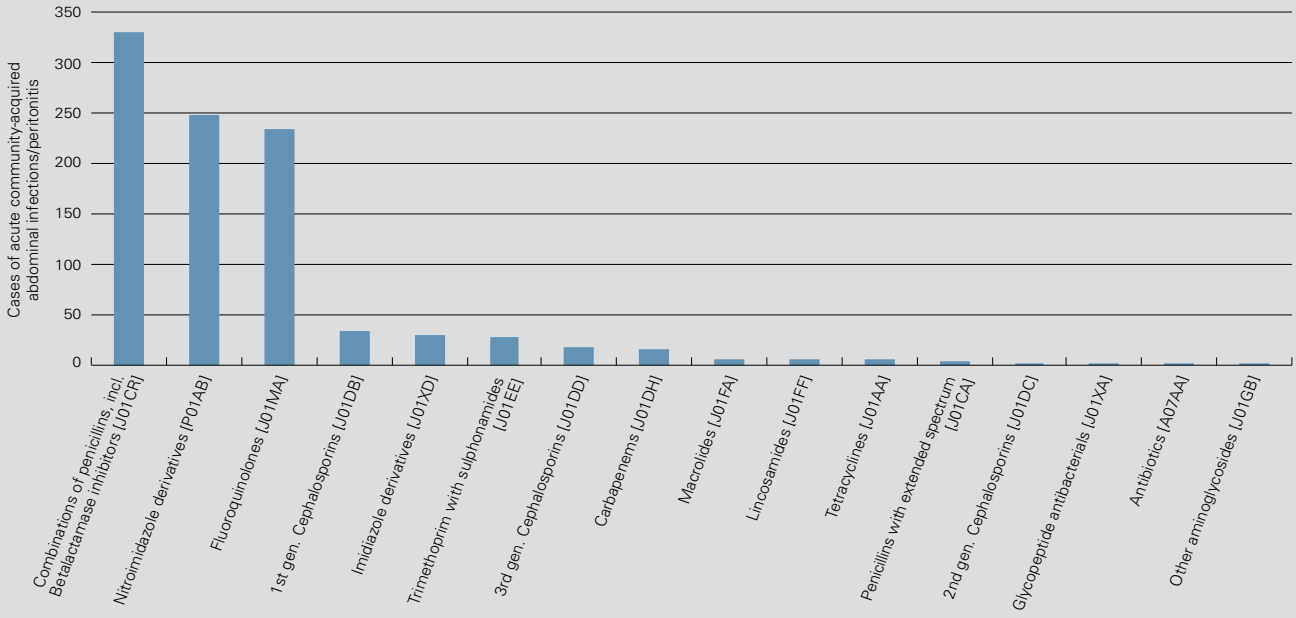


FIGURE 1. Number of cases of acute community-acquired abdominal infections/peritonitis treated with different classes of antibiotics in general surgery, Sahlgrenska University hospital January-May 2012. Total number of cases: 961.

Adverse reactions related to antibiotic use

Spontaneously reported drug-related adverse reactions are continuously entered into SWEDIS, a national database administered by the Swedish Medical Products Agency. The reports originate from health care professionals. The antibiotic related adverse reactions in the last five years, 2007-2011, were analysed for various groups of agents. The following organ system groups received most reports related to the use of systemic antibiotic drugs (J01): skin- and subcutaneous tissue disorders (n=682), hepato-biliary disorders (n=209), gastrointestinal disorders (n=270), general disorders (n=160), musculoskeletal disorders (n=72), blood disorders (n=133), and neurological reactions (n=114). The majority of the reports (60%) concern female patients, which is corresponding to the gender difference seen in the antibiotic use.

The 10 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 3.1.5.

TABLE 3.1.5. Most reported adverse drug reactions related to antibiotic agents to the Swedish Medical Products Agency 2007-2011.

Antibiotic	Total number of adverse drug reaction reports 2007 to 2011	Number of 'serious' reports	Number of fatal cases (causal relationship possible)
Flucloxacillin	135	81	3
Ciprofloxacin	134	83	4
Penicillin V	119	54	0
Nitrofurantoin	116	61	2
Trimethoprim with sulphonamides	99	60	1
Clindamycin	94	51	1
Doxycyclin	86	30	2
Amoxicillin	64	26	0
Piperacillin + tazobactam	56	32	2
Cefotaxime	48	25	0

We have previously reported that amended treatment recommendations resulted in changed prescription patterns for uncomplicated urinary tract infections. There was a decreased consumption of fluoroquinolones which is reflected in a decrease in reported adverse events. For nitrofurantoin which was increasingly prescribed a weak trend of a corresponding increase in the reporting of adverse reactions was noted. Due to the low number of reports and to the fact that data are based on spontaneous reporting, no clear conclusions can be made regarding these trends, Table 3.1.6.

TABLE 3.1.6. Number of most frequently spontaneously reported adverse events for fluoroquinolones and nitrofurantoin, during the period 2007 – 2011.

	2007	2008	2009	2010	2011	2007-2011
Fluoroquinolones (J01MA)						
Total no of reports	55	35	34	28	25	177
Number of reactions						
Musculoskeletal	13	9	9	5	6	42
tendinitis	7	2	3	3	2	17
tendon rupture	2	5	3	2	3	15
Skin- and subcutaneous tissue	12	4	7	8	5	36
Psychiatric disorders	4	2	1	3	3	13
Nitrofurantoin (J01XE01)						
Total no of reports	22	24	21	24	25	116
Number of reactions						
Respiratory system	3	6	8	6	3	26
dyspnoea	0	1	2	3	1	7
interstitial pneumonia	2	2	3	2	0	9
pulmonary fibrosis	0	0	0	0	0	0
Skin- and subcutaneous tissue	7	7	3	7	9	33
General disorders	6	7	5	9	7	34
fever	3	5	4	3	3	18

Antibiotic use in human and veterinary medicine

Increasing efforts are made to share experiences and coordinate initiatives regarding antibiotic policies between the human and veterinary medical sectors. This brief comparison of antibiotics prescribed in the two sectors is an attempt in that direction. Data collection and analysis have been done in collaboration between SMI (Swedish Institute for Communicable Disease Control) and the Strama-group for the veterinary medicine and the food industry, Strama VL. For more data on use of antibacterials in animals, please see SVARM 2011.

Figures reflecting total sales of antibiotics for systemic use in humans were retrieved as defined daily doses and recalculated as kilograms. Data on sales of antibiotics to animals are those presented in SVARM 2011. Sales for aquacultures are not included, nor are sales of medicines authorized for humans but sold for use in animals. The antibiotics included in the comparison are substances that are used in both disciplines and were sold in a quantity exceeding 1000 kg during 2011.

In total, 64.4 tons of antibiotics for systemic use (products indexed as ATC J01, excluding methenamine) were sold to humans. This is more than in 2010 and is consistent with the increase in number of DDD:s. When measuring the total antibiotic (J01 excl. mehtenamine) use in relation to estimated kg weight human in 2011, the total sale were 103.6 mg/kg weight. The corresponding figure for antibiotics for veterinary use (indexed QJ01) is 12.3 tons which is less than in 2010 and expressed as mg active substance (QJ01, QA07 and QJ51) per 'population correction unit' (PCU; estimated kg live-weight

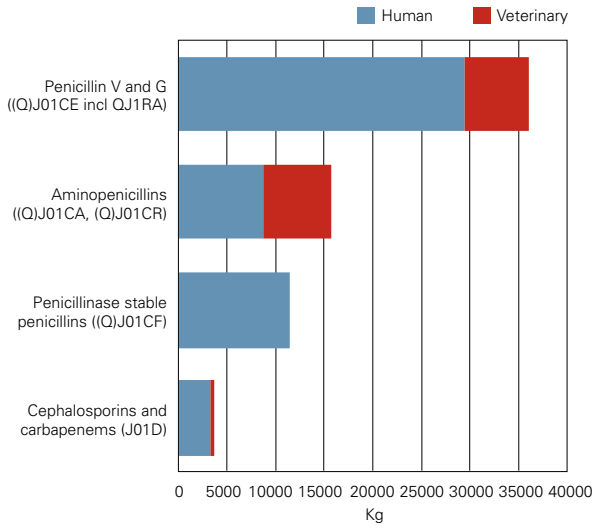


FIGURE 3.1.21. Amount of beta-lactam antibiotics in human and veterinary medicine, kg substance 2011. Please note the difference in indexation of the x-axis between figures3.1.21. and 3.1.22.

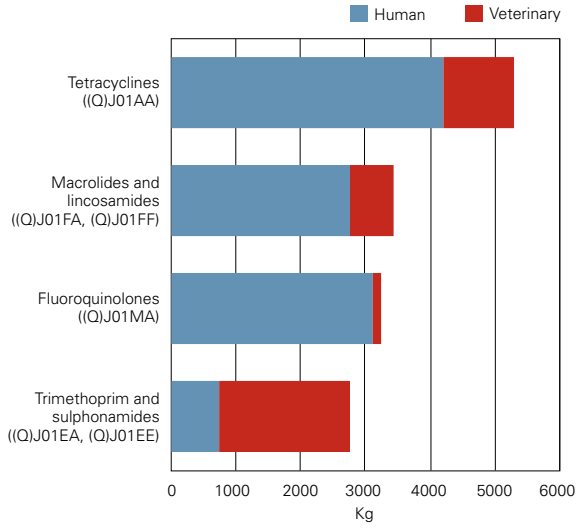


FIGURE 3.1.22. Amount of fluoroquinolones, macrolides, lincosamides, trimethoprim and sulphonamides, and tetracyclins in human and veterinary medicine, kg substance 2011. Please note the difference in indexation of the x-axis between figure 3.1.21. and 3.1.22.

of the populations of food producing animals), the sales in 2011 were 15.4 mg/PCU. Penicillins represent most of the weight in both categories; approximately 80 percent of human antibiotics and 60 percent of animal antibiotics.

Figure 3.1.21 displays the sales of beta-lactam antibiotics. These substances are by far the most used antibiotics in both human and veterinary medicine and also represent the largest amounts measured as kilograms. From an environmental and resistance perspective most of them are relatively harmless. However, the increasingly alarming global situation regarding carbapenem-resistance in *Enterobacteriaceae* must be kept in mind.

The substances in Figure 3.1.22 are sold in much smaller quantities (*n.b.* the difference in indexation of the x-axis between the figures), but their impact on the emergence of antibiotic resistance and the environment is more pronounced due to their chemical and pharmacological properties.

Human use makes up more than three quarters of all classes except trimethoprim and sulphonamides (J01EE and J01EA), where veterinary use represents 73.1 percent, Figure 3.1.22.

In a comparison of antibiotic use in human and veterinary medicine 2010 and 2011, the greatest change are shown in the use of narrow spectrum penicillins (J01CE) where the human use increased with 742 kg and the veterinary use decreased with 865 kg, Figure 3.1.23.

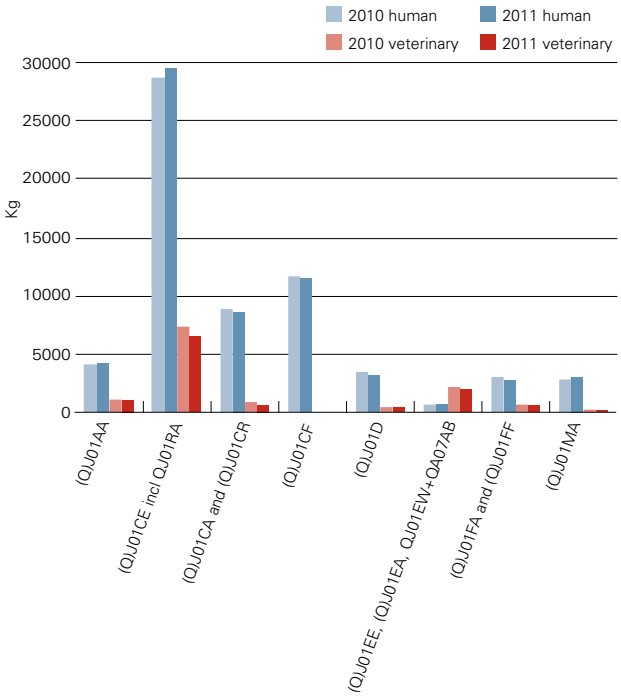


FIGURE 3.1.23. Kilograms of certain antibiotic classes in human and veterinary medicine 2010 and 2011.

3.2. Use of antifungals

Hospital care

Similar to the previous years there has been a small but steady increase from 2010 to 2011 in the use of antimycotic drugs for systemic use. The total use of antifungals is still low. In the year of 2010 there was an increase by 10% to 61.9 DDD per one million inhabitants and day, and during 2011 the increase was 4%, giving a total figure of 64 DDD per one million inhabitants and day. Fluconazole still constitutes the absolute majority of the antifungals used, 69% or 44 DDD per one million inhabitants and day. The increase of 4% in 2011 is related to an increased use of amphotericin B with 18%, and caspofungin with 18%. All other compounds have been stable during the last year. Use of amphotericin B was also increasing in 2010, but the reason for this trend i unknown. There has not been issued any new national guidelines that could explain the increased use. Most of the rise comes from the county of Stockholm which by far harbors the largest population. Since the overall figures are low the increase might be due to the treatment of only a few patients, but as there have been reports from other countries of increased azole resistance in *Aspergillus fumigatus* we currently cannot rule out that the increase in amphotericin

B is due to clinical failure with azole therapy.

It is of great importance to closely monitor the future development.

Fluconazole, which is a narrow spectrum antimycotic with effect towards candida species (excluding among others *C. krusei* and most strains of *C. glabrata*), stands for 69% of all consumption. It is a fungiostatic drug that is indicated for treatment of invasive non *krusei*, non *glabrata* candidosis in non neutropenic patients and for cryptococcosis. It is also used as prophylaxis against candida infection and as treatment for local infections such as thrush.

The new azoles; voriconazole which is regarded as treatment of choice for proven or probable aspergillosis, and posaconazole, increasingly used as prophylaxis against invasive fungal infection in certain high-risk neutropenic patients, both have excellent bioavailability after oral administration. Both drugs have good effect against the most common candida species with the possible exception of *C. glabrata*, which is an emerging pathogen in Sweden and now constitutes approximately 20% of all episodes of candidemia.

The use of voriconazole is still low in absolute numbers (2.44 DDD per one million inhabitants and day), and has been constant for the last few years. The total use in outpatient settings is three times higher and the absolute majority of voriconazole therapies are initiated and monitored by hospital physicians, so it is probably more correct to confer those data to hospital use rather than primary health care use.
Voriconazole is the only broad-spectrum antifungal drug that can be given orally and is therefore often used when the initial intravenous therapy is switched to oral, even in those cases when therapy was started with an echinocandin or amphotericin B. It is also used as secondary prophylaxis against aspergillus infections.

Posaconazole can also be given orally, as a suspension, but in Sweden it is only licensed as second line therapy for invasive fungal infection refractory to the first line treatment and as prophylaxis, so it is mainly used as prophylaxis in haematologic units. The total use increased by 61% in 2011. The total amount is still low; 1.3 DDD per one million inhabitants and day are used in hospital care, and 3.2 DDD per one million inhabitants and day are used in outpatients' settings. As for voriconazole it is probably more correct to confer all data to hospital use.

Since 2005 there has been a small but steady increase in the use of the echinocandins. In 2011 the use increased by 15%, making the total amount 5.7 DDD per one million inhabitants and day, and the group constitutes 8.9% of all systemic antifungals used in hospitals. Caspofungin which has been available in Sweden since 2002 is the most used, 88%. The echinocandins have a fungicide effect against candida species and a fungiostatic effect against *A. fumigatus*. Therefore those agents are increasingly used as first line therapy for patient with febrile neutropenia when antibiotics alone have not been successful and when there is a suspicion of infection with yeasts or mold. Both indications and side effects differ a little between the agents but the antifungal spectrum is similar.

Amphotericin B has for a long time been considered the golden standard for treatment of invasive fungal infection due to its broad spectrum and well documented effect against most yeasts and molds. However the tolerability is a problem. Side effects are common with nephrotoxicity and electrolyte imbalance as the most severe. Therefore amphotericin B is now mostly used in its liposomal form, which improves tolerability. The use has remained at the same level from 2005-2009 but increased substantially by 60% during 2010, followed by an 18% increase in 2011 making it now the most common broad spectrum antifungal drug in Swedish hospitals.

During the last years there have been many reports of a shift in the distribution of candida species, with an increase in non *albicans* species, especially *C. glabrata*, whose sensitivity to the azoles is debated. Two European centers have also reported the emergence of voriconazole resistance in *A. fumigatus* during azole therapy.

An increased awareness and monitoring of developing resistance to antifungal drugs is warranted.

Outpatient care

Seventy percent of all systemically administrated antifungal drugs are sold on prescription. The majority of those prescriptions were issued in primary health care. The most commonly prescribed drug is fluconazole, mainly for mucocutaneal infections.

There are many different topical applications containing imidazoles, with or without steroids, mainly used for dermatophyte infections of the skin or vaginal yeast infections. Some of those are sold on prescription and others are available as OTC drugs for self-medication.

Data comparing sales of antimycotic drugs between different countries are rare but recently ESAC published comparative data from different European countries, showing that the Swedish figures of sales are relatively low.

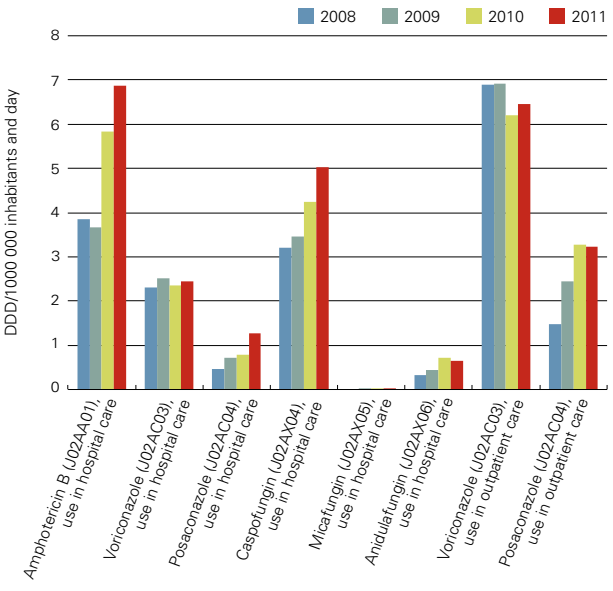


FIGURE 3.2.1. Use of broad spectrum antifungals in hospital care and in outpatient care, 2008-2011, DDD/1000 000 inhabitants and day.

4. Antimicrobial resistance

SWEDISH surveillance of antimicrobial resistance is normally based on testing of clinical samples and samples taken according to local screening programmes and outbreak investigations. Each part of the Swedish surveillance programme is based on data collected from all of the clinical microbiology laboratories. In these laboratories testing of clinical isolates for antibiotic susceptibility is routinely performed using the standardized disk diffusion method. In 2011, all laboratories have shifted to the recently standardized disk diffusion methodology as proposed by EUCAST (Appendix 4). Commercially available tests for MIC determination are also used, and in recent years there has also been an increase in the use of automated methods for susceptibility testing and categorization.

Notifications according to the Communicable Disease Act form the first part of the national surveillance programme. The first finding of a methicillin resistant *Staphylococcus aureus* (MRSA), a pneumococcus with decreased susceptibility to penicillin G (PNSP, MIC ≥ 0.5 mg/L), a vancomycin-resistant *Enterococcus faecalis* or *Enterococcus faecium* (VRE) or an *Enterobacteriaceae* producing extended-specrum betalactamases (ESBL) are notifiable according to the Communicable Disease Act, regardless of whether they were judged to cause a clinical infection or merely colonisation without infection. MRSA, PNSP and VRE require notifications by laboratories as well as by the diagnosing clinicians, whereas ESBL require laboratory notification only. The definition of an ESBL was altered in 2010 to encompass not only classical ESBLs which are inhibited by clavulanic acid ($ESBL_A$) but also plasmid-mediated AmpC-betalactamases ($ESBL_M$) and metallo-betalactamases / carbapenemases ($ESBL_{CARBA}$).

The annual resistance surveillance and quality control (RSQC) programme, initiated in 1994, form the second part of the national surveillance (Appendix 5). Well-characterized data on resistance in several commonly encountered bacterial species are now available from several years both at regional and national level.

Under the heading **Data on invasive isolates reported to ECDC/EARS-Net,** results from the Swedish part of the European Antimicrobial Resistance Surveillance Network are presented. Twenty of twenty-eight Swedish laboratories, covering approximately 75% of the population, regularly report susceptibility data on invasive isolates of seven defined bacterial species to ECDC/EARS-Net via the Swedish coordinator at SMI. Ten of these laboratories, with coverage of approximately 55% of the Swedish population, also deliver data on invasive isolates from all positive blood cultures (Appendix 5). For bacterial species other than those reported to ECDC/EARS-Net, data on resistance is presented under the heading **Surveillance of invasive isolates in addition to EARS-Net.**

One of the cornerstones in the battle against antibacterial resistance in Sweden has been the early identification of cases via screening programmes and contact-tracing around cases with notifiable resistance markers. The annual numbers of samples specifically registered by the laboratories to be analysed by screening methods for (multi-)resistant bacteria, MRB, is shown in Figure 4.1. Even though the screening programmes and criteria for registering analyses under this heading may vary between laboratories, they are fairly constant within each laboratory over time. In 2011 25 of 28 laboratories provided data on MRB- screening.

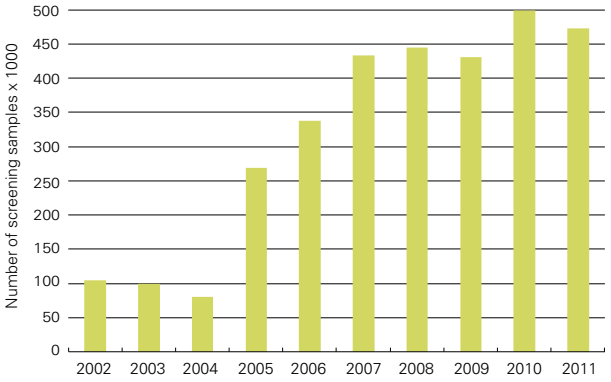


FIGURE 4.1. Annual number of recorded screening samples for multi-resistant bacteria 2002-2011.

Staphylococcus aureus including MRSA

Notifications of MRSA according to the Communicable Disease Act

MRSA has been mandatory notifiable since the year 2000. Infection control programmes have been developed and implemented locally under supervision of the County Medical Officers (CMO) and infection control teams. These programmes are based on early case-finding through extensive screening of patients with risk factors and contact tracing combined with infection control measures such as isolation of MRSA positive cases and intensive campaigns on basic hygiene precautions. The following presentation is based on data collected in the national web-based notification system SmiNet. During the last six years an active effort has been made to improve the quality of data and to collect missing data. The notifications have been reviewed and complemented with available relevant epidemiologic information from investigations around each case in collaboration with the CMOs.

In 2011 a total of 1884 cases of MRSA were notified, an increase by 304 cases (19%) compared to 2010, Figure 4.2.

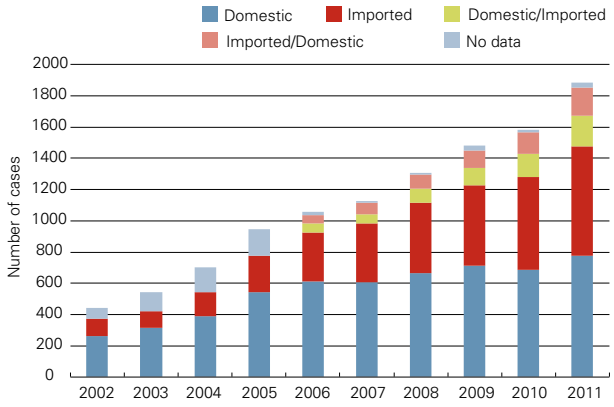


FIGURE 4.2. Number of MRSA cases annually notified in Sweden 2002-2011 by country of infection. "Domestic/Imported" and "Imported/Domestic" indicate several mentioned countries of infection with the most likely mentioned first.

In 2011, four of the Swedish counties, Skåne, Stockholm, Västra Götaland and Kronoberg, had a higher incidence than the average national incidence of 20 cases/100 000 inhabitants, Table 4.1.

During 2011, 41% (n=774) of all reported MRSA cases were domestically acquired and 37% (n=701) were acquired abroad. Iraq (45 cases), Philippines (42 cases), Serbia and Montenegro (40 cases), China (35 cases) and Thailand (32 cases) made up the five most common countries for imported MRSA infection. In 20% of the cases Sweden and at least one more country were mentioned as possible countries for acquisition of MRSA. When these reported secondary countries were also considered, the five most common countries were almost the same, but ranked differently: Philippines (93), Iraq (85), Thailand (52), India (50) and China (50). The country for acquisition was reported as "unknown" in 32 cases.

Among the domestic MRSA cases 2006-2011, the incidence was highest in the age group 80 years and older, Figure 4.3. Since 2006 there has been a decreasing incidence in this age group and an increasing incidence among children 0-6 years. In 2009 the incidences in these two age groups were almost identical (16-17), in 2010 they diverged, and in 2011 the incidences in both age groups approximated 19. In all other age groups the incidence of domestic MRSA has remained at a low and stable level around 5.

TABLE 4.1. MRSA notifications according to the Communicable Disease Act 2002-2011 by county.

	2002		2003		2004		2005		2006		2007		2008		2009		2010		2011	
County	**No**	**Inc**	**No**	**Inc**	**No**	**Inc**	**No**	**Inc**	**No**	**Inc**	**No**	**Inc**	**No**	**Inc**	**No**	**Inc**	**No**	**Inc**	**No**	**Inc**
Blekinge	4	2,7	2	1,3	3	2,0	9	6,0	4	2,6	16	10,5	10	6,6	11	7,2	8	5,2	17	11,1
Dalarna	2	0,7	2	0,7	3	1,1	6	2,2	11	4,0	15	5,4	23	8,3	27	9,8	27	9,7	38	13,7
Gotland	3	5,2	3	5,2	1	1,7	10	17,4	4	7,0	8	14,0	6	10,5	6	10,5	5	8,7	9	15,7
Gävleborg	12	4,3	6	2,2	5	1,8	22	8,0	18	6,5	12	4,4	26	9,4	12	4,3	26	9,4	36	13,0
Halland	13	4,7	13	4,6	4	1,4	21	7,3	23	8,0	18	6,2	16	5,5	45	15,2	40	13,4	51	16,9
Jämtland	2	1,6	5	3,9	1	0,8	7	5,5	3	2,4	24	18,9	31	24,4	18	14,2	28	22,1	19	15,0
Jönköping	5	1,5	24	7,3	14	4,3	40	12,1	42	12,7	17	5,1	20	6,0	66	19,6	54	16,0	61	18,1
Kalmar	5	2,1	6	2,6	16	6,8	23	9,8	26	11,1	36	15,4	29	12,4	42	18,0	72	30,8	45	19,3
Kronoberg	4	2,3	5	2,8	16	9,0	11	6,2	14	7,8	13	7,2	19	10,4	26	14,2	23	12,5	40	21,7
Norrbotten	6	2,4	9	3,6	7	2,8	8	3,2	5	2,0	10	4,0	16	6,4	13	5,2	21	8,4	20	8,1
Skåne	63	5,5	101	8,8	127	10,9	160	13,7	180	15,2	168	14,0	271	22,3	284	23,1	313	25,2	369	29,5
Stockholm	205	11,1	227	12,2	277	14,8	317	16,8	358	18,7	351	18,0	342	17,3	375	18,6	411	20,0	502	24,0
Södermanland	4	1,5	2	0,8	8	3,1	9	3,4	9	3,4	26	9,8	20	7,5	23	8,6	30	11,1	34	12,5
Uppsala	10	3,4	12	4,0	25	8,3	28	9,2	24	7,5	33	10,2	40	12,2	33	10,0	41	12,2	42	12,4
Värmland	5	1,8	11	4,0	18	6,6	9	3,3	13	4,8	32	11,7	22	8,0	33	12,1	28	10,2	48	17,6
Västerbotten	10	3,9	13	5,1	16	6,2	10	3,9	7	2,7	23	8,9	22	8,5	28	10,8	39	15,0	39	15,0
Västernorrland	7	2,9	10	4,1	5	2,0	4	1,6	8	3,3	22	9,0	35	14,4	43	17,7	30	12,4	24	9,9
Västmanland	7	2,7	11	4,2	12	4,6	36	13,8	48	19,3	54	21,7	23	9,2	46	18,3	32	12,7	28	11,0
Västra Götaland	47	3,1	61	4,0	117	7,7	126	8,2	176	11,4	177	11,4	243	15,6	257	16,4	264	16,7	347	21,8
Örebro	16	5,9	8	2,9	12	4,4	16	5,8	35	12,7	25	9,1	46	16,6	45	16,1	40	14,3	44	15,6
Östergötland	7	1,7	14	3,4	14	3,4	101	24,3	47	11,2	49	11,7	43	10,2	45	10,5	47	10,9	71	16,5
Total	437	4,9	545	6,1	701	7,8	973	10,8	1055	11,6	1129	12,3	1303	14,1	1478	15,8	1579	16,8	1884	19,9

Inc = Incidence (cases/100 000 inhabitants)

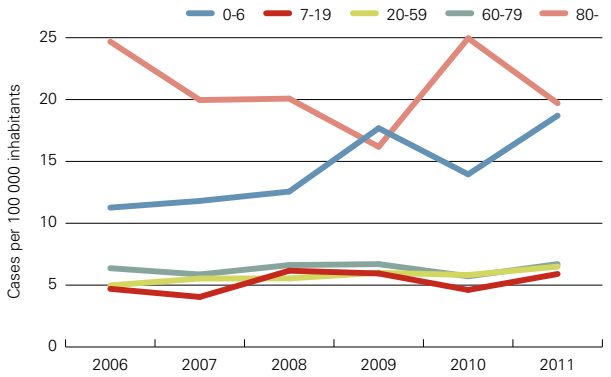


FIGURE 4.3. Age group adjusted incidence of notified domestic MRSA cases Sweden 2006-2011.

In 2011 42% of the domestic cases were identified through contact tracing, 9% in targeted screening, and 47% during investigations of clinical symptoms, Figure 4.4. For imported cases the corresponding figures were 13%, 49% and 37%, respectively. Invasive MRSA infection was reported in 28 cases 2011. 21 of those were newly notified cases 2011 and 7 occurred in patients previously known to carry MRSA.

Epidemiological classification of the acquisition of MRSA was based on information in the clinical notifications and from subsequent investigations by the CMOs, Figures 4.5 A and B.

Community-acquired infections dominated among domestic cases 2011 and comprised 68% (n=529) of all domestic cases, Figure 4.5 A. There has been a continuous increase in the proportion of community acquired cases since 2006, and in Sweden today MRSA is acquired primarily in the community. Among the imported cases the proportion of community acquired infections was 42% (n=295), Figure 4.5 B. Community acquisition was reported in 74% of the cases for which it was uncertain whether MRSA was acquired domestically or imported (n=280, not presented graphically).

Hospital acquired MRSA was comparatively more common in imported cases, 33% (n=235), than among domestic cases, 7% (n=52). The number of domestic cases with hospital acquired MRSA decreased from 64 to 52 compared with 2010 and the number of domestic hospital acquired cases has been more than halved as compared to 2006 and 2007, when 135 and 127 cases were reported, respectively.

The number and the proportion of domestic cases with MRSA acquired in healthcare/care outside hospital was reduced to 75 (10%) in 2011 compared to 102 (15%) in 2010. During 2011 only minor outbreaks in different counties were reported from the Swedish healthcare system and from long-term care facilities.

Epidemiological typing of MRSA

The primary method used at SMI for epidemiological typing of MRSA isolated from newly reported cases is *spa* typing. This method replaced pulsed-field gel electrophoresis (PFGE) in 2006. An important advantage of *spa* typing is that it is a sequence based method with a standardised nomenclature (http://spaserver.ridom.de). This nomenclature (Ridom nomenclature) is unambiguous, easy to communicate and internationally well recognised. In addition to *spa* typing all isolates are tested by PCR for presence of genes encoding the toxin PVL (Panton-Valentine Leukocidin).

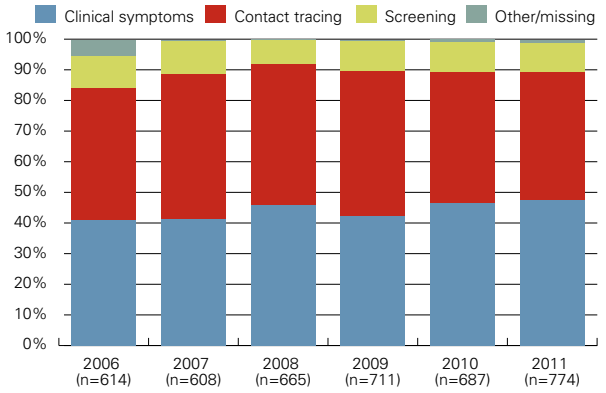


FIGURE 4.4. The reasons for detection of domestic MRSA cases in Sweden 2006-2011. n refers to the number of reported cases each year.

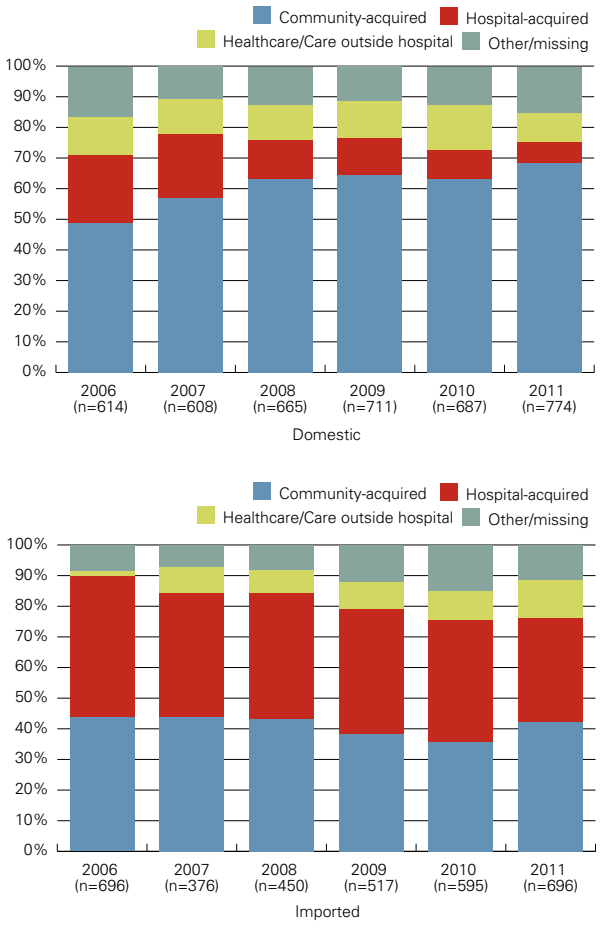


FIGURE 4.5. A and B. Epidemiological classification of the acquisition of domestic (A, top) and imported (B, bottom) MRSA, Sweden 2006-2011. n= number of notified cases each year.

In total, 316 *spa* types were seen among MRSA isolated from the 1884 newly reported cases in 2011. The ten most common *spa* types in 2007-2011 are listed in Table 4.2. In 2011, 864 cases (46%) had a top ten MRSA *spa* type. Eight of the most common *spa* types in 2011 were among the top ten also in 2010. One noticeable change between 2010 and 2011 was the continued decrease of t032 MRSA. From being the most common *spa* type in 2007, t032 was only seen in MRSA isolated from 22 cases in 2011. This *spa* type is associated with MLST sequence type (ST) 22 and PFGE pattern UK E15 (SMI nomenclature; EMRSA-15, international nomenclature). Another change in 2011 was the increased number of MRSA belonging to *spa* types t690 and t790. In 2010 these *spa* types were seen in MRSA from 21 and 19 cases, respectively. PVL positive variants of t690 MRSA have been isolated in Sweden since 2003 and PVL negative variants since 2005. MRSA belonging to *spa* type t790 have been isolated in Sweden since 2007. All these isolates have been PVL negative.

TABLE 4.2. The ten most common *spa* types in 2007-2011 listed in decreasing order per year. Numbers of notified cases are shown in brackets for 2009-2011. For 2011 numbers of PVL positive / PVL negative / PVL data missing are shown in square brackets.

2007	2008	2009	2010	2011
t032	t002	t008 (157)	t008 (150)	t008 (167) [139 / 24 / 4]
t008	t008	t044 (108)	t002 (100)	t002 (166) [47 / 117 / 2]
t044	t044	t002 (106)	t044 (98)	t019 (130) [125 / 4 / 1]
t002	t019	t019 (59)	t019 (65)	t044 (92) [85 / 2 / 5]
t037	t032	t015 (58)	t223 (53)	t223 (76) [5 / 71 / 0]
t015	t127	t437 (53)	t437 (52)	t127 (69) [8 / 59 / 2]
t437	t437	t127 (44)	t127 (51)	t437 (49) [36 / 13 / 0]
t690	t024	t223 (46)	t032 (35)	t690 (46) [30 / 12 / 4]
t024	t015	t032 (38)	t015 (32)	t015 (37) [0 / 36 / 1]
t019	t037	t037 (27)	t021 (26)	t790 (32) [0 / 32 / 0]

The proportion of PVL positive MRSA among all tested isolates (n=1793) was 41%. This was an increase from 36% in 2010. In 2011 a PVL positive MRSA most often belonged to *spa* types t008, t019 or t044. The two most common *spa* types, t008 and t002, were seen both in PVL positive and PVL negative MRSA. Some PVL positive t008 MRSA isolates had PFGE pattern SE03-5 (SMI nomenclature). This pattern is indistinguishable from that of the USA300 MRSA prototype strain. However, since PFGE is no longer performed on all isolates the actual number of USA300 MRSA in Sweden is unknown.

Since 2006 there has been focus on the zoonotic potential of MRSA, especially on livestock associated MRSA belonging to MLST clonal complex (CC) 398 that have been causing problems in the Netherlands, Denmark and other European countries. In Sweden 2006-2011, MRSA belonging to a CC398 associated *spa* type have been isolated from 44 human cases; t034 (n=29), t011 (n=10), t571 (n=3) and t108 (n=2). The majority of these isolates were PVL negative. None of the PVL positive isolates (t034, n=13) came from cases with known animal contact. Six of the t034 cases (five PVL negative and one PVL positive), three of the t011 and one of the t571 cases were reported in 2011. During 2006-2011 only two cases, both with t011 MRSA, have had known contact with horses or other domestic animals.

In 2011 researchers from the UK, Denmark, Germany and Ireland presented the DNA sequence of a novel *mecA* homologue, $mecA_{LGA251}$. This *mecA* variant was first seen in MRSA isolated from bovine samples, cow's milk, and later also from human samples. MRSA with $mecA_{LGA251}$ have been isolated from 15 human cases in Sweden 2011. The following nine *spa* types were seen: t373, t528, t843, t9122, t9268, t9716, t978, t3391 and t9111. The first six are associated with MLST CC130 and the remaining three to MLST CC1943. Only three *spa* types were seen in MRSA from more than one case, t843 (5 cases), t3391 (2 cases) and t9111 (2 cases).

Antibiotic resistance in MRSA

All MRSA isolates were investigated with regard to resistance to antibiotics other than beta-lactam antibiotics. Out of 1492 isolates tested (representing MRSA from all counties except Skåne and Örebro), 647 (43%) had no other resistance marker than the *mecA* gene defining them as MRSA. Among the remaining 845 strains, macrolide resistance (resistance to erythromycin and/or clindamycin) was still the single most frequently seen resistance marker (n=547) in MRSA of many different *spa* types, indicating that this type of resistance is very widespread. Resistance to ciprofloxacin was the second most common resistance marker (n=301), followed by resistance to gentamicin and other aminoglycosides (n=212), resistance to fusidic acid (n=143), and to a much lesser degree resistance to rifampicin or to mupirocin. This trend was described in previous SWEDRES reports and is still valid.

MRSA of the ten most common *spa* types often had quite stable antibiotic resistance patterns. Four of them were only resistant to beta-lactam antibiotics (t019, t223, t015 and t790), whereas the others had various combinations of resistance to ciprofloxacin, erythromycin/clindamycin and fusidic acid. Resistance to kanamycin, an aminoglycoside antibiotic not used in clinical practice, was frequent in t044 and appeared also in t008, t002, t127 and t437. Multi-resistance, when defined as beta-lactam resistance and resistance to at least three other antibiotic classes (represented by ciprofloxacin, erythromycin /clindamycin, gentamicin/kanamycin, fusidic acid or rifampicin), was found in a total of 197 isolates (13% of tested isolates).

Annual Resistance Surveillance and Quality Control (RSQC) programme

Staphylococcus aureus from skin and soft tissue infections has been included in the annual RSQC programme since 2001 (Appendix 5). In 2011 23 laboratories, representing 20 of the 21 counties, provided data on 200 consecutive isolates using the disk diffusion method for cefoxitin (screening disk for detection of MRSA), clindamycin, erythromycin, fusidic acid, and an aminoglycoside (gentamicin or tobramycin). Norfloxacin was used as screening disk for detection of fluoroquinolone resistance. The average resistance rates, as retrieved from ResNet, are shown in Figure 4.6.

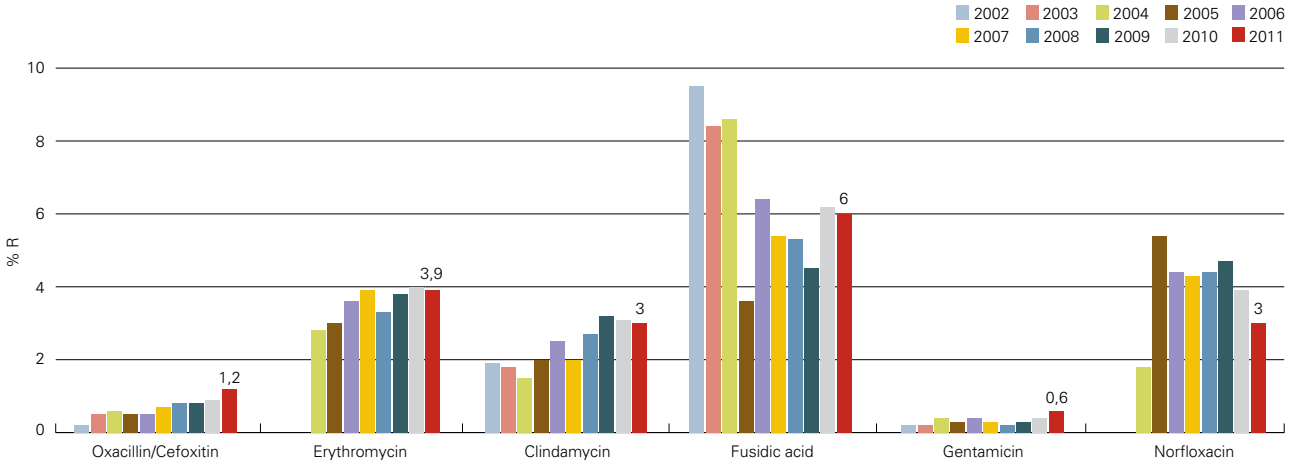


FIGURE 4.6. Resistance rates for *Staphylococcus aureus* from skin and soft tissue infections 2002–2011 (data from the annual RSQC programme, 3000-5000 isolates per year). In 2005 resistance rates were recorded in *S.aureus* isolated from skin and soft tissue infections from elderly (> 65 years) people only.

The frequency of MRSA in skin and soft tissue infections (SSTI) (cefoxitin used as test compound) has increased slowly, and in 2011 it exceeded 1% for the first time. The average resistance rates for erythromycin (3.9%), clindamycin (3%) and fusidic acid (6%) were practically the same as in the previous 2 years. Almost no resistance to aminoglycosides was seen in bacteria from SSTI. Fluoroquinolone resistance had decreased to 3%.

Data on invasive isolates reported to ECDC/EARS-Net

In 2011, 0.8% of the invasive *S. aureus* isolates were MRSA (identified by the cefoxitin screen disk test and confirmed by detection of the *mecA* gene), Table 4.3. This low level has remained during the eleven years of mandatory reporting, indicating that infection control measures to prevent MRSA from spreading in the hospital environment have been successful.

TABLE 4.3. Invasive isolates of *Staphylococcus aureus* tested by disk diffusion and number and percentage of methicillin resistant isolates (R, confirmed by presence of the *mecA* gene). Data from Sweden 2002-2011 reported to ECDC/EARS-Net and retrieved from the EARS-Net database 2012-05-23.

Year	R	Total number
2002	11 (0.6%)	1836
2003	16 (0.9%)	1855
2004	14 (0.7%)	1906
2005	18 (1.0%)	1774
2006	16 (0.9%)	1967
2007	10 (0.5%)	2163
2008	16 (0.7%)	2409
2009	25 (1.0%)	2457
2010	14 (0.5%)	2856
2011	25 (0.8%)	3143

Streptococcus pneumoniae

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 addition invasive infections with *S. pneumoniae*, regardless of resistance, became notifiable in 2004. Pneumococci have been part of the annual RSQC programme since 1994.

Notifications according to the Communicable Disease Act

In 2011 there were 314 PNSP cases notified in Sweden, a decrease by 23% compared with 2010, Figure 4.7. Forty-nine percent of the cases had been infected domestically and 16% of the cases in a foreign country. In the remaining 111 cases no country for acquisition was given.

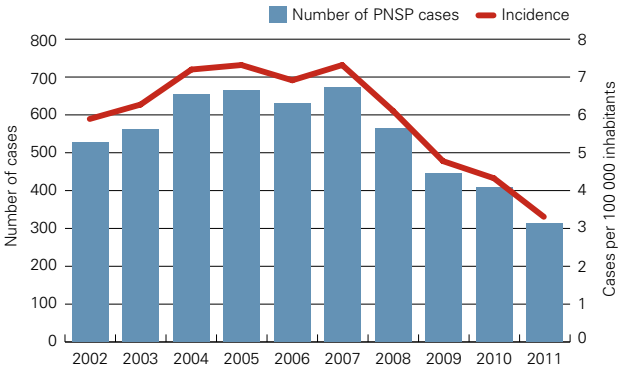


FIGURE 4.7. Number of cases of *S. pneumoniae* with reduced susceptibility to penicillin, MIC ≥ 0.5 mg/L (left) and cases per 100 000 inhabitants (right), Sweden 2002-2011.

The incidence of PNSP in Sweden 2011 was 3.3 cases per 100 000 inhabitants. Previous analyses have indicated that the declining incidence was related to a concurrent decrease in nasopharyngeal culturing propensity. The majority of PNSP cases, independent of year observed, were found in the age group 0-4 years, Figure 4.8. Since 2007, the decrease in the number of reported cases was found primarily in this age-group. There was no difference in the proportion of the reported cases with regard to gender.

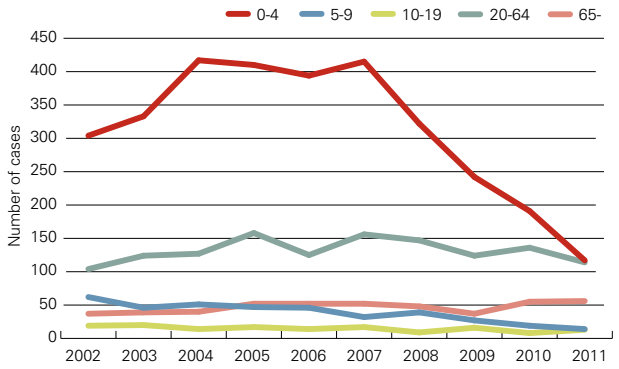


FIGURE 4.8 Age-group distribution among all cases reported with PNSP in Sweden 2002-2011.

PNSP were reported from all Swedish counties, with Stockholm (101 cases) and Skåne (58 cases) accounting for 51% of all notifications (but only 34% of the Swedish population). In these two counties, the number of notifications decreased by 46% in Skåne and by 41% in Stockholm, compared with 2010.The remaining counties reported 1-26 cases each. Due to regional differences in general culturing propensity, case finding intensity as well as presence of targeted screening programmes, a comparison of regional incidences is not meaningful.

The majority, 63% of all notifications of PNSP, were found in cultures from the nasopharynx. In 50% of all cases the detection of PNSP was due to clinical infection, and in 16% due to targeted screening including contact tracing. In the remaining cases another reason for sampling was stated (4%) or the information was missing (29%).

Serotype distribution

In 2011, 21 cases of invasive PNSP infections were reported, and in 20 of these, bacteria were isolated from blood. Serotypes of these 20 cases show that the dominating serotype, like in previous years, was serotype 14 (seven cases), followed by type 9V (four cases). The serotype distribution among all PNSP 2011 had changed somewhat compared to 2010. The preliminary results for the most commonly found serotypes (254 isolates sent to SMI and tested so far) were, in decreasing order, type 19F (23%), followed by non-typeable (NT) (18%), 35B (11%), 14 (9%), 19A (7%), 6B and 23F (6% each), and 9V (5%).

Annual Resistance Surveillance and Quality Control (RSQC) programme

The isolates collected during the RSQC surveys were mainly derived from nasopharyngeal cultures. In most years a total of approximately 3000 consecutive isolates from all clinical laboratories have been tested for susceptibility to penicillin (by means of oxacillin 1 µg screen disk), erythromycin, clindamycin (since 2004), tetracycline, trimethoprim-sulfamethoxazole, and norfloxacin (since 2005, used as indicator for fluoroquinolone resistance) using the disk diffusion method. In 2011 21 laboratories delivered data according to the newly introduced EUCAST methodology (Appendix 4), and 2081 isolates were included in the analysis. The national summary of the results, as retrieved from ResNet, are shown in Figure 4.9. During most of the previous years there has been an increase in the rates of resistance for all tested antibiotics. However, since 2010 this successive increase has stopped for all tested antibiotics except for oxacillin/penicillin.

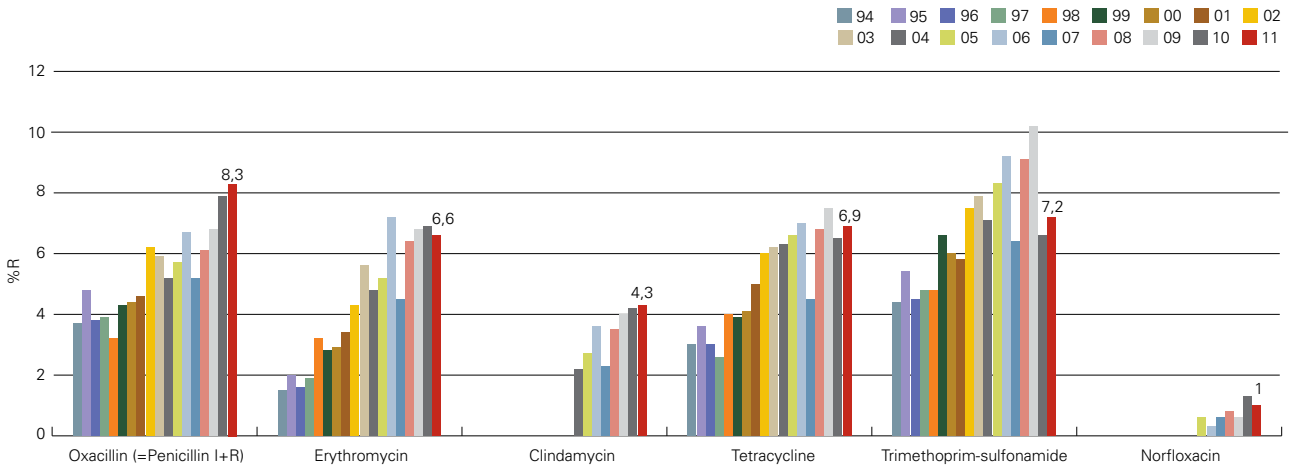


FIGURE 4.9. Resistance rates for *Streptococcus pneumoniae* 1994-2011 (data from the annual RSQC programme, 2-3000 isolates per year).

Data on invasive isolates reported to ECDC/EARS-Net

The Swedish data on susceptibility to penicillin and erythromycin among invasive isolates for 2002-2011 are given in Tables 4.4. A and B. Levels of resistance were lower among invasive isolates than in the nasopharyngeal isolates from the RSQC programme (see above). One explanation, although not proven, could be that asymptomatic carriers diagnosed during contact tracing are included in the RSQC programme. Not only are the resistance levels lower, but there has also been no increased resistance among invasive isolates, neither for penicillin nor erythromycin.

TABLE 4.4. A AND B. Invasive isolates of *Streptococcus pneumoniae* tested for susceptibility to penicillin (A) and erythromycin (B). Number of strains tested and percentage SIR are given. Data from Sweden 2002-2011 reported to ECDC/EARS-Net and retrieved from the EARS-Net database 2012-05-23.

	Penicillin * (I+R = PNSP)			
Year	**S%**	**I%**	**R%**	**Total**
2002	97.6	2.0	0.4	830
2003	95.3	4.3	0.4	917
2004	96.8	2.8	0.4	955
2005	96.4	3.1	0.5	1017
2006	97.9	1.3	0.8	993
2007	97.0	2.9	0.1	1028
2008	98.0	1.6	0.4	1213
2009	96.7	0.8	2.5	1060
2010	96.3	1.5	2.3	960
2011	96.5	2.6	0.9	1019

* S < 0.12 mg/L; I 0.12 - 1 mg/L; R > 1 mg/L

	Erythromycin			
2002	94.4	0.3	5.3	683
2003	95.4	0.1	4.5	760
2004	94.7	0.1	5.2	869
2005	94.3	0.3	5.4	932
2006	95.2	0.3	4.5	943
2007	94.7	0.1	5.2	926
2008	94.4	0.4	5.2	1129
2009	95.9	0.2	3.9	1010
2010	96.0	0.1	3.9	955
2011	95.3	0.2	4.5	936

Enterococcus faecalis and *Enterococcus faecium*

Background

Vancomycin resistant enterococci (VRE) have become important causes of nosocomial infections in many parts of the world, usually involving high-risk populations 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.

From 2000 to 2006 only low numbers (18-35 per year) of VRE-cases were reported in Sweden. In 2007, reports came from Stockholm County about an increase in the number of VRE-cases, and the total yearly count was 53 cases. An increased occurrence of VRE was also reported from Västmanland, Halland and Uppsala counties during 2008-2009. This was the beginning of an outbreak that would last until 2011, when it was finally declared to have come to an end in all four affected counties. The total number of cases with an *Enterococcus faecium* with *vanB* belonging to this outbreak was 872. A majority of the reported cases were domestic and healthcare-related. Epidemiological typing of these *Enterococcus faecium vanB* showed that all examined isolates from Västmanland and Halland, as well as the majority of isolates from Stockholm County, had closely related PFGE patterns, suggesting spread of the same strain. The recognition of the outbreak led to intensified control measures, such as contact tracing and improved screening methods.

Notifications of VRE according to the Communicable Disease Act

During 2011 a total of 122 cases were reported, a decrease by 43% compared to 2010. VRE cases were reported from 17 of the 21 Swedish counties. The average national incidence of VRE was 1.3. The highest incidence 15.3 was reported from Västernorrland County. This was explained by an outbreak that started in 2010 and included two regional hospitals. The strain which was isolated from most of the cases was a new *Enterococcus faecium vanB* strain, i.e. not related to the previously reported outbreak strain. Cases belonging to this new outbreak were also reported during the first half of 2011, but discontinued during the second half of the year, and the outbreak was then declared to be over. The number of cases belonging to the outbreak was estimated to 100.

The counties of Stockholm and Skåne also had incidence figures slightly above the national average, with 1.9, and 1.4 cases per 100 000 inhabitants, respectively.

In Figure 4.10 the epidemic curve of the first outbreak strain prevailing in 2007-2010 is shown. The number of cases had decreased significantly in 2010, although isolates with the typical PFGE pattern of this strain were still detected. During the first 11 months of 2011 no cases with the previous outbreak strain were reported, but in December a minor outbreak of 8 new cases was detected in Stockholm County.

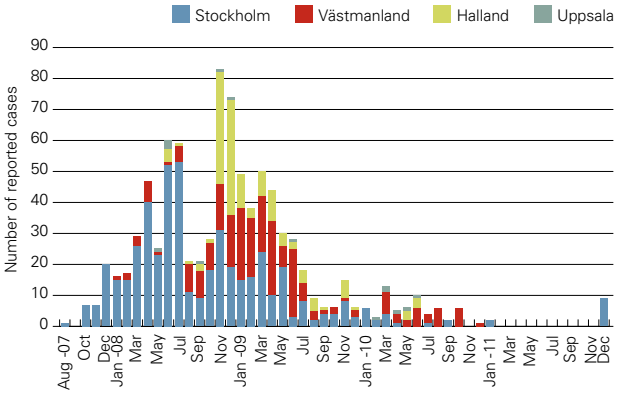


FIGURE 4.10. Epidemic curve for spread of domestic *Enterococcus faecium* with *vanB* with PFGE-pattern SE-EfmB-0701.

Of all cases 2011, 59% (n=72), were reported as domestic, and 80% of those (n=58) were health-care related. For the remaining 14 domestic cases the route of transmission was not known. In 35% (n=43), VRE had been acquired abroad, and 20 different countries were stated. In seven cases the country of acquisition was unknown. Thirty-five of the imported cases were healthcare related.

The domestic VRE cases were detected due to contact tracing in 82% (n=59), screening in 7% and clinical symptoms in 8%. For 3% another reason for detection was stated. The majority of the imported cases (81%, n=35) were detected through screening, 12% due to clinical symptoms and 2% due to contact tracing. For 5% another reason for detection was stated.

In 2011, 111 cases had *Enterococcus faecium*. Of these, 70 carried the *vanB* gene and 38 *vanA*. Information was missing for three cases. *Enterococcus faecalis* was reported in 11 cases, eight with a *vanA* gene and two with *vanB*. In one case the resistance gene was not reported. The species and resistance genotype distribution per county for domestic and healthcare related cases in 2011 are presented in Table 4.5.

TABLE 4.5. Species and resistance genotypes for VRE cases 2011.

County	Total number of cases	Efm [a], vanB	Efm, vanA	Efs [b], vanB	Efs, vanA	No data
Dalarna	1	-	-	1	-	-
Gotland	1	1	-	-	-	-
Gävleborg	1	1	-	-	-	-
Halland	4	1	3	-	-	-
Jämtland	1	-	-	-	-	1
Jönköping	3	2	1	-	-	-
Kalmar	2	-	2	-	-	-
Kronoberg	1	-	-	-	1	-
Norrbotten	1	-	-	-	-	1
Skåne	17	3	12	-	2	-
Stockholm	40	26	13	-	1	-
Södermanland	1	-	-	-	-	1
Värmland	2	-	2	-	-	-
Västernorrland	37	33	-	1	3	-
Västmanland	2	1	1	-	-	-
Västra Götaland	6	2	3	-	1	-
Östergötland	2	-	2	-	-	-
Total	122	70	39	2	8	3

[a] Efm = *Enterococcus faecium*, [b] Efs = *Enterococcus faecalis*

Distribution between genders was even, and the median age for women was 74 years and for men 69 years. According to the first laboratory notification for each case the majority of isolates were from faeces (56%), followed by rectum 15%, "other" 13%, and urine in 3% of the cases. Isolation site was missing for 13%. No invasive VRE infections were reported in 2011. The findings of VRE in faeces or rectum in more than 70% of the cases indicated that most of the cases were detected by screening or contact tracing.

Epidemiological typing of VRE

For enterococci PFGE is still used as the standard typing method. Isolates from notified cases in all counties from 2007 and onwards have been analysed, and comparisons with isolates from previous years have also been performed. Only a minor set of strains from Stockholm County was available for analysis, but exchange of information has taken place to clarify the epidemic situation.

From this national strain collection and PFGE database it could be shown that the *Enterococcus faecium* with *vanB* gene causing the outbreak situation 2007-2010 had not been detected before 2007. It has been named SE-EfmB-0701 to indicate species (Efm), resistance gene (B), year of detection (07) and a serial number (01). Several smaller outbreaks in Sweden during 2000 – 2006 were caused by strains of different PFGE-types, and they have been given names retrospectively.

In 2010-2011, a new extensive outbreak occurred in Västernorrland County, and the PFGE pattern of this strain was named SE-EfmB-1001.

Sporadic cases of *Enterococcus faecium* with *vanA* gene have been notified since 2000. PFGE analyses of those indicated that the majority were single cases with unique PFGE patterns. However, at least two small outbreaks occurred in 2010, caused by SE-EfmA-1003 in Norrbotten (5 cases) and SE-EfmA-1007 in Västmanland (7 cases). In 2011 a few small outbreaks (2-3 cases) were identified in different counties, but with no further spread.

Data on invasive isolates reported to ECDC/EARS-Net

Enterococcus faecalis and *Enterococcus faecium* have been reported to EARSS/EARS-Net since 2001 (Appendix 5). The main focus has been on vancomycin resistance, but also on high-level resistance to aminoglycosides (HLAR).

In 2003 the first four Swedish vancomycin-resistant invasive isolates of *Enterococcus faecium* were reported (2.2%), followed by three isolates (1.2%) in 2004, two isolates (0.3%) in 2006, five isolates (1.5%) in 2008, one isolate (0.4%) in 2009 and one isolate (0.3%) in 2010. In 2011 no invasive VRE were detected, Tables 4.6 and 4.7. Molecular typing of the vancomycin-resistant isolates showed that the isolates from 2008 all had the same PFGE pattern as the recent epidemic strain described above (SE-EfmB-0701), whereas the others were singletons.

HLAR was more prevalent in *Enterococcus faecium* (26.4%) than in *Enterococcus faecalis* (16.6%) in 2011. This shift among the species was seen already in 2008. From 2006 and onwards all laboratories who reported HLAR used gentamicin (GEN) as test disk for detection, and almost all isolates were tested.

TABLE 4.6 Resistance among invasive isolates of *Enterococcus faecalis* (number of strains and percentage). Data from Sweden 2002-2011 reported to ECDC/EARS-Net and retrieved from the EARS-Net database 2012-05-23.

Year	Vancomycin-R (%)	HLAR (%)	Total number (number tested for HLAR by GEN)
2002	0	nd	430 (235)
2003	0	16.6	593 (440)
2004	0	15.6	592 (533)
2005	0	18.9	567 (492)
2006	0.2	20.0	578 (561)
2007	0	16.1	651 (632)
2008	0	20.1	720 (703)
2009	0	18.6	718 (627)
2010	0	15.2	776 (687)
2011	0	16.6	824 (711)

TABLE 4.7. Resistance among invasive isolates of *Enterococcus faecium* (number of strains and percentage). Data from Sweden2002-2011 reported to ECDC/EARS-Net and retrieved from the EARS-Net database 2012-05-23.

Year	Vancomycin-R (%)	HLAR (%)	Total number (number tested for HLAR by GEN)
2002	0	6.3	181 (96)
2003	2.2	11.2	231 (170)
2004	1.2	7	260 (227)
2005	0.8	4.3	253 (211)
2006	0.3	11.9	302 (286)
2007	0	14.4	279 (263)
2008	1.5	24.8	333 (331)
2009	0.5	24.1	311 (274)
2010	0.3	21.8	339 (319)
2011	0	22.0	406 (346)

Extended spectrum beta-lactamase-producing *Enterobacteriaceae* (ESBL)

Background

ESBL-producing *Enterobacteriaceae* became notifiable according to the Communicable Disease Act in February 2007. Notifications of ESBL-producing bacteria are limited to clinical laboratories. As a result, epidemiological information on ESBL cases is restricted to data on age, gender and cultured material while information on reasons for sampling or place of acquisition is not available. In 2007, Strama proposed an action plan with the aim to keep the proportion of *Escherichia coli* and *Klebsiella pneumoniae* producing ESBL in blood isolates as low as possible, and also in urine cultures in order to maintain the current treatment recommendations for lower urinary tract infections. During 2009, a supplement to the action plan was published where the definition of ESBL was broadened. Valid from 2010, the definition of an ESBL included not only classical ESBLs which are inhibited by clavulanic acid ($ESBL_A$) 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, coupled to a demand for contact tracing by the local authorities. During 2012 an updated version of the action plan will be published.

Notifications according to the Communicable Disease Act

A total of 5666 cases were notified during 2011, an increase with 14% compared to the 4983 cases in 2010. Reports came from all 21 counties of Sweden, corresponding to a national incidence of 60 cases per 100 000 inhabitants, Figure 4.11. Almost all Swedish counties had an increased incidence. The highest incidence 2011 was found in Jönköping County (121 cases per 100 000 inhabitants).

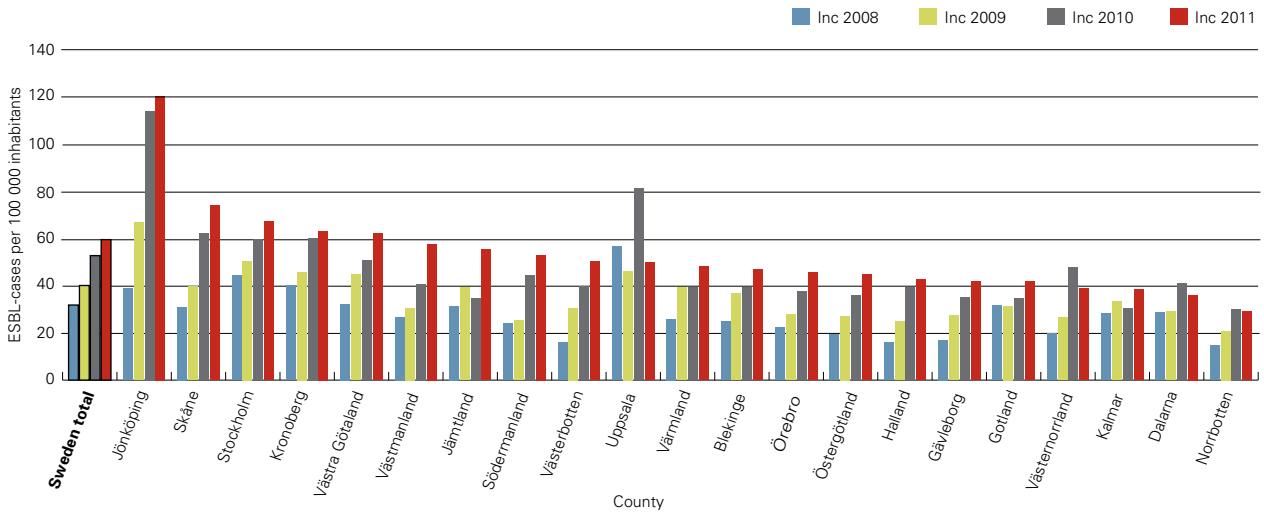


FIGURE 4.11. The incidence (Inc) of ESBL in Swedish counties 2008-2011, arranged according to incidence 2011.

The most commonly reported species with ESBL was *E. coli*, accounting for 87% of all cases, followed by *K. pneumoniae* with 7%, (Table 4.8). 21 cases of *Salmonella* species with ESBL were reported in 2011. They are commented upon in the chapter on *Salmonella* and *Shigella*.

TABLE 4.8. Distribution of species among cases of ESBL-producing bacteria 2011.

Escherichia coli	5068
Klebsiella pneumoniae	418
Proteus mirabilis	32
Citrobacter species *	19
Salmonella species	21
Miscellaneous *Enterobacteriaceae* *	243
Species not reported	45
Total number reported	5846**

* Distinction between an ESBL and a chromosomally mediated AmpC was not made for these species.

** In 137 patients two or more ESBL-producing species were reported resulting in a higher number of isolates than number of cases reported.

ESBL-producing bacteria were detected in urine samples in 63% of the cases. The second most common source was faecal samples with 14%. Isolates from rectum and wound samples constituted 8% and 3% respectively, and blood isolates 4% of the cases. Invasive infections with ESBL-producing bacteria, all in blood and cerebrospinal fluid, were notified in 312 persons during 2011, as compared to 225 persons (all in blood) in 2010. Among these, 271 were new cases for 2011 and 41 were known carriers of ESBL, notified during the previous year.

The type of ESBL according to the extended definition was reported in 25% (n=1419) of all cases. Of those, 1256 were of $ESBL_A$-type and 138 of $ESBL_M$-type. Sixteen cases were reported as $ESBL_{CARBA}$. In 13 cases more than one type of ESBL was reported.

The incidence in age groups and gender differed between species and is shown in Figure 4.12. ESBL-producing *E. coli* were derived from women in 67% of all *E. coli* cases. They had a median age of 50 years compared to 63 years for men. The *K. pneumoniae* ESBL cases were equally distributed between sexes, with median ages of 61 years both for women and men.

Carbapenemases, the most recent threat

The nation-wide problem with ESBL-producing bacteria in Sweden continues to be a larger problem than that of MRSA, both in numbers of cases and severity of infections. Concomitant resistance to several other antibiotics in many isolates (data not shown) limits the options for treatment. As described above there are several types of ESBLs, and their common feature is that they confer resistance to broad-spectrum cephalosporins.

Betalactamases which also affect carbapenem antibiotics, so called carbapenemases, pose an even greater threat because they limit the treatment options even further. Carbapenemases of clinical importance belong to one of two kinds, either KPC (*K. pneumoniae* Carbapenemase) or MBLs (Metallo-BetaLactamases). Both types are characterised as $ESBL_{CARBA}$ according to the newly extended definition of ESBL.

Thirty-five cases of $ESBL_{CARBA}$ have been encountered in Sweden 2007-2011, Figure 4.13. In 2007 the first isolates of *K. pneumoniae* with KPC-2 and with VIM metallo-betalactamase were detected, and in 2008 the first isolate of *K. pneumoniae* with a NDM-1 enzyme. Two isolates with OXA-48 were detected in 2011, but in retrospect two more isolates (*E. coli* and *Enterobacter aerogenes*) from 2009 were also identified. All these types of $ESBL_{CARBA}$ have been found also in 2011, but isolates with KPC or NDM enzymes were most frequently found. In a majority of the cases there was a history of healthcare related contacts abroad, with Greece often mentioned in relation to KPC or VIM, and the Indian subcontinent in relation to NDM. All isolates with $ESBL_{CARBA}$ were multiresistant, leaving very few options for treatment.

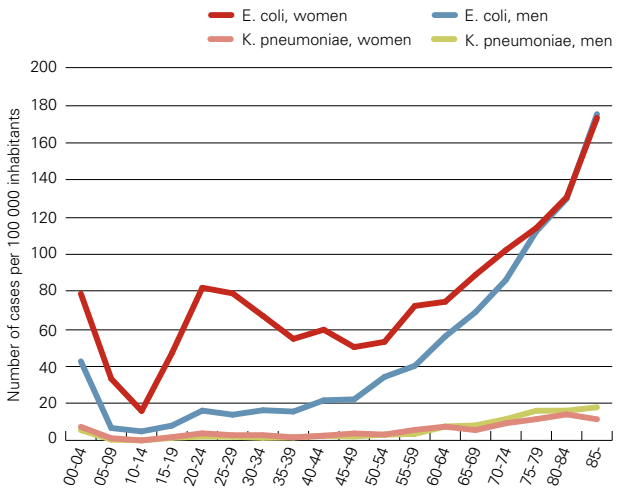


FIGURE 4.12. Age and gender distribution of *E.coli* and *K. pneumoniae* ESBL cases 2011.

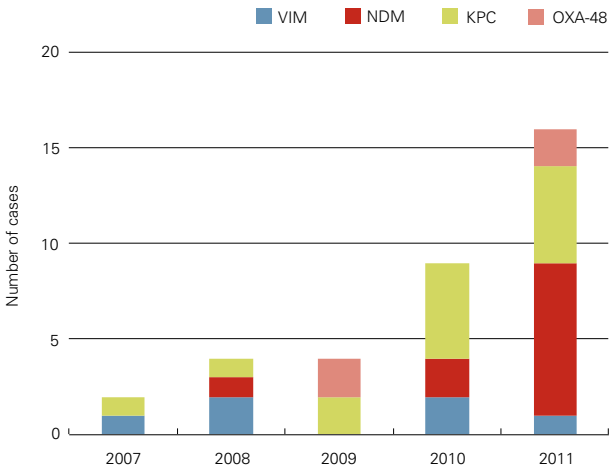


FIGURE 4.13. Numbers and types of $ESBL_{CARBA}$ in *Enterobacteriaceae* in Sweden 2007-2011.

Escherichia coli

Annual Resistance Surveillance and Quality Control (RSQC) programme

Escherichia coli, mainly derived from urinary tract infections, has been included in the national surveillance program regularly since 1996 and every year since 2001. Resistance to commonly prescribed oral antibiotics for treatment of urinary tract infections (UTI) has been tested each year. The number of isolates tested by each laboratory was increased from 100 to 200 from 2006 in order to increase the statistical validity of the data.

In 2011 24 laboratories delivered data according to the newly introduced EUCAST methodology (Appendix 4), and 5892 isolates were included in the analysis.

The average resistance rates to **ampicillin** have increased yearly, from 22 to 31.6% (Figure 4.14). A similar trend has been seen for trimethoprim, for which the rates have increased from 14 to 20.3%. Resistance to **nitrofurantoin,** another therapeutic option for uncomplicated urinary tract infections, is still very rare (less than or equal to 1%).

For cefadroxil, mecillinam and fluoroquinolones, please see Detailed analyses of RSQC data for *Escherichia coli* on pages 40-41.

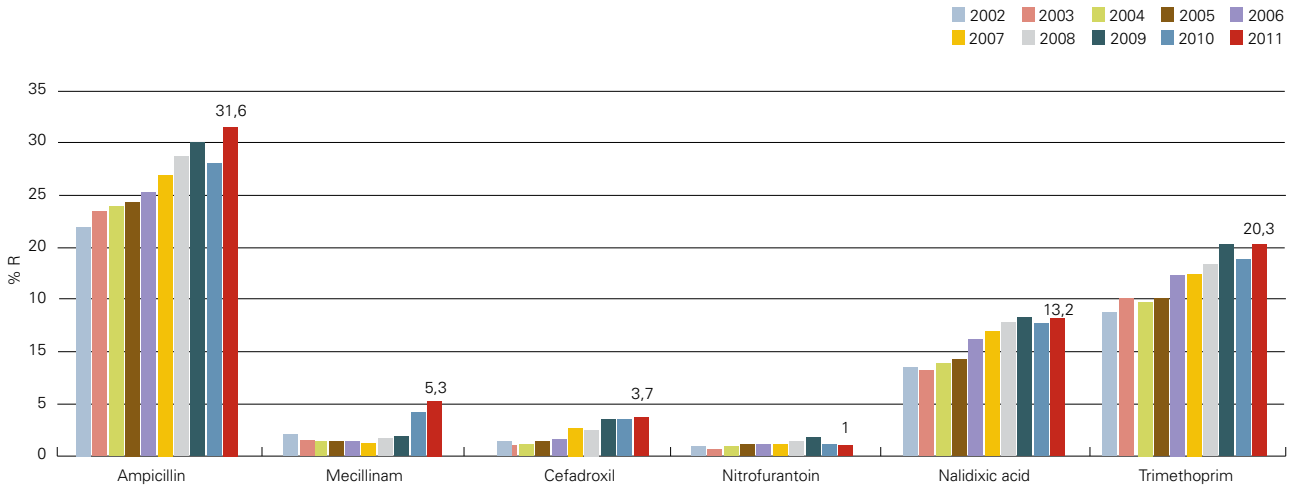


FIGURE 4.14. Resistance rates for UTI antibiotics in *E. coli* 2002-2011. Nalidixic acid was used as a screening disk for detection of resistance to fluoroquinolones.

Data on invasive isolates reported to ECDC/EARS-Net

Escherichia coli derived from invasive infections (blood isolates) have been part of the European Antimicrobial Resistance Surveillance System (EARSS/EARS-Net) since 2001. The surveillance system has focused on resistance to beta-lactam antibiotics, especially resistance caused by ESBLs, and on resistance to aminoglycosides and fluoroquinolones. Results for 2001-2011 are presented in Table 4.10.

Ampicillin resistance, caused by production of plasmid-mediated beta-lactamase (most often of TEM-type) was slightly higher in blood isolates than in the urine isolates tested in the RSQC programme, 35% versus 32%. However, this difference must be interpreted with caution since only 20% of the blood isolates were tested against ampicillin. The ampicillin resistance rates in Sweden are still much lower than in most other European countries where ampicillin resistance often exceeds 50%.

The level of resistance to third generation cefalosporins among blood isolates had reached 4% in 2011, thus a significant increase compared to 3.2% in 2010. In the majority of the cefotaxime-resistant isolates this resistance was attributed to the presence of an ESBL of the CTX-M type.

Aminoglycoside resistance in *E. coli* has shown an increasing trend for the last couple of years and reached 5.1% in 2011. Genes coding for aminoglycoside resistance often co-exist with genes coding for ESBL enzymes and other resistance markers which make these bacteria multi-resistant.

Reduced susceptibility and resistance to fluoroquinolones (I/R) has increased every year, but contrary to cephalosporins and aminoglycosides, the resistance rate was found to be lower in 2011 (10.4%) than in 2010 (14%).

TABLE 4.10. Resistance among invasive isolates of *Escherichia coli* (number of isolates tested and percentage R). Data from Sweden 2002-2011, reported to ECDC/EARS-Net And retrieved from the EARS-Net database 2012-05-23.

Year	Ampicillin-R (%)	Cefotaxime-R (%)	Amino-glycoside-R (%) **	Fluoro-quinolone-I/R (%) ***	Total number of isolates
2002	24.9	0.3	0.5	7.2	3062
2003	28.5	0.4	1.3	8.3	3300
2004	23	0.7	1.5	11.1	3336
2005	26	1.3	1.6	8.9	3212
2006	28.1	1.5	1.6	11.1	3514
2007	32.9	2.3	2.2	13.3	3745
2008	31.9	2.3	2.3	14.4	4028
2009	32.8	2.9	3.3	13.7	4423
2010	34	3.2	4.5	14.0	4991
2011	35 *	4.0	5.1	10.4	5066

*Only 20% of isolates were tested against ampicillin; **gentamicin or tobramycin, *** ciprofloxacin

Detailed analyses of RSQC data for *Escherichia coli*

RESISTANCE to **cephalosporins** (cefadroxil tested), although much less prevalent than ampicillin resistance, had shown a more pronounced increase already from 2007 and had reached 3.7% in 2011. This rise in resistance was caused by the increasing prevalence of ESBL-producing strains, especially among *E. coli* from the urinary tract (see also Characterization of ESBLs in Sweden through extended RSQC programmes 2007, 2009 and 2011, p. 42-43). The data from the RSQC programme is also coherent with the increasing incidence of ESBL-producing bacteria as seen from the notified cases (above) and of reports to EARS-Net for invasive isolates.

Resistance to **mecillinam,** one of the primary therapeutic options for uncomplicated urinary tract infections, showed a sudden increase in resistance, from a level of approximately 2% during 1996 to 2009 to a level of approximately 5% from 2010 and onwards. Inhibition zone histograms from 4 years, derived from ResNet, making up the background data on which the calculations of percentage of resistance are made, are presented in Figures 4.15 A-D. In 2007 the standard methodology for susceptibility testing in Sweden comprised the use of IsoSensitest agar, and the zone breakpoints were correlated to the MIC breakpoints S ≤ 1 mg/L / R ≥ 8 mg/L. Resistance was calculated to 1.4%, but in retrospect it might be assumed that the rather large intermediate category (Figure 4.15A) could have hidden some strains which more correctly should have tested R. In 2009 the MIC breakpoints, now defined by EUCAST, had been adjusted to S ≤ 8 mg/L / R > 8 mg/L and stated to be valid only for *E. coli* from uncomplicated urinary tract infections. This change did not alter the percentage of strains being classified as resistant (Figure 4.15B). In 2010 and 2011 the new standard methodology for disk diffusion tests, as recommended by EUCAST and adopted by all laboratories, was based on a different medium (Mueller Hinton agar), and a more dense bacterial inoculum was used. These two changes, together with the increased prevalence of ESBL-producing strains as described for cefadroxil above, have most certainly resulted in the increased resistance rate for mecillinam. The figure was 4.6% resistance in 2010 (Figure 4.15C) and 5.3% in 2011 (Figure 4.15D). However, this could also be expressed as 95% of *E. coli* from uncomplicated urinary tract infections still being susceptible to mecillinam.

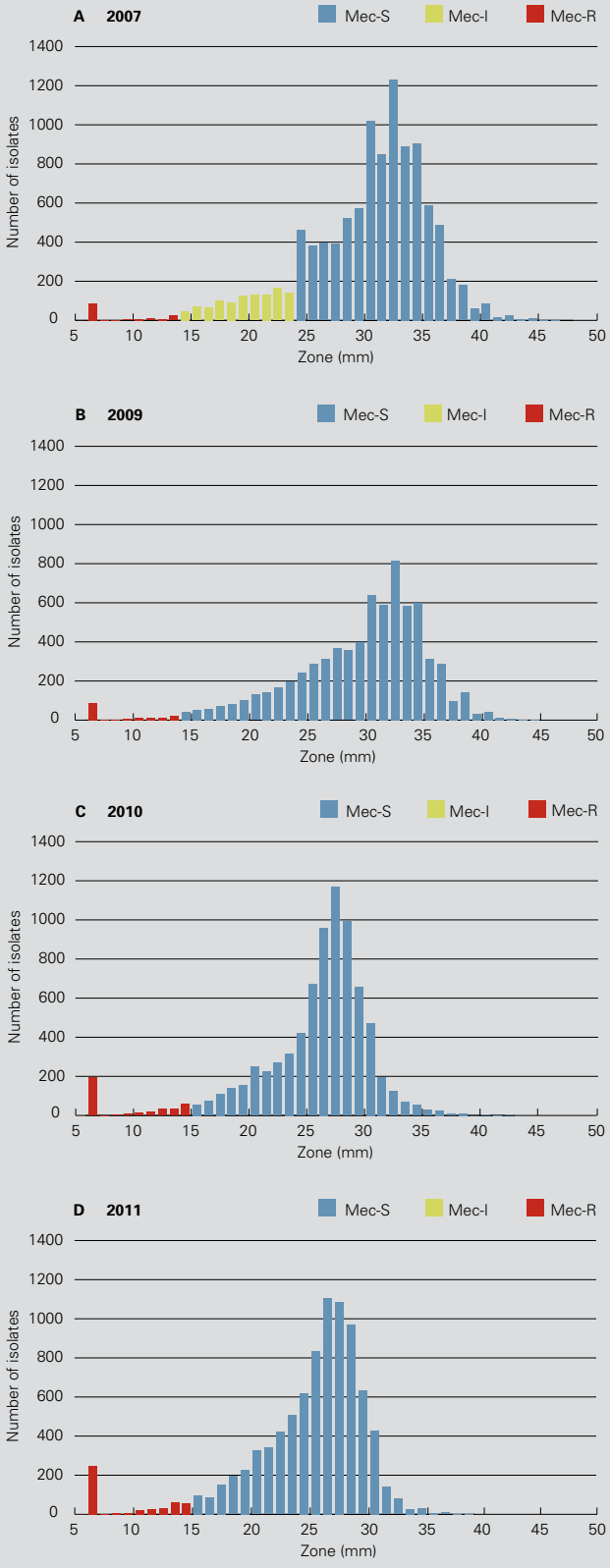
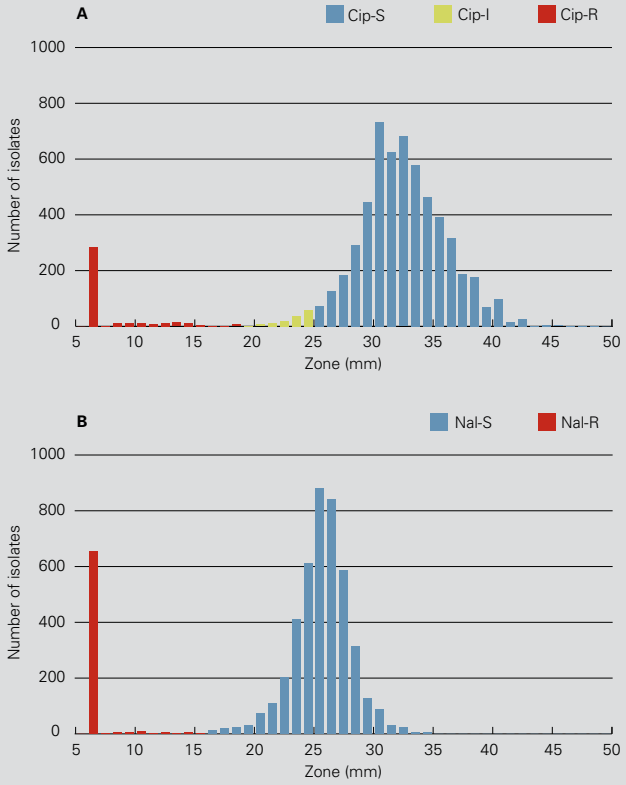


FIGURE 4.15. A-D. Zone histogram distributions of mecillinam 10 µg on 5-6000 urine isolates of *E. coli* from the RSQC programmes 2007 (A), 2009 (B), 2010 (C) and 2011 (D).

Fluoroquinolone resistance, detected by the **nalidixic acid** screening disk since 2002, has also increased during the surveillance period and is now approximately 13%, using the zone breakpoint R < 16 mm. In 2011, 18 laboratories tested nalidixic acid and **ciprofloxacin** disks in parallel on a total of 5082 isolates. The EUCAST zone breakpoint for ciprofloxacin (R < 19 mm) resulted in a resistance rate of only 6.4%, Figures 4.16 A and B. By applying the EUCAST WT zone breakpoint for ciprofloxacin (R < 25 mm) the frequency of resistance increased by only 2 percent. The difference in resistance between ciprofloxacin and nalidixic acid is explained by the fact that the breakpoint for ciprofloxacin correlates with the clinical breakpoint of R > 1 mg/L, whereas the nalidixic acid breakpoint includes all non-wildtype isolates (ciprofloxacin MIC > 0.06 mg/L) in the resistant category.



FIGURES 4.16. A and B. Zone histogram distributions of ciprofloxacin 5 µg (A) and nalidixic acid 30 µg (B) on 5082 urine isolates of *E. coli* from the RSQC programme 2011.

Characterization of ESBLs in Sweden through extended RSQC programmes 2007, 2009 and 2011.

THE EPIDEMIOLOGY of *Enterobacteriaceae* with ESBL, especially the two most common species *E. coli* and *K. pneumoniae*, needs to be followed on a national level. It is important to understand both the genetic background of the bacterial strains and also the character of the bacterial enzymes causing resistance to betalactam antibiotics. By collecting representative bacterial isolates regularly and performing phenotypic and genotypic analyses, we have achieved an increasingly better understanding of the epidemiology of these resistant bacteria, both in Sweden and at an international level.

During three years, 2007, 2009 and 2011, in connection to the yearly RSQC programme, we have asked all laboratories to collect consecutive cefadroxil-resistant (R < 13 mm) isolates of *E. coli* and *K. pneumoniae* during a one-month period and send them to SMI for further analysis of ESBL epidemiology.

In 2011 a total of 508 *E. coli* were collected and tested with phenotypic and genotypic methods. 82% of all the cefadroxil-resistant isolates had an ESBL, a figure which was similar to the two previous collections (Figure 4.17). Of the *E. coli* isolates from 2011 93.3% had $ESBL_A$, 6.3% had $ESBL_M$, and 0.5% had both $ESBL_A$ and $ESBL_M$ (Figure 4.18). Among the $ESBL_A$, CTX-M belonging to group 1 was the most prevalent enzyme (73.5%), followed by CTX-M group 9 (24.5%), and other type(s) (3%). *E. coli* isolates with $ESBL_M$ harboured plasmid-mediated AmpC-enzyme of the type CIT (originating from *Citrobacter* species).

A total of 34 *K. pneumoniae* were collected in 2011 and tested with phenotypic and genotypic methods (Figure 4.19). 73.5% (n=25) of the isolates had $ESBL_A$, and two of these also carried an $ESBL_M$ of type DHA. Nine isolates had no ESBL-activity. Of isolates with $ESBL_A$, 72% had CTX-M group 1, 8% had CTX-M group 9, and 20% had SHV (Figure 4.20).

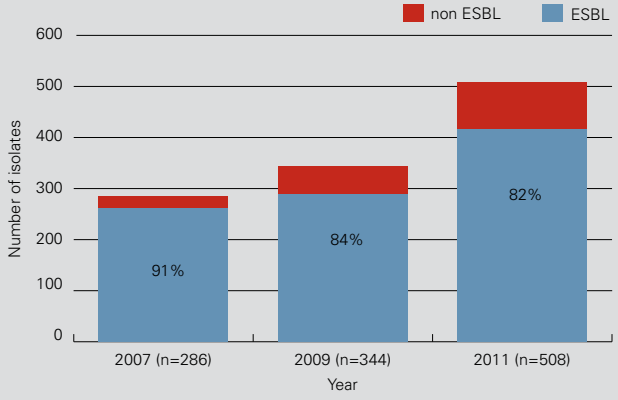


FIGURE 4.17. Number of ESBL-producing and/or cefadroxil-resistant *Escherichia coli* urine isolates collected during one month in addition to the yearly RSQC programmes in 2007, 2009 and 2011.

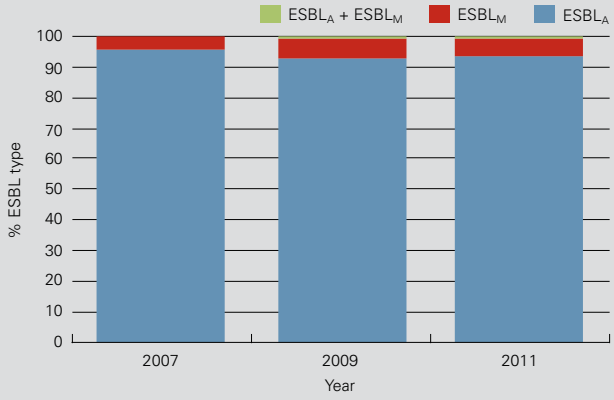


FIGURE 4.18. Distribution of ESBL types among the ESBL-positive *Escherichia coli* isolates from the extended RSQC programmes in 2007, 2009 and 2011.

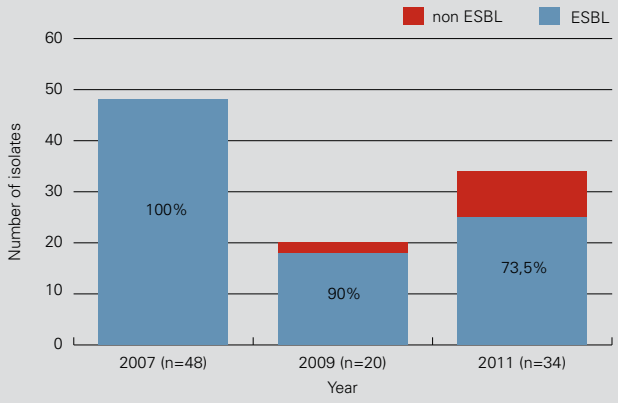


FIGURE 4.19. Number of ESBL-producing and/or cefadroxil-resistant isolates among all *Klebsiella pneumoniae* isolates collected during one month in addition to the yearly RSQC programmes in 2007, 2009 and 2011.

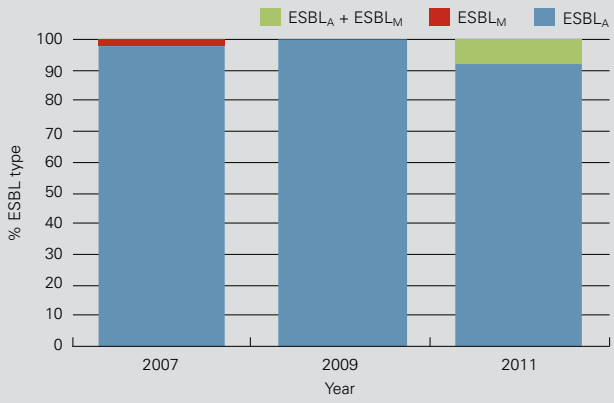


FIGURE 4.20. Distribution of ESBL types among the ESBL-positive *Klebsiella pneumoniae* isolates in the extended RSQC programmes in 2007, 2009 and 2011.

Susceptibility testing was performed on all isolates with an ESBL, and percent resistance (R) to all the tested antibiotics for both *E. coli* and *K. pneumoniae* from the three years are summarized in Table 4.9. It is shown that ESBL-producing isolates are often resistant also to aminoglycosides (gentamicin and/or tobramycin) with the exception of amikacin, and often resistant to ciprofloxacin and trimethoprim. In the investigated collections there were no isolates resistant to carbapenems.

TABLE 4.9. Antibiotic resistance of *Escherichia coli* and *Klebsiella pneumoniae* with $ESBL_A$ within the RSQC programmes 2007, 2009 and 2011.

	Escherichia coli (% R)			***Klebsiella pneumoniae*** (% R)		
Antibiotic	**2007** (n=249)	**2009** (n=270)	**2011** (n=390)	**2007** (n=47)	**2009** (n=18)	**2011** (n=25)
Cefotaxime	96.4	99.6	99.2	95.8	100	100
Ceftazidime	49.0	66.5	72.8	59.6	88.9	88.0
Piperacillin/tazobactam	4.5	7.0	14.6	19.1	0	36.0
Imipenem	nt	0	0	nt	0	0
Meropenem	nt	0	0	nt	0	0
Gentamicin	31.4	43.7	39.7	25.5	50.0	44.0
Tobramycin	20.9	47.2	47.2	14.9	44.0	80.0
Amikacin	0	6.7	0.8	0	22.2	8.0
Ciprofloxacin	77.1	66.2	60.8	53.2	50.0	68.0
Nitrofurantoin	6.4	7.8	2.8	nt	nt	nt
Trimethoprim	71.1	73.3	70.5	76.6	77.8	88.0
Tigecycline	nt	0	0	nt	0	12
Colistin	nt	0.7	0.8	nt	0	4.0

Klebsiella pneumoniae

Annual Resistance Surveillance and Quality Control (RSQC) programme

Klebsiella pneumoniae is one of the most important bacterial species from a hospital infection control point of view. It has been included in the RSQC programme and in EARSS/EARS-Net since 2005.

As for *E. coli*, the RSQC 2011 programme for *K. pneumoniae* was mainly focused on urine samples, Figure 4.21. Twenty-two laboratories delivered data according to the newly introduced EUCAST methodology (Appendix 4), and 2646 isolates were included in the analysis. The results indicated that the levels of resistance to all tested antibiotics were the same or slightly lower than in 2010.

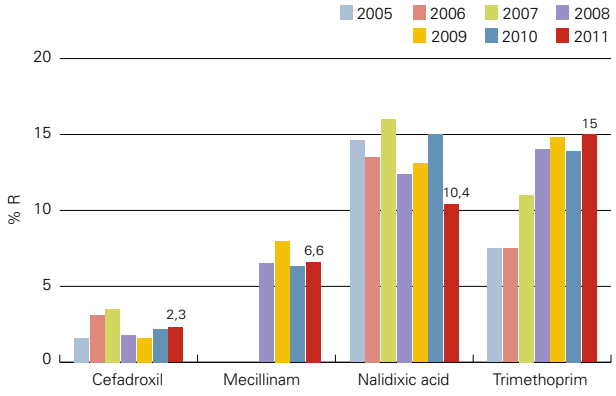


FIGURE 4.21. Resistance rates for antibiotics commonly used to treat urinary tract infections, *Klebsiella pneumoniae* 2005-2011. Nalidixic acid was used as a screening disk for detection of resistance to fluoroquinolones.

Data on invasive isolates reported to ECDC/EARS-Net

Klebsiella pneumoniae derived from invasive infections (blood isolates) have been included in the European Antimicrobial Resistance Surveillance System (EARSS/EARS-Net) yearly since 2006. The rates of cephalosporin and aminoglycoside resistance were as low 2011 as in 2010, Table 4.11. All cephalosporin resistance was caused by ESBLs of the CTX-M type. Fluoroquinolone resistance (I/R) had decreased compared to 2010. Carbapenem resistance has so far not been detected in an invasive isolate of *Klebsiella pneumoniae* in the Swedish part of the EARS-Net surveillance.

TABLE 4.11. Resistance among invasive isolates of *Klebsiella pneumoniae* (number of isolates tested and percentage R). Data from Sweden 2006-2011, reported to ECDC/EARS-Net And retrieved from the EARS-Net database 2012-05-23.

Year	Cefotaxime-R (ESBL)	Amino-glycoside-R (%) *	Fluoro-quinolone-I/R (%) **	Total number of isolates
2006	1.5	0.3	8.5	610
2007	1.4	1.1	10.8	649
2008	2.3	1.1	12.9	826
2009	1.8	1.0	12.2	755
2010	2.3	2.0	8.5	908
2011	2.2	2.1	5.0	934

*gentamicin or tobramycin, ** ciprofloxacin

Pseudomonas aeruginosa

Annual Resistance Surveillance and Quality Control (RSQC) programme

Pseudomonas aeruginosa has since 2003 been included yearly in the RSQC programme, except for 2005 and 2008. Laboratories have been asked to test 100 consecutive isolates of *P. aeruginosa* with the exclusion of respiratory isolates. Resistance to the tested antibiotics is shown in Figure 4.22. Aminoglycoside resistance (gentamicin and/or tobramycin tested) seemed stable around 1%. Four beta-lactam antibiotics were tested; one cephalosporin, one penicillin-inhibitor combination, and two carbapenems. For ceftazidime, resistance levels were slowly increasing but remained below 5%, and for piperacillin-tazobactam (only tested in 2010 and 2011) the resistance had stabilized around 7%. For the carbapenems, resistance to imipenem was higher (7.6%) than to meropenem (5.1%), both in 2010 and 2011. Resistance to ciprofloxacin had decreased slightly to approximately 9%.

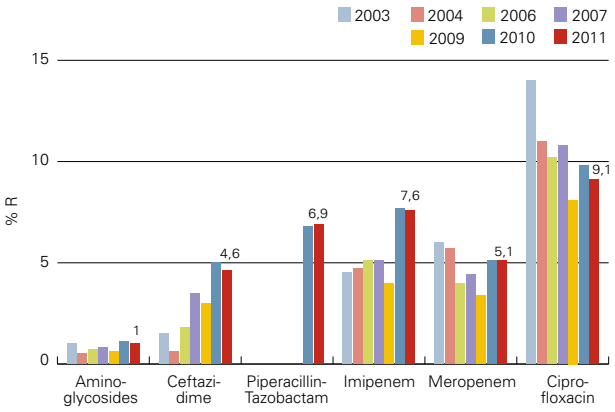


FIGURE 4.22. Resistance rates for four groups of antibiotics tested against *Pseudomonas aeruginosa* 2003-2011. Aminoglycoside resistance was detected by gentamicin or tobramycin. *P. aeruginosa* was not included in the RSQC programme in 2005 and 2008.

Data on invasive isolates reported to ECDC/EARS-Net

Pseudomonas aeruginosa derived from invasive infections (blood isolates) have been included in the European Antimicrobial Resistance Surveillance System (EARSS/EARS-Net) yearly since 2006. The levels of resistance to beta-lactam antibiotics (ceftazidime and carbapenems) were in the range 3-7% for all

TABLE 4.12. Resistance among invasive isolates of *Pseudomonas aeruginosa* (number of isolates tested and percentage R). Data from Sweden 2006-2011, reported to ECDC/EARS-Net And retrieved from the EARS-Net database 2012-05-23.

Year	Ceftazidime-R (%)	Carba-penem-R (%) *	Amino-glycoside-R (%) **	Fluoro-quinolone -I/R (%) ***	Total number of isolates
2006	5.7	4.7	0.5	7.7	297
2007	4.5	7.1	0	10.4	335
2008	5.2	4.0	0	7.6	309
2009	6.9	7.7	0	10.1	326
2010	2.9	6.7	3	10.1	337
2011	5.2	7.2	1	7.0	402

* imipenem, meropenem, ** gentamicin, tobramycin, *** ciprofloxacin

six years, Table 4.12. A slight reduction in resistance rate had occurred for fluoroquinolones (7%), and the aminoglycoside resistance level was still low.

Acinetobacter spp.

Questionnaire on the inclusion of *Acinetobacter* in surveillance programmes

In January 2012 the EARS-Net team at ECDC distributed a questionnaire to EARS-Net coordinators in all EU member states on *Acinetobacter* species. In order to have an accurate background for the reply from Sweden to ECDC we forwarded an extra question to the yearly collection of nominator data from Swedish clinical microbiology laboratories. We asked for the number of *Acinetobacter* isolates in blood cultures and in all clinical samples in 2011. Information on the approximate coverage for each laboratory (number of people) and the number of positive blood cultures was collected from Table App 2.4 on denominator data from laboratories.

Responses on the specific *Acinetobacter* questions were received from 24 out of 28 laboratories. The total number of blood cultures growing *Acinetobacter* species was 123 (range 0-12 per laboratory, average 5.1) and the total number of positive cultures from any clinical sample was 2657 (range 23-227 per laboratory, average 111). These figures were compared to the total number of positive blood cultures from these 24 laboratories which far exceeded 50.000.

The conclusion from Sweden to ECDC was that *Acinetobacter* species, especially in blood cultures, so far seemed to be a minor problem in Sweden.

Haemophilus influenzae

Annual Resistance Surveillance and Quality Control (RSQC) programme

Haemophilus influenzae was included in the RSQC programme on antibiotic resistance in 2011 as a follow-up to 2008-2010 when a marked increase in rates of penicillin-resistant and trimethoprim-sulfamethoxazole-resistant isolates was seen (Figure 4.23). In 2011, 25 laboratories delivered data according to the newly introduced EUCAST methodology (Appendix 4), and 2812 isolates were included in the analysis. The methodological changes introduced (for description see www.srga.org) made results for beta-lactam resistance more difficult to interpret, but by correlating beta-lactamase producing isolates to 6 mm only of penicillin G 1 unit disk, it was possible to get a percentage of the prevalence of this resistance mechanism (Figure 4.23). Other mechanisms of betalactam resistance were then assumed if zones of penicillin G 1 unit disk were 7-11 mm, allowing for a rough estimation of the frequencies of BLNAR. By doing so the results indicated a dramatic increase in BLNAR during the last couple of years, a fact which needs to be verified and further investigated.

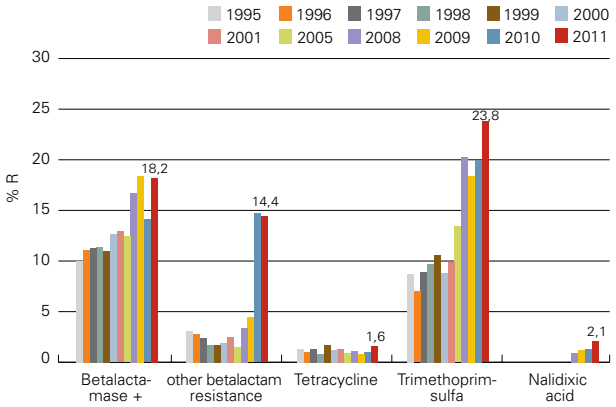


FIGURE 4.23. Resistance rates for *Haemophilus influenzae* 1995-2011 (no data collected in 2002-04 and 2006-07). In 2010-2011 betalactamase producing isolates were separated from isolates with other betalactam resistance mechanisms by use of penicillin G 1 unit disk using the following interpretation: 6 mm = betalactamase production, 7-11 mm = other betalactam resistance.

In 2011 the previously high rates of resistance to trimethoprim-sulfamethoxazole had increased further and reached 23.8%. Tetracycline resistance in *Haemophilus influenzae* was still rare (1.6%). Approximately 2% fluoroquinolone resistance, detected by the nalidixic acid screening disk, was found.

Surveillance on invasive isolates additional to EARS-Net

Data on consecutive blood isolates were obtained from 10 laboratories covering approximately 55% of the population. Only 76 of 16.969 (0.5%) were *Haemophilus influenzae*. Fourteen isolates (18.4%) were ampicillin-resistant, and two of these also had cefotaxime MICs of 0.25 mg/L, indicating that they were BLNAR. Twelve isolates (15.8%) were resistant to trimethoprim-sulfamethoxazole, which is similar to the results from previous years. One blood isolate was resistant to fluoroquinolones as judged by the nalidixic acid screen disk.

A majority of the isolates were retrieved from adults (> 50 years), and only two were isolated from children 0-9 years.

Streptococcus pyogenes

Surveillance on invasive isolates additional to EARS-net

Data on consecutive blood isolates were obtained from 10 laboratories covering approximately 55% of the population. One hundred and eighty-eight of 16.969 (1.1%) were *Streptococcus pyogenes* (GAS). This was in the same order of magnitude as in the previous four years with 1.8, 1.2, 1.2 and 1.0% GAS, respectively. All GAS isolates were susceptible to penicillin. Six isolates (3.2%) were resistant to erythromycin and clindamycin, indicating that they possessed *erm* genes (MLS_B type of resistance). This was a notable increase compared with 1.7% in 2010. Twenty-five isolates (13.3%) were resistant to tetracycline which was similar to the previous four years (range 8.0 -14.6%). A majority of the isolates were retrieved from adults (> 50 years), and only 3.7% of the isolates was from children 0-9 years.

Streptococcus agalactiae

Surveillance on invasive isolates additional to EARS-net

206/16.969 (1.2%) of consecutive blood isolates from the participating 10 laboratories were *Streptococcus agalactiae* (GBS). This was in the same order of magnitude as the previous four years with 1.0, 1.3, 1.1 and 1.4% GBS, respectively. All GBS isolates were susceptible to penicillin/ampicillin. Fourteen of the isolates (6.8%) were resistant to erythromycin; twelve of those were also resistant to clindamycin. This indicated, but has not been confirmed, that the isolates harboured either *erm* genes (MLS_B type of resistance affecting both erythromycin and clindamycin) or *mef* genes (efflux-mediated resistance affecting only erythromycin). The figure for 2011 was comparable to those from the previous four years (range 6.5 - 8.8%). A majority of the isolates were retrieved from adults (> 50 years), but 19 (9.2%) were isolated from children less than 2 months, a decrease from 2010 (13.2%) but the same as in 2009 (9.2%). Two of the isolates from newborns were resistant to erythromycin.

Clostridium difficile

The *Clostridium difficile* surveillance programme in Sweden

A national surveillance programme for *Clostridium difficile* was initiated by the Swedish Institute for Communicable Disease Control (SMI) in 2009. The programme included both a voluntary laboratory reporting system of all new cases of *C. difficile* infection (CDI) through SmiNet2 and a determination of resistance and epidemiological typing of isolates from the clinical microbiology laboratories. All *C. difficile* strains isolated during weeks number 11 and 39 were sent to SMI 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, also susceptibility to moxifloxacin, clindamycin and erythromycin, as indicators of selective pressure, was tested. All isolates were tested using Etest on Mueller Hinton agar.

Distribution of resistant *Clostridium difficile* isolates in 2011

In the national surveillance programme 2011 a total of 426 isolates from all counties except Gotland were characterised. No isolate was resistant to the current treatment options, metronidazole or vancomycin. The proportions of *C. difficile* isolates resistant to moxifloxacin, clindamycin, and erythromycin decreased slightly in 2011 compared to 2010, Table 4.13. As in previous years, most of the resistant isolates were associated with four types: PCR ribotype 012, 017, 046 and 231/SE37. Similar to what was found in 2009, *C. difficile* isolates with resistance to moxifloxacin and other tested antibiotics were clustered in geographical regions (Figure 4.24; $p < 0.001$, Fisher's exact test). Also, as found in 2008-2010, the use of moxifloxacin differed between Swedish counties.

TABLE 4.13. *Clostridium difficile* types resistant to erythromycin, clindamycin and moxifloxacin in Sweden 2011 (n=426).

PCR ribotype	no. of isolates tested	Moxifloxacin No. (%) of R	Clindamycin No. (%) of R	Erythromycin No. (%) of R
012	23	19	19	17
017	8	6	6	5
046	13	9	8	8
231/SE37	8	8	7	7
Other	374	16	22	27
Total	426	58 (13.6)	62 (14.6)	64 (15)
Comparison 2010		(15.9)	(17.4)	(19.8)

The following MIC-breakpoints were used: moxifloxacin R > 4, clindamycin R > 16 and erythromycin R > 2.

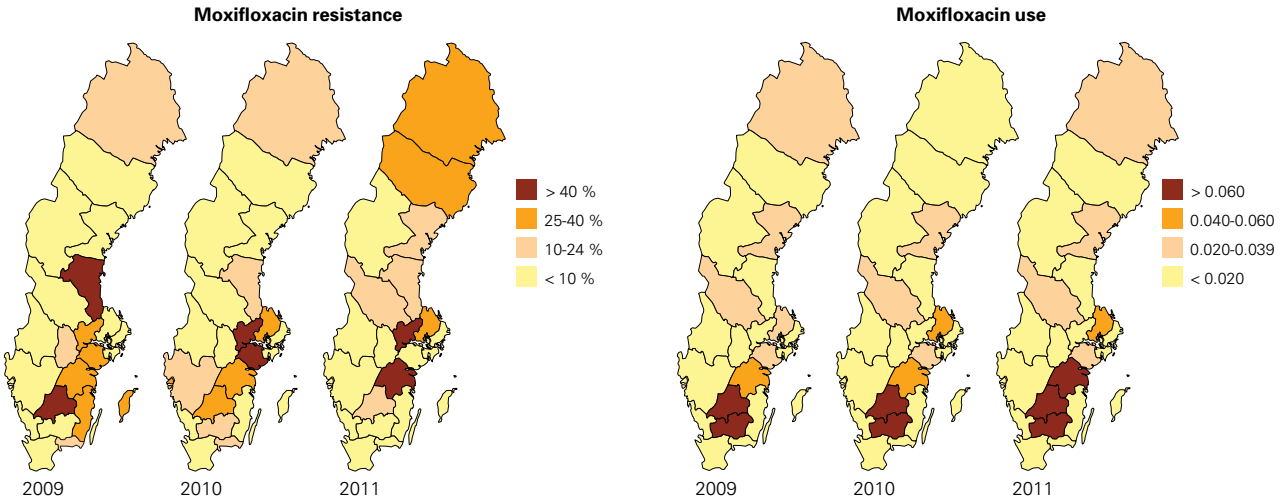


FIGURE 4.24. Proportion of *Clostridium difficile* isolates with resistance to moxifloxacin per county 2009-2011 and sales of moxifloxacin in DDD/1000 inhabitants and day.

Helicobacter pylori

Annual Resistance Surveillance

Helicobacter pylori derived from gastric biopsies have been monitored locally at a few laboratories. In vitro resistance to metronidazole has been reported in 10-40 % of Scandinavian isolates but is no longer tested. Resistance to clarithromycin has been increasing and locally, at one laboratory, it has reached over 10% for several years. Frequencies of resistance to clarithromycin and metronidazole during 2002-2011 in clinical isolates from south Sweden, representing a population of approximately 300 000, are presented in Table 4.14. Resistance to clarithromycin suddenly increased to more than 26% in 2011.

TABLE 4.14. Resistance rates of *Helicobacter pylori* at University Hospital MAS, Malmö, Sweden2002-2011

Year	Total number tested	Clarithromycin-R (%)	Metronidazole-R (%)
2002	124	9.0	44.1
2003	112	7.2	42.6
2004	151	11.6	41.0
2005*	217	11.2	nt
2006	257	16.0	nt
2007	375	9.8	nt
2008	156	5.2	nt
2009	151	10.6	nt
2010	175	15.9	nt
2011	219	26.3	nt

* Molecular biology technique from 2005

Campylobacter spp.

Annual Resistance Surveillance

Campylobacter spp. derived from patients with diarrhoea has been monitored locally at a few laboratories, and *Campylobacter* spp growing from clinical samples have been subjected to susceptibility testing. Approximately 50% of *Campylobacter* strains are imported. Since resistance to fluoroquinolones is of major concern worldwide it is interesting to notice that the small decline in fluoroquinolone resistance among *Campylobacter* isolates noticed a few years ago has now regained the former level of about 50%. The nalidixic acid screen disk method was introduced in Sweden in 2001, but it has been shown by parallel testing that nalidixic acid and ciprofloxacin are equally able to detect fluoroquinolone resistance in *Campylobacter*, Table 4.15.

TABLE 4.15. Resistance rates of *Campylobacter jejuni/coli* at University Hospital MAS, Malmö, Sweden 2002-2011 tested by disk diffusion.

Year	Nalidixic acid	Ciprofloxacin	Tetracycline	Erythromycin
2002	29	28	30	0.5
2003	48	46	22	0
2004	50	47	29	2
2005	57	52	18	1
2006	50	44	21	4
2007	49	45	31	7
2008	65	62	36	7
2009	57	52	21	1
2010	50	48	26	8
2011	69	68	37	7

Salmonella and *Shigella* spp.

Annual Resistance Surveillance

Salmonella spp. and *Shigella* spp. derived from faecal cultures have been monitored locally by a few laboratories. Since most of the *Salmonella* and more than 90% of the *Shigella* strains isolated in Sweden originate from tourists returning home, the resistance patterns reflect the geographical origin. Too few strains are included in the Swedish survey to obtain conclusive results. Fluoroquinolone resistance is however high, 20-25% among *Salmonella* strains and 15-20% among *Shigella* spp. The fluoroquinolone resistance is not only seen in ESBL producing strains.

Salmonella is since many years a notifiable disease, and in addition ESBL-producing *Salmonella* should be notified by laboratories as ESBL-producing *Enterobacteriaceae*, Table 4.8. In 2011 21 *Salmonella* isolates with ESBL were reported. They were almost all imported cases with Thailand as the most frequently reported country of infection. A few reports mentioned other Southeast Asian countries or North African countries. Five of the isolates were available for analysis of ESBL type. Four of them carried CTX-M group 1 enzymes and one isolate carried a plasmid-mediated AmpC.

Neisseria gonorrhoeae

Notifications according to the Swedish Communicable Diseases Act

Gonorrhoea is a notifiable infection/disease in Sweden and in 2011 951 cases (10 cases per 100 000 inhabitants) of the infection were reported. Most of the cases were identified in the three largest counties of Sweden, which comprise the cities Stockholm, Gothenburg, and Malmö, respectively. Clinical isolates are in the present report described from the WHO Collaborating Centre for Gonorrhoea and other STIs, Swedish Reference Laboratory for Pathogenic Neisseria (an external body of the Swedish Institute for Communicable Disease Control [SMI]), Department of Laboratory Medicine, Clinical Microbiology, Örebro University Hospital, Örebro; Clinical Microbiology Malmö, Skåne University Hospital, Malmö; and Karolinska University Hospital, site Huddinge and site Solna, Stockholm.

In 2011, a total of 805 different *N. gonorrhoeae* strains from the notified cases were characterised at these laboratories, representing 85% of the notified cases.

Antimicrobial susceptibility testing was performed according to standardized methodology using Etest for MIC deter-

mination of ampicillin, cefixime, ceftriaxone, azithromycin, ciprofloxacin, and spectinomycin. The used SIR criteria have been determined by The Swedish Reference Group for Antibiotics (SRGA) and The European Committee on Antimicrobial Susceptibility Testing (EUCAST). Production of beta-lactamase was examined by nitrocefin discs.

Results for 2011 are compared with those from 2005 to 2010, Table 4.16. Notably, the levels of resistance to all antimicrobials previously used in the traditional gonorrhoea treatment (penicillins and ciprofloxacin) remained high. The levels of resistance to azithromycin and cefixime have substantially increased during the recent three to four years. Notably, most of the azithromycin resistant cases were identified in Stockholm, which may reflect an overuse of azithromycin in the treatment of gonorrhoea and/or other sexually transmitted infections, in particular, urogenital chlamydial infections. It is of grave concern that resistance to ceftriaxone, which is the last remaining option for empirical treatment of gonorrhoea, has occurred and been increasingly detected in the last two years. No resistance to spectinomycin has still been detected in Sweden, however, the availability of spectinomycin is highly limited (in Sweden as well as worldwide), and it is not suitable for treatment of pharyngeal gonorrhoea.

Neisseria meningitidis

Notifications according to the Swedish Communicable Diseases Act

Invasive meningococcal disease is a notifiable disease, and in 2011 a total of 68 clinical cases (incidence 0.7) of the disease were reported. All together 61 clinical isolates from blood or cerebrospinal fluid (one per patient) were analysed at the Swedish Reference Laboratory for Pathogenic Neisseria (an external body of the Swedish Institute for Communicable Disease Control [SMI]), Department of Laboratory Medicine, Clinical Microbiology, Örebro University Hospital.

Susceptibility testing was performed according to standardized methodology using Etest on Mueller Hinton II agar with 5% horse blood and NAD for determinations of MICs of bensylpenicillin, cefotaxime, meropenem, chloramphenicol, ciprofloxacin and rifampicin. Production of beta-lactamase was examined by nitrocefin discs.

None of the isolates produced beta-lactamase. Seven isolates (11%) had reduced susceptibility to bensylpenicillin (MIC >0.064 mg/L). All isolates were fully susceptible to all other tested antimicrobials. Accordingly, all isolates had MICs of cefotaxime <0.016 mg/L and ciprofloxacin < 0.008 mg/L. The range of meropenem MICs was 0.002-0.032 mg/L, chloramphenicol MICs 0.25-2 mg/L, and rifampicin MICs 0.002-0.064 mg/L.

Mycobacterium tuberculosis

During 2011 in total 595 cases of tuberculosis (TB) were reported compared to 683 cases during 2010, representing a decrease by 13%.

The number and proportion of culture confirmed cases were 476 (80%) compared to 527 (77%) in 2010. *Mycobacterium tuberculosis* was identified in 473 cases, *Mycobacterium africanum* in one patient and *Mycobacterium bovis* in two patients. In one of the cultures with confirmed *M. tuberculosis* it was not possible to perform a drug resistance test due to poor growth of the strain. The proportions of cases diagnosed with isoniazid resistant TB in 2011 were 12% (57/473) and MDR 3.6% (17/473).

Isolates of *M. tuberculosis* and *M. africanum* resistant to at least one of the four first line drugs (isoniazid, rifampicin, ethambutol or pyrazinamid) were identified in 73 patients corresponding to 15.4% of the 473 with culture confirmed TB, Table 4.17. The two patients with *M. bovis* were not included since these strains are naturally resistant to pyrazinamid. As always the most common resistance was that against isoniazid. Among the patients born in Sweden 9/43 (21%) had resistant TB and 6 of those were resistant to isoniazid. This increase of resistance among cases born in Sweden is unexpected but at least 3 of the 9 cases have most likely been infected abroad and two elderly patients only had resistance against pyrazinamid. This type of resistance has increased in general this year and might be due to methodological reasons/difficulties. Nearly 90% of the TB patients in Sweden were born in another country. In this group 64/430 (15%) had some kind of resistant TB and 17 of those 64 had MDR-TB, which makes 4% (17/430). Of the culture confirmed cases 35/473 (7.4%) had a history of previous treatment for TB after 1949 at which time effective medication became available. Out of these 35 cases, 8 (22.9%) had strains resistant to any of the first line drugs including 6 (17%) MDR-TB. The corresponding figures for cases with no reported previous treatment were 65/438 (14.8%) out of which 11 (2.5%) were MDR-TB.

None of the 17 cases of MDR-TB were born in Sweden. The majority (14/17) came to Sweden 2006 or later. In total 11 of the 17 cases had pulmonary manifestations among which four were smear positive.

Genetic typing with RFLP (restriction fragment length polymorphism) has been performed on 71 of the 73 resistant strains so far. The typing of the remaining two is ongoing. This is done to help detect clusters which could indicate ongoing spread of resistant strains. Thirty six of the 71 examined strains belong to 31 different clusters with two or more patients in each cluster. For two patients there was a family connection. The majority of the clustering cases belong to clusters with no resistant strains which make recent spread unlikely, the common factor in the cluster most often being the same country of origin.

The proportion of patients with *M. tuberculosis* resistant against isoniazid has gradually increased from 7.5% in 2003 to 12% in 2011. The annual proportion of MDR-TB increased from 0.8% in 2006 to 4.2% in 2007, dropped in 2009 but increased again to 3.6% in 2011.

TABLE 4.16. Resistance rates (%) and beta-lactamase production of Swedish *Neisseria gonorrhoeae* strains 2005-2011.

	2005 (n=497)	**2006** (n=352)	**2007** (n=406)	**2008** (n=447)	**2009** (n=384)	**2010** (n=618)	**2011** (n=805)
Beta-lactamase positive	23	30	30	28	44	29	23
Ampicillin	23	30	30	28	44	31	24
Cefixime*	0	0	<1	1	5	6	8
Ceftriaxone*	0	0	0	<1	0	2	2
Azithromycin*	<1	5	7	13	6	12	11
Ciprofloxacin	49	61	70	63	75	56	55
Spectinomycin	0	0	0	0	0	0	0

* For cefixime, ceftriaxone and azithromycin, new SIR criteria were introduced in 2009 and the results from previous years have been recalculated.

TABLE 4.17. Drug resistant tuberculosis in Sweden 2002-2011.

Year of diagnosis	**2002**		**2003**		**2004**		**2005**		**2006**		**2007**		**2008**		**2009**		**2010**		**2011**	
Culture confirmed *M. tuberculosis* or *M. africanum*	346		345		368		448		395		361		434		510		523		473	
	No	%	No	%	No	%	No	%	No	No	%	%	No	%	No	%	No	%	No	%
Any resistance	36	10.4	32	9.3	43	11.7	52	11.6	43	10.9	49	13.6	57	13.1	58	11.4	68	13.0	73	15.4
Isoniazid	34	9.8	26	7.5	35	9.5	46	10.3	38	9.6	46	12.7	51	11.8	51	10.0	57	10.9	57	12.0
Rifampicin	4	1.2	10	2.9	6	1.6	5	1.1	6	1.5	15	4.2	15	3.5	14	2.7	20	3.8	19	4.0
Ethambutol	1	0.3	5	1.4	3	0.8	3	0.7	1	0.3	7	1.9	6	1.4	7	1.4	12	2.3	10	2.1
Pyrazinamid	4	1.2	7	2.0	12	3.3	6	1.3	6	1.5	11	3.0	18	4.1	15	2.9	20	3.8	27	5.7
Isoniazid + rifampicin (MDR)	4	1.2	8	2.3	5	1.4	4	0.9	3	0.8	15	4.2	14	3.2	13	2.5	18	3.4	17	3.6

Appendix 1 – Abbreviations

ABU	Asymptomatic bacteriuria
AST	Antibiotic susceptibility testing
ATC	The Anatomical Therapeutic Chemical classification system
BLNAR	Beta-lactamase negative ampicillin resistant
CDCDC	County Department for Communicable Disease Control
DDD	Defined daily dose
CDI	*Clostridium difficile* infection
DST	Drug susceptibility testing
EARSS/EARS-Net	European Antimicrobial Resistance Surveillance System/Network
ESBL	Extended spectrum beta-lactamase
GAS	Group A streptococci or *Streptococcus pyogenes*
GBS	Group B streptococci or *Streptococcus agalactiae*
MDR	Multidrug resistance
MIC	Minimal inhibitory concentration
MRB	Multi-resistant bacteria
MRSA	Methicillin resistant *Staphylococcus aureus*
NordicAST	Nordic committee on antimicrobial susceptibility testing
PFGE	Pulsed-field gel electrophoresis
PNSP	Penicillin non-susceptible pneumococci, MIC ≥0,5 mg/L
PRIS	Primary care record of infection in Sweden
PVL	Panton-Valentine Leukocidin
RFLP	Restriction fragment length polymorphism
RSQC	Resistance surveillance and quality control programme
RTI	Respiratory tract infection
SRGA-M	The Swedish Reference Group of Antibiotics - subcommittee on Methodology
SSTI	Skin and soft tissue infection
ST	Sequence type
Strama	Swedish strategic programme against antibiotic resistance
TB	Tuberculosis
UTI	Urinary tract infection
VRE	Vancomycin resistant enterococci

Appendix 2 – Demographics and denominator data

TABLE APP 2.1. Population by county and age group, December 31st 2011.

	0-6 y	7-19 y	20-59 y	60-79 y	80 y -	All ages
Blekinge	11470	22192	75416	34827	9322	153227
Dalarna	20171	41513	134443	63515	17405	277047
Gotland	3877	8509	28367	13238	3278	57269
Gävleborg	19863	41098	135163	63587	16797	276508
Halland	24721	47807	148083	62136	16737	299484
Jämtland	9557	18421	62540	28104	8069	126691
Jönköping	27296	53799	168484	67204	20083	336866
Kalmar	16086	34452	113202	54636	15160	233536
Kronoberg	14622	28096	92269	37750	11203	183940
Norrbotten	17193	36477	124009	57217	13713	248609
Skåne	104332	182128	650369	240055	66445	1243329
Stockholm	193460	304453	1132294	338944	85192	2054343
Södermanland	21323	42139	132243	59840	15193	270738
Uppsala	28092	50976	179493	62235	15086	335882
Värmland	19149	40217	135036	61513	17350	273265
Västerbotten	19824	38806	134009	52718	13929	259286
Västernorrland	18075	35650	117863	56242	14795	242625
Västmanland	19390	38502	126332	54154	14378	252756
Västra Götaland	129813	236132	829367	301980	83005	1580297
Örebro	21880	42623	140832	58836	16059	280230
Östergötland	33830	65550	220801	85756	23705	429642
Sweden	774024	1409540	4880615	1854487	496904	9415570

TABLE APP 2.2. Population in Sweden 2000-2011. Numbers represent the population by December 31st 2011.

	2000	2001	2002	2003	2005	2006	2007	2008	2009	2010	2011
Population	8861426	8882792	8909128	8940788	9011392	9047752	9113257	9182927	9256347	9340682	9415570

TABLE APP 2.3. Number of admissions and patient-days in somatic medical care, 2010. Numbers represent production by acute care hospitals in the counties.

	Patient-days	Admissions
Blekinge	113419	22091
Dalarna	209018	48637
Gotland	43145	9715
Gävleborg	190412	42486
Halland	193859	43406
Jämtland	95195	18497
Jönköping	252181	53626
Kalmar	164929	40333
Kronoberg	138534	26694
Norrbotten	188884	39337
Skåne	928285	194412
Stockholm	1094024	266716
Södermanland	198471	38858
Uppsala	322071	60287
Värmland	188980	38480
Västerbotten	282422	52587
Västernorrland	173487	37131
Västmanland	178713	37978
Västra Götaland	1174573	246416
Örebro	228299	50123
Östergötland	281134	65254
Sweden	6640035	1433064

TABLE APP 2.4. Denominator data from the microbiological laboratories 2011.

	Number of analyses 2011									Number of positive samples 2011	Number of positive cultures 2011				
Laboratory	**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* (toxin-positive)**
Aleris Medilab	776	0	10787	4233	10248	18031	41414	7897	1278	112	4654	854	963	10202	218
Borås	17682	204	3019	2989	6341	2096	24548	5523	1814	2823	4444	601	540	6879	214
Eskilstuna (Unilabs)	11210	215	6251	2922	6507	1934	27826	4219	1772	1994	3851	582	645	7730	307
Falun	13863	441	2365	1438	10926	3949	26890	3767	1749	1735	4419	520	445	7549	312
Gävle	12692	161	2063	933	11284	2883	22257	2929	1780	1259	4214	405	345	7322	359
Göteborg	37496	1495	2713	3257	17706	38472	71540	12719	4281	5557	9926	792	766	16649	266
Halmstad	12073	231	2341	2702	7393	8270	23995	5297	2112	1639	3632	603	476	6903	390
Jönköping	18700	265	5387	3526	13039	19151	34295	6911	2613	3150	6400	655	430	10650	786
Kalmar	11221	119	3984	2550	6825	3022	24884	4097	1366	1571	4095	637	551	7697	271
Karlskrona	6240	51	1703	1359	5237	1463	14568	2422	1369	674	1938	255	204	4043	195
Karlstad	16342	168	1997	2199	11398	8991	33327	3774	1872	1641	5362	469	380	8221	257
Karolinska Stockholm	75138	2576	31067	9436	76946	206384	139852	20515	11090	9041	28828	2957	3037	36543	1545
Linköping	18351	944	6172	3446	18957	8640	39727	6807	3907	1719	6919	682	752	10710	693
Malmö	65399	1722	19092	15641	33309	48014	162598	28633	11044	7903	22535	2891	3653	42594	1975
Skövde (Unilabs)	13261	175	3559	3206	8395	10241	48557	6841	2363	2859	4933	590	394	10787	385
S:t Göran (Unilabs)	9570	99	7479	3547	10650	38424	45822	8750	1670	1411	5865	913	736	10791	207
Sunderby Luleå	9661	136	2893	2865	8223	3607	27776	3647	1620	NA	NA	NA	NA	NA	NA
Sundsvall	10656	156	2046	1400	6726	11983	26978	4368	1986	1281	3858	374	449	7540	222
NÄL Trollhättan	18278	237	1563	2102	8391	9147	33440	4160	1524	2057	4804	501	321	9318	177
Umeå	14642	631	3702	2354	20348	6599	32762	4748	1729	1515	4732	651	399	9918	124
Uppsala	19801	1028	6049	2523	15118	5787	33735	5581	3701	2202	5617	654	624	9034	891
Visby	3840	321	2170	643	2634	NP	6253	1073	689	447	1324	203	265	2022	87
Västerås	12077	190	2499	1725	9494	4992	27996	4434	1941	1804	4086	335	251	8245	390
Växjö	8813	81	2519	1999	5818	2409	20389	3046	1487	1050	2722	499	305	5500	237
Örebro	16591	288	10472	1778	14363	5789	32762	5225	2463	1823	6068	644	1174	8227	404
Östersund	5963	64	2390	1096	5172	2549	15670	2387	970	1549	3187	368	127	6067	128
Total	460336	11998	146282	81869	351448	472827	1039861	169770	70190	58816	158413	18635	18232	271141	11040

NP, not performed
NA, data not available

Appendix 3 – Surveillance of antibiotic consumption

Sources of data

Data on sales of antibiotics in outpatient care is obtained from Apotekens Service AB, the core infrastructure supplier for all pharmacies in Sweden. Measures used are defined daily doses per 1000 inhabitants and day (DDD/1000 and day) and prescriptions per 1000 inhabitants. 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.

Antibiotic use in hospital care is measured as DDD/1000 and day and DDD/100 patient-days or admissions to hospitals. The number of DDDs is obtained from Apotekens Service AB 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.

When this report is compiled, data on patient-days and admissions in 2011 is not available. Therefore, data from 2010 is used. The number of patient-days and admissions represent production of somatic medical care by each county (to be distinguished from consumption of the county's inhabitants). This gives a more accurate comparison of antibiotic use in hospitals, since the amount of medicines used is related to the quantity of medical care produced.

The ATC classification system and defined daily doses (DDD)

Since 1988, the Anatomical Therapeutic Chemical (ATC) classification system recommended by the WHO is used in Sweden for national drug statistics. 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 Apotekens Service AB are upgraded yearly according to the recommendations made by the WHO Collaborating Centre for Drug Statistics methodology in Oslo, Norway. The sales of drugs are presented as number of DDDs per 1000 inhabitants and day (DDD/1000 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.

Swedish national statistics on drug utilisation

Since 1975, the National Corporation of Swedish Pharmacies regularly produces sales statistics on drugs, 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 includes information on the sales of drugs dispensed on prescription by all Swedish pharmacies by the prescription survey, running since 1974. The statistical material was until 1995 built of samples of dispensed prescriptions. From 1996 all prescriptions dispensed by pharmacies are included. From 1999, ApoDos (individually packed doses of drugs 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 and day or number of prescriptions/1000 inhabitants. Hospital care data includes drugs delivered by all hospital pharmacies to the hospital departments. The system also produces sales statistics for each hospital department and on national and county sales to hospitals. The sales are expressed as cash value, number of packages and number of defined daily doses.

Following the re-regulation 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 AB.

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 gives information on the number of individuals treated with at least one course of antibiotics during a specific period of time, i.e. number of users per 1000 inhabitants 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 once a year data to the National Patient Register kept by The National Board on Health and Welfare. Administrative data within hospital care include, among others, date of admission, date of discharge and length of stay. Since data for 2011 is not available until August denominator data from 2010 and sales data from 2011 are used in some figures in this report. The number of admissions and patient-days in Swedish somatic medical care (produced by acute care hospitals) 2010 is shown in Appendix 2, Table App 2.3. The National Board of Health and Welfare keeps a searchable database at the web, http://www.socialstyrelsen.se/statistik.

Appendix 4 – Antibiotic Susceptibility testing

THE MICROBROTH DILUTION METHOD is the internationally accepted reference method for susceptibility testing to which other methods are compared. Clinical microbiological laboratories in Sweden have a long tradition of using **paper 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 Nordic AST 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. In 2010 several laboratories had already 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), and from 2011 all laboratories use this methodology. 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, whereas quality assurance is one of the features of the Swedish "100-strains", also referred to as ResNet or RSQC programme".

Appendix 5 – 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 Eenterobacteriaceae*, 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 Swedish Institute for Communicable Disease Control (SMI). Notifications, with the exception of STI, are done with full person 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 bensylpenicillin MIC $\geq$ 0.5 mg/L (PNSP) have been notifiable since 1996. Methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *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, SmiNet2. At the SMI, 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 MRSA, VRE and PNSP isolates are sent to SMI for epidemiological typing. For MRSA *spa* typing is the primary typing method, for VRE it is pulsed-field gel electrophoresis (PFGE), and for PNSP serotyping. Depending on needs also other molecular biology methods are used, e.g. MLST.

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 SMI. All resistant isolates are sent to SMI for epidemiological typing, using restriction fragment length polymorphism (RFLP).

The feedback of notification data is done monthly on the SMI homepage (http://www.smi.se) and yearly in "Communicable Diseases in Sweden – the Yearly Report (in Swedish)" and in this report. Data on drug-resistant TB is 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.

Swedish combined surveillance and QC programme (RSQC surveys) further developed into ResNet since 2002

In 1994 a model for the concomitant surveillance of antimicrobial resistance and quality assurance of antimicrobial susceptibility testing was devised. In Sweden there are at present 28 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 antimicrobial 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 microbiological laboratories (see also Appendix 4).

Each year the laboratories are 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.

From 2002 web-based software (ResNet) will receive 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 or MICs together with the relevant demographic data are directly accessible. The software will accept both MIC and zone distributions of well-characterized data sets. 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). A recently introduced feature enables each laboratory to view all its own data and also to link this information to a website of its own local health care system.

EARS-Net

The European network of national surveillance systems of antimicrobial resistance (EARSS) performed on-going surveillance of invasive infections of *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Escherichia coli*, and *Enterococcus faecalis/faecium*, and monitors variations in antimicrobial resistance

over time and place. From 2005 invasive isolates of *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* are also part of the scheme.

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 twenty laboratories in Sweden is coordinated through the SMI, 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 additional to EARS-Net data

Data on invasive isolates on all positive blood cultures were obtained from ten laboratories that are using the same laboratory information system (ADBakt). Their total catchment population is at present 5 millions, thus representing more than 55% of the Swedish population. From these laboratories data for the pathogens specified by the EARS-Net network are retrieved, but also data on all other bacterial pathogens consecutively isolated from blood cultures. In the SWEDRES reports from 2007 to2011 data for *Streptococcus pyogenes*, *Streptococcus agalactiae* and *Haemophilus influenzae* are presented.

Sentinel surveillance

A national surveillance programme for *Clostridium difficile* was initiated by SMI in 2009. The programme included both a voluntary laboratory reporting system of all new cases of *C. difficile* infection (CDI) through SmiNet2 and a determination of resistance and epidemiological typing of isolates from the clinical microbiology laboratories. All *C. difficile* strains isolated during weeks number 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 by clinical laboratories. Existing data are mainly derived from special investigations by devoted researchers / laboratories.

In order to get a national overview of the situation, the ResNet software developed by SMI (see above) is available also for data on these pathogens, as well as for national quantitative data on *Neisseria gonorrhoeae* and *N. meningitidis* performed by the reference centre in Örebro. Also collections of quantitative susceptibility data on other pathogens of general interest are suitable for entering and displaying in ResNet.

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SMITTSKYDDSINSTITUTET
Swedish Institute for Communicable Disease Control

SVARM 2011

Swedish Veterinary Antimicrobial Resistance Monitoring

NATIONAL VETERINARY INSTITUTE

Swedish Veterinary Antimicrobial Resistance Monitoring - SVARM

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Acknowledgements
Several people have in various ways been involved in the work with SVARM and we express our gratitude to all who have contributed.

Suggested citation: SVARM 2011, Swedish Veterinary Antimicrobial Resistance Monitoring. The National Veterinary Institute (SVA), Uppsala, Sweden, 2012. www.sva.se, ISSN 1650-6332.

This report is available at www.sva.se
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Content

NATIONAL VETERINARY INSTITUTE

Printed by Edita Västra Aros, Västerås, Sweden ISSN 1650-6332
Produced by SVA
Graphic production by Edita Västra Aros, Västerås, Sweden
Photographs by Bengt Ekberg, Märit Pringle and Anna Duse, SVA.

Preface

THE INTRODUCTION of antimicrobials some 70 years ago was a true paradigm shift with immense impact on the possibility to treat infectious diseases in human medicine. Soon antimicrobials were introduced also in animal health care and not the least, these drugs came into use in the breeding of animals for food production.

Unfortunately use and misuse of antimicrobials for humans and animals have diminished the usefulness of the miracle drugs by selecting for antimicrobial resistance. The impact of resistance is vast and goes beyond therapeutic failures in single cases. Virtually the foundation of human healthcare as perceived today is being undermined by emergence of resistance. Likewise, modern companion animal healthcare relies on access to effective therapy of infectious diseases as does food production based on breeding of production animals. Not surprisingly emergence of antimicrobial resistance is often described as one of the greatest current global threats and challenges to man.

To recapture the usefulness of antimicrobials for treatment of man and animals, joint actions on several levels are needed. This is generally recognized and was recently addressed by the European Commission in its "Action plan against the rising threats from antimicrobial resistance" released in November 2011 (COM 2011 748). The plan acknowledges a holistic approach comprising actions in several different sectors such as medicine, veterinary medicine, animal husbandry, agriculture, environment and trade.

Among the 12 urgently needed key actions described in the plan is research and development of new antimicrobials to replace drugs that have become obsolete by emerging resistance. This is easily understood but the plan goes further and proposes actions in several other fields. Among these are measures to prevent infectious diseases in man and animals and measures to promote and ascertain prudent use of antimicrobials in human and veterinary medicine. Surveillance of antimicrobial use and of resistance in human as well as veterinary medicine are also among the key actions proposed. Also it is emphasised that harmonisation of monitoring is vital because it increases the usefulness for risk assessment and management of the data generated.

It is in this context the reports from SWEDRES and SVARM should be perceived. To be effective, relevant actions against resistance must be based on sound knowledge of the current situation and of trends over time. For more than a decade the reports have yearly documented the national situation with regard to antimicrobial use and prevalence of resistance. The data generated so far, and in the future, is urgently needed as guidance for actions and initiatives to mitigate antimicrobial resistance as well as for designing strategies on a national level.

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Guidance for readers

Cut-off values for resistance

In SVARM, isolates of indicator bacteria and zoonotic bacteria are classified as susceptible or resistant by epidemiological cut-off values (ECOFF) issued by European Committee on Antimicrobial Susceptibility Testing (EUCAST) and available online at www.eucast.org. Also, animal pathogens are classified by ECOFFs when such values are available and suitable for the concentration range tested. Cut-off values used are given in Appendix 4.

ECOFFs classify isolates with acquired reduced susceptibility as non-wild type, in SVARM called "resistant". This classification is relevant for monitoring purposes, but it should be understood that "resistance" does not always imply clinical resistance.

Since the first report from SVARM, some cut-off values for resistance have been changed. To facilitate comparisons when retrospect data are presented in SVARM 2011, levels of resistance have been recalculated using current cut-off values if not otherwise stated.

Indicator bacteria

In SVARM, *Escherichia coli*, *Enterococcus faecalis* and *Enterococcus faecium* serve as indicators for presence of antimicrobial resistance in the enteric flora of healthy animals and in the flora contaminating retail meat. The prevalence of acquired resistance in such commensal bacteria indicates the magnitude of the selective pressure from use of antimicrobials 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 bacteria contaminating meat indicates the magnitude of the potential human exposure to such reservoirs in food producing animals.

Presentation of MIC distributions

Susceptibility data 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 substance and vertical bold lines indicate cut-off values used to define resistance.

The percentage of isolates with a certain MIC of an antimicrobial is given in the corresponding white field. For MICs above the range tested of an antimicrobial (>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 antimicrobial (≤Y mg/L) the percentage is given as the lowest tested concentration, i.e. in the first white field of the tested range.

Multiresistance

The term "multiresistance" is used in SVARM with a meaning as proposed by Schwarz et al. (2010). Briefly, isolates with phenotypically identified acquired resistance to three or more antimicrobial classes are deemed multiresistant. This implies for example that resistance to ciprofloxacin, enrofloxacin and nalidixic acid represents resistance to one class of antimicrobials.

Antimicrobial abbreviations

Am	ampicillin	Fu	fusidic acid
Ba	bacitracin	Gm	gentamicin
Ce	ceftiofur	Km	kanamycin
Ci	ciprofloxacin	Na	narasin
Cl	clindamycin	Nal	nalidixic acid
Cm	chloramphenicol	Ox	oxacillin
Col	colistin	Pc	penicillin
Ct	cephalothin	Sm	streptomycin
Ctx	cefotaxime	Su	sulphonamide
Ef	enrofloxacin	Tc	tetracycline
Em	erythromycin	Tm	trimethoprim
Fox	cefoxitin	Va	vancomycin.
Ff	florfenicol	Vi	virginiamycin

Other abbreviations

ESBL	extended spectrum beta-lactamase
MRSA	meticillin resistant *Staphylococcus aureus*
MRSP	meticillin resistant *Staphylococcus pseudintermedius*
MIC	minimum inhibitory concentration
VRE	vancomycin resistant enterococci

Example of a table with distributions of MICs:

Antimicrobial	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				

Summary

THE 2011 REPORT FROM SVARM shows that the situation regarding antimicrobial resistance in bacteria from animals remains favourable from an international perspective. However, the importance of continuous monitoring as a tool to discover appearance of new types of resistance and to identify trends is again manifested. In SVARM 2011, transferable resistance to third generation cephalosporins (ESBL) in *Escherichia coli* from pigs in Sweden is reported for the first time as is the first isolation of methicillin resistant *Staphylococcus aureus* from dairy cows.

These examples illustrate a dynamic and gradually deteriorating situation. They are also examples of the complex and multifactorial background to emergence and spread of antimicrobial resistance. To guide actions to counteract resistance, it is important to fully understand the interaction of the factors involved. This is also important for assessment of the risks for animal and human health as a consequence of resistance in bacteria from animals.

However, of key importance for emergence as well as for spread of resistance is the selection pressure exerted by use of antimicrobials. The stable or declining use of antimicrobials for animals in Sweden reported in SVARM 2011 is therefore encouraging and signifies that activities to promote "prudent use" in veterinary medicine are successful. From an international perspective the level of antimicrobial use for animals in Sweden is outstandingly low.

The total amount of antimicrobials used for animals was 12 606 kg in 2011. When data were expressed as mg active substance per 'population correction unit' (PCU; estimated kg live-weight of the populations of food producing animals), the sales in 2011 were 15.4 mg/PCU which is 26% lower than in 2007 and more than 50% lower than in 1992. Decreases are seen for all antimicrobial classes and for all major animal species. Sales of products for group medication are only about 10% of the total sales.

Salmonella is rare in Swedish animals and most incidents involve susceptible isolates. In 2011, 72% of the isolates were susceptible to all antimicrobials tested. Only four of 43 isolates from food producing animals and three of 28 isolates from companion animals and wildlife were multiresistant. Resistance to third generation cephalosporins was not observed. Only one incident involved multiresistant *S.* Typhimurium DT 104 but multiresistant monophasic *Salmonella* subspecies I, O 4,5,12:i- was found in one incident in cattle and also in a dog. There are no indications of increased occurrence of resistance, but in view of the public health consequences vigilance towards resistant *Salmonella* in food-producing animals is warranted.

In pigs, all isolates of ***Campylobacter coli*** were susceptible to erythromycin but a large proportion was resistant to quinolones (37%). This is in agreement with previous findings and probably caused by use of quinolones (enrofloxacin) in sows and piglets.

Methicillin resistant *Staphylococcus aureus* (MRSA) in animals is notifiable to the Board of Agriculture. In 2011, MRSA was confirmed in one cat, two horses and in four milk samples from dairy cows. Since first reported in 2006 and until the end of 2011, MRSA has been isolated from 18 dogs, 5 cats, 17 horses, 4 dairy cows and in one sample from pigs. The four isolates from cows were of *spa*-types t524 and t9111 and were the first findings of MRSA from cattle in Sweden. They were also the first isolations of MRSA with the divergent *mecA* homologue, $mecA_{LGA251}$ from Swedish animals. Most isolates from horses and the isolate from pig were of *spa*-type t011 and belonged to the livestock associated CC398. This type is common in several animal species in other countries but rare among humans in Sweden. In contrast, most isolates from dogs and cats were of *spa*-types that are common among MRSA from humans in Sweden. Since there is a zoonotic aspect to MRSA in animals, the situation should be closely monitored and measures to hinder spread, such as improved biosecurity and infection control, is of utmost importance.

Resistance in indicator bacteria (*Escherichia coli* and *Enterococcus* spp.) from the intestinal flora of healthy animals, are believed to reflect the antimicrobial selective pressure in an animal population. At slaughter, intestinal bacteria can contaminate carcasses and subsequently be passed along the food chain. Resistance in indicator bacteria on food can therefore be used to assess exposure of humans to resistant bacteria from food animals.

In an international perspective, resistance in indicator bacteria from pigs and pig meat was low and at similar levels as in previous years. However, resistance to ampicillin, trimethoprim or sulphonamides in *E. coli* from pigs has gradually increased since monitoring started in 2000. These three antimicrobials are commonly used in pig production and the increase is probably due to direct selection. Co-selection probably enhances selection since these three resistance traits are common in multiresistant isolates.

By screening of samples from pigs with sensitive selective cultures, *E. coli* with ESBL resistance was found in 1.6% of the samples. This is the first finding of ESBL resistance in *E. coli* from pigs in Sweden. Notably, use of cephalosporins in pigs is insignificant in Sweden. In broilers, selective culture confirmed previous findings of *E. coli* with ESBL or AmpC

resistance in intestinal content in a large proportion of birds. These findings cannot be explained by antimicrobial use in broiler production in Sweden and preliminary findings indicate introduction and spread from imported breeding stock.

The overall resistance situation in **pathogenic bacteria from food-producing animals** in Sweden is favourable. Resistance was most common in isolates of *E. coli* from pigs and calves where resistance to ampicillin, streptomycin, tetracycline or trimethoprim-sulphonamides was not unusual. Forty percent of isolates from calves and 25% of isolates from pigs were multiresistant, which are increasing figures compared to previous years.

Resistance was rare in isolates of *Actinobacillus pleuropneumoniae* and *Pasteurella* spp. from the respiratory tract of pigs, in isolates of *Pasteurella* spp. from the respiratory tract of calves as well as in isolates of *Streptococcus equisimilis* from joints of piglets. Resistance to penicillin was not detected in these species, supporting the view that penicillin is the substance of choice for treatment of respiratory and joint infections. However, penicillin resistance was confirmed in *Mannheimia haemolytica* from calves in one herd, emphasizing the importance of monitoring.

In isolates of *Brachyspira* spp. from pigs, resistance to tiamulin occurred in *B. pilosicoli* but was not observed in *B. hyodysenteriae*. However, the majority of isolates of *B. pilosicoli* and *B. hyodysenteriae* was resistant to tylosin.

In *Aeromonas salmonicida* subsp. *achromogenes*, *Flavobacter columnare* and *Flavobacter psychrophilum* from farmed fish, deviating high MICs to florfenicol, tetracycline or nalidixic acid in some isolates indicate acquired resistance to these antimicrobials.

The resistance situation in **pathogenic bacteria from companion animals** is worrisome concerning *Staphylococcus pseudintermedius* from the skin of dogs. Most isolates were resistant to penicillin through beta-lactamase production and resistance to clindamycin, erythromycin, fusidic acid or tetracycline was also common. Multiresistance occurred in 36% of the isolates and 7% were resistant to five or more antimicrobials. In Sweden, isolates of methicillin resistant *S. pseudintermedius* (MRSP) are notifiable. During 2011, 53 cases were reported to the Board of Agriculture. Since first detected in 2008, ESBL resistance has been confirmed in 19 isolates of *Enterobacteriaceae*. Isolates of *Pseudomonas aeruginosa* from the external ear of dogs were susceptible to polymyxin B, but resistance to gentamicin and enrofloxacin occurred.

Resistance in **pathogenic bacteria from horses** is mostly in level with previous years. However, ESBL resistance has been confirmed in 33 isolates of *Enterobacteriaceae* since 2008, and the situation must be closely monitored. In isolates of *E. coli*, resistance to streptomycin and trimethoprim-sulphonamides was most common. Resistance to penicillin through beta-lactamase production in isolates of *Staphylococcus aureus* from skin samples occurred in 20% of the isolates. Isolates of *Streptococcus zooepidemicus* from the respiratory tract were uniformly susceptible to penicillin, but resistance to trimethoprim-sulphonamides occurred.

Sammanfattning

SVARM 2011 visar att resistensläget hos bakterier från djur är fortsatt gynnsamt ur ett internationellt perspektiv. Men trots att den samlade bilden är positiv har för första gången MRSA påvisats hos svenska kor och *Escherichia coli* med överförbar resistens mot tredje generationens cefalosporiner (ESBL) hos svenska grisar.

Båda fynden visar att resistensläget är föränderligt och de belyser därmed vikten av kontinuerlig övervakning för att förändringar ska upptäckas tidigt. Baserat på sådan kunskap kan åtgärder för att bromsa spridning av resistenta bakterier vidtas i ett tidigt skede och har då störst möjlighet att bli effektiva.

Försäljningen av antibiotika för djur var totalt 12 606 kg under 2011. Uttryckt som mg aktiv substans per skattade kilo levandevikt av livsmedelsproducerande djur var försäljningen 2011 15.4 mg/kg vilket är 26 % lägre än 2007 och mer än 50 % lägre än 1992. Minskad försäljning noterades för alla antibiotikaklasser och för alla djurslag. Försäljning av antibiotika för inblandning i foder eller vatten stod endast för cirka 10% av den totala försäljningen.

Fynd av **meticillinresistent *Staphylococcus aureus* (MRSA)** hos djur är anmälningspliktiga till Jordbruksverket. Under 2010 påvisades MRSA hos en katt, två hästar och i fyra mjölkprover från kor. Sedan det första fallet hos svenska djur 2006 har MRSA konfirmerats hos 18 hundar, 5 katter, 17 hästar, 4 mjölkkor och i ett prov från grisar till och med 2011. De fyra isolaten från kor var av *spa*-typerna t524 och t9111 och var de första fynden av MRSA från nötkreatur i Sverige. De var också de första isolaten av MRSA med den avvikande *mecA*-genen, $mecA_{LGA251}$, från svenska djur. De flesta isolat från hundar och katter och isolatet från gris var av *spa*-typ t011 och tillhörde den stordjursassocierade varianten av MRSA, CC398. Denna variant är vanlig hos framför allt livsmedelsproducerande djur i många länder men är ovanlig hos människor i Sverige. Isolaten från hundar och katter var av *spa*-typer som är vanliga hos människor i Sverige, vilket indikerar smittspridning mellan människa och djur. MRSA betraktas som ett zoonotiskt smittämne och läget i djurpopulationer bör därför övervakas. Åtgärder för att hindra smittspridning är mycket viktiga.

Salmonella är ovanligt hos svenska djur och de fall som inträffar orsakas oftast av antibiotikakänsliga stammar. Under 2011 var 72 % av isolaten känsliga för alla testade antibiotika. Bara fyra av 43 isolat från livsmedelsproducerande djur och tre av 28 isolat från sällskapsdjur och vilda djur var multiresistenta. Inget isolat var resistent mot tredje generationens cefalosporiner. Endast ett fall av multiresistent *S.* Typhimurium DT 104 påvisades. Multiresistent monofasisk *Salmonella* subspecies I, O 4,5,12;i- påvisades i ett fall hos nötkreatur och dessutom hos en hund. Sedan 2006 har totalt åtta fall med multiresistenta isolat av denna salmonellatyp påvisats hos svenska lantbruksdjur.

Alla isolat av ***Campylobacter coli*** från gris var känsliga för erytromycin men en stor andel var resistent mot kinoloner (37 %). Kinolonresistensen hos isolat från grisar har varit vanlig även tidigare år vilket troligen beror på att kinoloner (enrofloxacin) används för behandling av smågrisar och suggor.

Resistens hos indikatorbakterier (*Escherichia coli* och *Enterococcus* spp.) från tarmfloran hos friska djur anses återspegla selektion av resistens som följd av användning av antibiotika till djuren. Indikatorbakterier på livsmedel ger en uppfattning om vilka resistenta bakterier från lantbruksdjur som kan nå människor via livsmedelskedjan.

Resistens hos indikatorbakterier från såväl tarminnehåll från grisar som från griskött är ovanlig och av samma storleksordning som tidigare år. I ett internationellt perspektiv är förekomsten liten. Sedan övervakningen startade 2000 har dock resistens mot ampicillin, trimethoprim och sulfonamid hos *E. coli* successivt ökat. Dessa tre antibiotika används för att behandla sjuka grisar och ökningen är sannolikt en följd av direkt selektion. Men troligen har ko-selektion också betydelse eftersom det inte är ovanligt att multiresistenta isolat av *E. coli* är resistenta mot alla tre substanserna.

Med känslig selektiv odlingsmetod påvisades *E. coli* med överförbar resistens mot tredje generationens cefalosporiner i en liten andel (1,6 %) prov av tarminnehåll från grisar men i en stor andel sådana prov från slaktkyckling. Det är första gången denna typ av resistens påvisas hos tarmbakterier från svenska grisar medan undersökningen av slaktkyckling konfirmerar resultatet från undersökningarna i SVARM 2010. I Sverige används cefalosporiner mycket sällan till grisar och inte alls i uppfödningen av slaktkyckling. Preliminära resultat visar att orsaken till förekomst hos svensk slaktkyckling sannoliokt är spridning av resistenta bakterier från importerade avelsdjur.

Resistensläget hos **sjukdomsframkallande bakterier från livsmedelsproducerande djur** i Sverige är generellt sett gynnsamt. Resistens var vanligast hos isolat av *E. coli* från grisar och kalvar där resistens mot ampicillin, streptomycin, tetracyklin eller trimetoprim-sulfonamid var vanligast. Fyrtio procent av isolaten från kalvar och 25 % av isolaten från grisar var multiresistenta vilket är en ökning jämfört med tidigare år.

Resistens var ovanligt hos isolat av *Actinobacillus pleuropneumoniae* och *Pasteurella* spp. från luftvägarna hos grisar, hos isolat av *Pasteurella* spp. från luftvägarna hos kalvar och hos isolat av *Streptococcus equisimilis* från lederna hos smågrisar. Resistens mot penicillin påvisades inte hos dessa bakteriearter, vilket stödjer ståndpunkten att penicillin bör vara förstahandsval vid antibiotikabehandling av luftvägs- och ledinfektioner. Penicillinresistens påvisades dock hos *Mannheimia haemolytica* från kalvar i en besättning vilket belyser vikten av resistensundersökning.

Hos isolat av *Brachyspira* spp. från grisar förekom resistens mot tiamulin hos *B. pilosicoli* men kunde inte påvisas hos *B. hyodysenteriae*. Majoriteten av isolaten av *B. pilosicoli* och *B. hyodysenteriae* var resistent mot tylosin.

Hos *Aeromonas salmonicida* subsp. *achromogenes*, *Flavobacter columnare* och *Flavobacter psychrophilum* från odlad fisk förekom avvikande höga MIC-värden för florfenikol, tetracyklin eller nalidixansyra hos några isolat, vilket indikerar överförbar resistens mot dessa antimikrobiella substanser.

Resistensläget hos **sjukdomsframkallande bakterier hos sällskapsdjur** är oroande vad gäller *Staphylococcus pseudintermedius* från huden på hundar. De flesta isolat var resistenta mot penicillin genom betalaktamasproduktion och resistens mot klindamycin, erytromycin, fusidinsyra eller tetracyklin var också vanligt. Multiresistens förekom hos 36 % av isolaten och 7 % var resistenta mot fem eller fler antibiotika. I Sverige är fynd av meticillinresistent *S. pseudintermedius* (MRSP) anmälningspliktigt. Under 2011 anmäldes 53 fall av MRSP till Jordbruksverket. Resistens av ESBL-typ hos *Enterobacteriaceae* har påvisats hos 19 isolat från hundar och katter sedan 2008. Isolat av *Pseudomonas aeruginosa* från hörselgången hos hundar var känsliga för polymyxin B men resistens mot gentamicin och enrofloxacin förekom.

Resistensläget hos **sjukdomsframkallande bakterier från hästar** är i huvudsak jämförbart med tidigare år. ESBL-producerande isolat av *Enterobactericeae* har dock påvisats 33 gånger och noggrann övervakning av läget är viktigt. Hos *E. coli*-isolat var resistens mot streptomycin och trimetoprim-sulfonamid vanligast. Resistens mot penicillin genom betalaktamasproduktion hos isolat av *S. aureus* från hudprover förekom hos 20 % av isolaten. Alla isolat av *Streptococcus zooepidemicus* från luftvägarna var känsliga för penicillin men resistens mot trimetoprim-sulfonamid förekom.

Use of antimicrobials

STATISTICS ON TOTAL SALES of antimicrobials for use in animals in Sweden are available since 1980. For a review of the data from 1980-2000 as well as references to publications on which that review is based, see SVARM 2000. Data represent an approximation of the real use of antimicrobials, assuming that the amount sold is also used during the observation period. Data for 2011 were provided by Apotekens Service AB and represent sales for terrestrial animals. Data on prescription of antimicrobials for farmed fish are collected through the Fish health control program and are commented in the section 'Comments on trends by animal species'. Details on source of data and inclusion criteria are given in Appendix 2 and on antimicrobial agents with general marketing authorisation in Sweden in Appendix 5.

Trends in animal populations

Changes in the numbers of animals may affect trends in statistics on use of antimicrobials. The number of beef cows have increased by 5% in five years (i.e. since 2007), but the number of dairy cows has decreased by 6%. The number of pigs slaughtered has decreased by 5%, while the number of broilers was 5% higher in 2010 than in 2007. The number of horses was 349 000 in 2010, an estimated increase by 10-20% since 2004. Details on animal numbers are found in Appendix 1.

Completeness of data

The data coverage for products with general Swedish marketing authorisation is assumed to be 100%. However, during the analysis of data for 2011, it became clear that the data for products sold with special license (prescribed and sold on exemption from general Swedish marketing authorisation) and sold for the first time in 2010 or 2011 were not included in the retrieved data. Furthermore, a comparison of data retrieved for some products sold with special license before 2010 with sales figures for 2011 showed that the sale from drug companies to pharmacies (in number of product packages) was much larger than sales from pharmacies (in number of product packages). The difference is deemed to be larger than what can be expected to be kept in stock at the pharmacies.

In conclusion, data for products sold with special license are less complete than before 2010. In 2009, about 10% of the overall sales expressed in kg active substance were products of this type. Major antimicrobials sold with special license are products for group medication with tetracyclines, amoxicillin or colistin and products for injection with long acting penicillins. These products are mainly sold for use in pigs and poultry, and the uncertainty about completeness of data will therefore hamper assessment of trends for these animal species.

Overall use

The total yearly sales of antimicrobials over the last decade are presented in Table AC I. The potency of different antimicrobials is not equal and therefore each class should be evaluated separately. Trends in sales of individual classes from 1980 are shown in Figure AC I.

Changes in the numbers of animals over time will influence the statistics on use of antimicrobials. To correct for this, the method of estimating the weight at treatment of livestock and of slaughtered animals described in a recent publication from the European Medicines Agency was applied (EMA 2011). The term used for the total estimated weight is "population correction unit" (PCU) which is a purely technical unit of measurement. In Figure AC II, the sales of antimicrobials for animals from 1980 are presented as mg active substance per PCU. The overall sales have decreased more than 50% compared to the average figures for 1980-1984 (i.e. before the Swedish ban on growth promoting antimicrobials in 1986). This is explained both by the removal of growth promoting antimicrobials in 1986 and by a major gradual decrease from the mid 90s of the sales of veterinary products for medication via feed or water (group medication). Today, the sales of prod-

TABLE AC I. Yearly sales of antimicrobial drugs for veterinary use expressed as kg active substance. For penicillins, tetracyclines, aminopenicillins and polymyxins data on sales of products sold with special license may be incomplete for 2011 (indicated in red).

ATCvet code	Antimicrobial class	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
QJ01AA, QG01A	Tetracyclines[a]	1 415	1 307	1 329	1 562	1 516	1 853	1 649	1 174	1 115	1 073
QJ01CE, -R, QJ51	Benzylpenicillin[a,b]	8 179	7 579	7 814	7 571	7 860	7 582	7 758	7 721	7546	6 696
QJ01CA, QJ01CR	Aminopenicillins[a]	767	870	875	911	920	927	938	1 068	907	723
QJ01D	Cephalosporins	676	832	928	1 009	1 217	954	820	738	575	498
QA07AA, QJ01G, -R, QJ51R	Aminoglycosides and polymyxins[a]	753	645	606	762	750	718	643	609	557	503
QA07AB, QJ01E	Sulphonamides	2 477	2 326	2 462	2 535	2 543	2 427	2 303	2 128	1 998	1 867
QJ01E	Trimethoprim & derivatives	414	381	406	437	450	438	416	379	357	338
QJ01F	Macrolides & lincosamides	1 412	1 124	1 095	1 080	1 254	1 520	1 096	988	739	648
QJ01MA	Fluoroquinolones	185	184	187	184	195	180	169	164	148	120
QJ01XX92, - 94	Pleuromutilins	988	744	387	338	459	506	572	398	174	140
Total		*17 266*	*15 992*	*16 089*	*16 389*	*17 164*	*17 106*	*16 364*	*15 368*	*14 117*	*12 606*

[a] Includes drugs marketed with special licence prescription; [b] Also includes small amounts of penicillinase stable penicillins.

ucts for medication of groups of animals are less than 10% of what it was on average before 1986 (counting the sum of veterinary medicines and growth promoters).

Of the total sales expressed as kg active substance, about 90% are products formulated for treatment of individual animals (injectables, tablets, intramammaries) and about 10% for treatment of groups or flocks (premixes, oral powders, solutions for water medication). In table AC II, the sales of products for use in individual animals, excluding topical, intrauterine and intramammary use are presented. The sales of cephalosporins (almost entirely first generation cephalosporins) have decreased by 48% in five years, almost entirely related to decreased prescription of first generation cephalosporins for dogs. The sales of fluoroquinolones for therapy of individual animals have decreased by 33% since 2007. This is explained both by a marked decrease in sales of fluoroquinolones for oral use in dogs and cats (32% decrease of that subset) and of products for injection (34% decrease of that subset).

Data on sales of antimicrobials formulated for medication of groups of animals are given in Table AC III. Data for 1984 are given as historical reference. As noted above, data on products sold with special license is slightly incomplete for 2011 which hampers assessment of trends of some classes. For further comments see pig and poultry below.

TABLE AC II. Yearly sales of antimicrobial drugs authorised for individual treatment expressed in kg active substance. Only products for systemic use (QJ01) or for use as intestinal anti-infective (QA07) are included. For penicillins, tetracyclines aminopenicillins and intestinal anti-infectives, data on sales of products sold with special license may be incomplete for 2011 (indicated in red).

ATCvet code	Antimicrobial class	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
QA07A	Intestinal anti-infectives[a]	594	594	586	496	434	372	364	355	302	280
QJ01A	Tetracyclines	628	606	611	623	609	632	605	576	538	520
QJ01CE	Benzylpenicillin[a, b]	8 127	7 536	7 769	7 493	7 777	7 504	7 671	7641	7 492	6 627
QJ01CA -CR	Aminopenicillins	767	870	875	911	909	899	828	802	742	687
QJ01D	Cephalosporins	676	832	928	1 009	1 212	950	817	735	575	498
QJ01E	Sulfonamides & trimethoprim	2 483	2 280	2 427	2 610	2 689	2 619	2 486	2 270	2 138	2 023
QJ01F	Macrolides & lincosamides	477	430	382	400	417	413	352	332	311	287
QJ01G	Aminoglycosides[c]	460	367	344	362	345	343	318	301	274	246
QJ01M	Fluoroquinolones	178	177	180	179	190	177	164	159	144	118
QJ01X	Pleuromutilins	49	77	32	29	39	36	36	28	17	13
Total		*14 439*	*13 769*	*14 134*	*14 112*	*14 622*	*13 944*	*13 640*	*13 198*	*12 532*	*11 300*

[a] Drugs marketed with special licence prescription are included; includes aminoglycosides, formolsulfatiazole and colistin; [b] The amount includes QJ01R; [c] Does not include the aminoglycosides in QA07A, intestinal anti-infectives.

TABLE AC III. Yearly sales of antimicrobial drugs authorised for group treatment and ionophoric anticoccidials sold expressed as kg active substance. For penicillins, tetracyclines, aminopenicillins and intestinal anti-infectives, data on sales of products sold with special license may be incomplete for 2011 (indicated in red).

ATCvet code	Antimicrobial class	1984	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
QA07A	Intestinal anti-infectives[a]					163	170	158	106	107	119	77
QJ01A	Tetracyclines[a]	12 300	777	695	712	934	903	1 217	1 040	594	575	552
QJ01C	Penicillins incl. aminopenicillins[a]						11	28	111	266	164	36
QJ01F	Macrolides & lincosamides	607	935	694	713	680	837	1 107	744	657	427	361
QJ01MA	Fluoroquinolones		7	8	7	5	5	3	5	5	4	2
QJ01MQ	Quinoxalines[b]	9 900										
QJ01XX91	Streptogramins[c]	8 800										
QJ01XX92, -94	Pleuromutilins		939	667	355	309	420	471	536	370	157	127
QP51AA	Nitroimidazoles	1 440										
	Feed additives[d]	700										
Total		*33 747*	*2 658*	*2 064*	*1 787*	*2 091*	*2 346*	*2 984*	*2 543*	*1 999*	*1 447*	*1 154*
QP51AH	Ionophoric antibiotics (coccidiostats)[d, e]	7 900	8 439	10 920	10 486	11 095	12 335	12 527	13 376	12 471	15 325	NA[e]

[a] Drugs with special licence prescription are included from year 2005, includes aminoglycosides and colistin; [b] Years 1980-1984 sold as feed additives, thereafter on veterinary prescription at therapeutic dosages until 1997; [c] Feed additives other than quinoxalines and streptogramins: avoparcin, bacitracin, nitrovin, oleandomycin and spiramycin; [d] Figures are from the Feed Control of the Board of Agriculture (www.sjv.se); [e] Not available at the time of publication.

FIGURE A

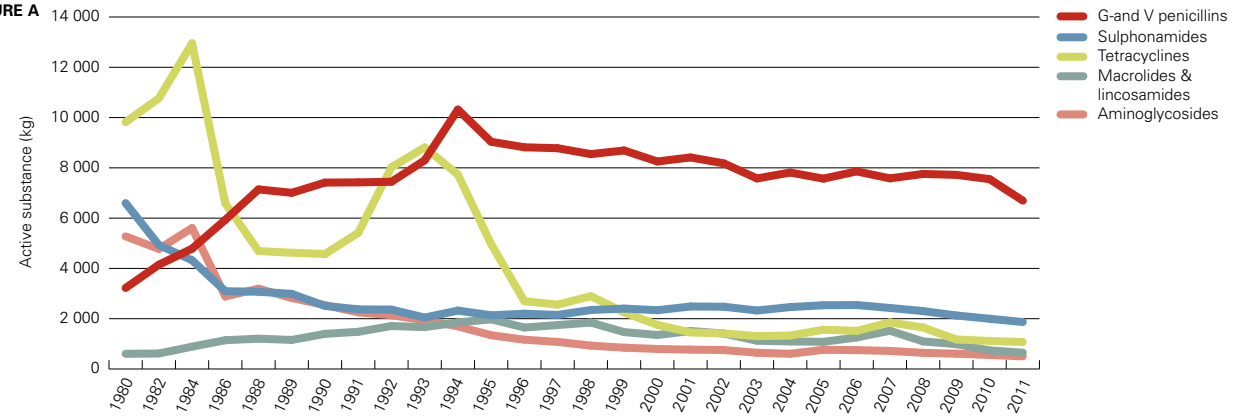


FIGURE B

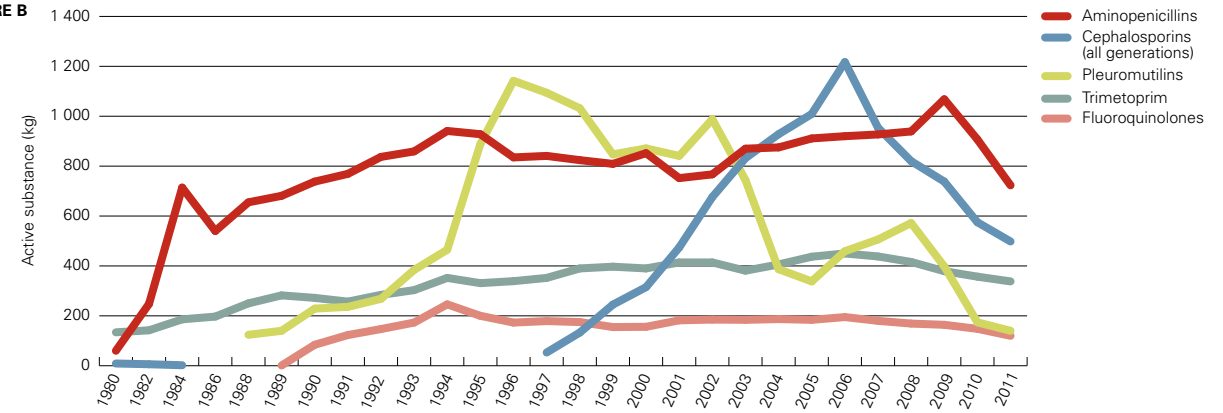


FIGURE AC I A & B. Sales of antimicrobials for animals. Amphenicols, nitroimidazoles, streptogramins, quinoxalines and other feed additives were withdrawn from the market during the time period and are not shown. Note that the scales on the Y-axis are different in figure a and b. For penicillins, tetracyclines and aminopenicillins, data on sales of products sold with special license may be incomplete for 2010 and 2011.

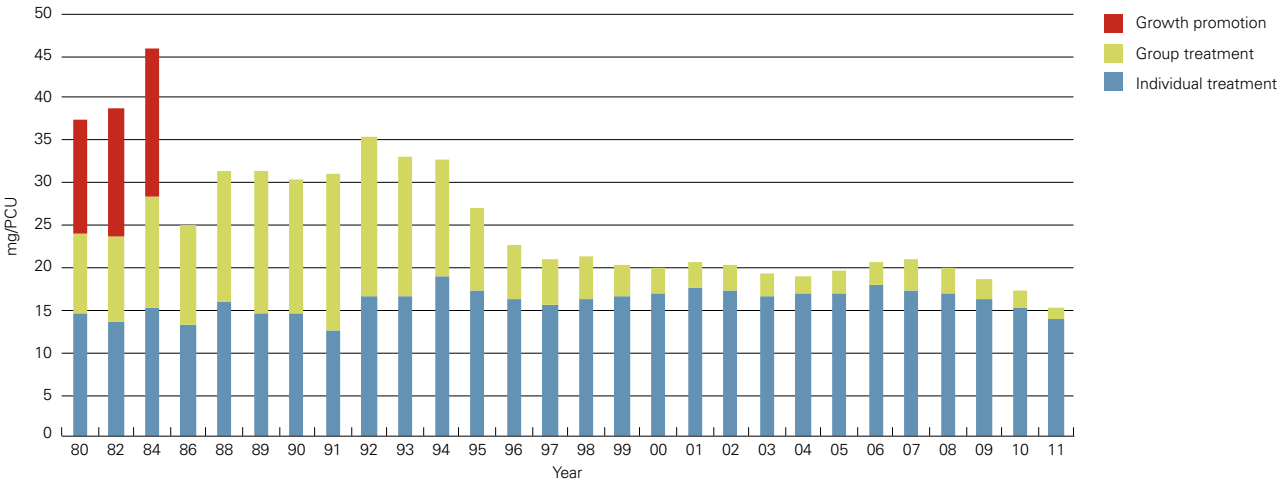


FIGURE AC II. Sales of antimicrobials for animals expressed as mg per population correction unit (PCU).

Comments on trends by animal species

Information on the volumes of antimicrobials sold for different animal species as given on the prescription is available from the Swedish Board of Agriculture. The results for years 2009-2011 have been summarised in Table AC IV as percent of the total volume sold per class. A large proportion of the aminopenicillins (76%) and cephalosporins (97%) are used for companion animals. Also, macrolides & lincosamides and fluoroquinolones are to a considerable extent sold for use in dogs and cats (39 and 30%, respectively). The current system does not permit a full stratification of the antimicrobials sold for specific food producing animal species. Therefore, non companion animal species are given as one group in Table AC IV.

In the following, trends in the use of various classes for different animal species are commented based on information from different sources, e.g. species when given on the prescriptions, knowledge on how different products are generally used in Sweden and on other available information. The comments have varying degrees of uncertainty, depending on the source of information used.

Dairy cows

The Swedish Dairy Association publishes a yearly report related to the organization's work to improve animal health and welfare in dairy cows (Swedish Dairy Association, 2011). The reporting year is from September to August which in the following will be given as, e.g., 2009/10. For statistics specifically on antimicrobial treatments, full years are reported and the latest year is 2010. The report includes statistics on disease incidence in dairy cows enrolled in the Swedish milk recording scheme. Data are mainly retrieved from a database with veterinary reported disease events and treatments (Jansson Mörk, 2010).

The by far most common indication for treatment of dairy cattle is clinical mastitis and other udder conditions. The reported incidence of clinical mastitis in dairy cows was 13.0 per 100 completed/interrupted lactations in 2010/11 which is lower than in 2009/10 (14.2 per 100). In Sweden, mastitis is generally treated systemically and any changes in treatment incidence, treatment length or choice of antimicrobial for this condition will have a noticeable influence on the statistics on sales of antimicrobials. Treatment with penicillin was by far the most common, and the decreased incidence of clinical mastitis tallies with a decrease in sales of penicillins for systemic use (Table AC II) where products with a general marketing authorisation in Sweden have decreased by 11% between 2010 and 2011. The incidence of treatment of dairy cows with third generation cephalosporins has decreased from 0.82 per 100 cow-years in 2007 to 0.32 per 100 cow-years. The reported incidence of treatment of dairy cows for mastitis with fluoroquinolones has been roughly unchanged over the last years, around 2.5 treatments per 100 cow-years. In the sales statistics from pharmacies, 13.3 kg of third generation cephalosporins and 72 kg of fluoroquinolones were recorded as sold for cows, horses or unknown animal species. This represents a decrease since 2007 by 49 and 33%, respectively.

The Swedish Dairy Association reports a 30% treatment incidence at drying off for cows enrolled in the Swedish milk recording scheme. The number of dose-applicators of intramammary products for drying off corresponds to a treatments incidence of 19.6%, assuming that four applicators are used per cow. The discrepancy in figures might be explained by fewer applicators being used per cow (e.g. only subclinically infected quarters treated) or by products formulated for use during lactation being used to some extent for this indication, or a combination of both. Products with penicillin combined with aminoglycosides are by far the most commonly used for prevention around drying off.

Pigs

The problems with retrieval of data on sales of products sold with special license mentioned above will in particular affect the statistics on sales of products with tetracycline, aminopenicillins or colistin for group medication and long acting penicillin for injection of pigs. The sales of fluoroquinolones for pigs were 12.5 kg in 2011, 38% lower than in 2007. The sales of third generation cephalosporins were insignificant (0.01 kg).

The continued drop in use of macrolides for group medication (Table AC III; 67% lower in 2011 than in 2007) is likely to reflect improved knowledge on how to manage problems with concomitant infections in herds with postweaning multisystemic wasting syndrome. This includes the introduction of vaccination strategies and an awareness that in most cases, antimicrobials have no or a limited effect. The sales of pleuromutilins also continue to decrease and the sales are 73% lower in 2011 compared to 2007. The main indication for pleuromutilins (tiamulin, valnemulin) is swine dysentery. Efforts to control the disease through e.g. a certification programme have resulted in a decreased need to treat swine dysentery, leading to overall declining sales figures since the mid 90s (Figure AC I). Further comments on trends in sales of antimicrobials for pigs 2006-2010 are presented in the Highlight 'Antimicrobials for pigs'.

Poultry

The problems with retrieval of data on sales of products sold with special license mentioned above will in particular affect the statistics on sales of pencillin V and aminopenicillins for group medication of poultry.

Antimicrobials are rarely used for treatment of bacterial diseases in commercially reared *Gallus gallus*. Localized outbreaks can therefore have a major influence on the sales in a specific year. Over the last five years, the yearly sales of fluoroquinolones for *Gallus gallus* have been below or much below 1.5 kg and in 2011 there were no sales of this class. Cephalosporins are never used.

From 2011, the Swedish poultry meat association requests all treatments of broilers, parents and grandparents to be reported as part of the Poultry health control programme. According to the reports, a total of six of 3 185 broiler flocks (0.2%) were treated with antimicrobials because of outbreaks

of botulism. In two flocks, amoxicillin was used and in four tylosin. In addition to this, one flock each of grandparent (penicillin V) and parent (amoxicillin) birds were treated. These figures are well in line with the sales statistics, keeping in mind that all the quantity sold will not be used.

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

Horses

Around 60% of the sales of trimethoprim-sulphonamides are products for oral use in horses (paste or powder). The sales of such products increased steadily until 2006 but since, there has been a decrease by 27%. Over the same time period, the total number of horses has increased but the number of mares covered has decreased by 31% (Anonymous 2012). Among the indications for trimethoprim-sulphonamides in horses are reproductive disorders and various conditions in foals. Thus, it is probable that the decrease in sales of trimethoprim-sulphonamides is explained by the lower number of mares covered and a lower number of foals born.

The sales of other antimicrobials for horses is difficult to estimate, as they are frequently administered by the veterinarian in connection with an examination, either in ambulatory practice or in clinics or hospitals.

Dogs

In 2006, the total sales of antimicrobials for oral use in dogs corresponded to 562 packages per 1000 dogs. Since, the sales expressed as total number of packages has decreased by 32%. The dataset includes products authorised for oral use in animals (ATC vet code QJ01 and QA07) as well as for humans (ATC code J01) and corresponds to out-patient use for dogs. The most recent estimate of the dog population in Sweden is from 2006, but there are no indications that the number of animals has decreased.

In figures AC III, the sales of the major classes of antimicrobials are shown. The most prominent changes relative to 2006 is noted for cephalosporins (-62%), aminopenicillins with clavulanic acid (-44%), and fluorquinolones (-40%). Figures on sales of antimicrobials for dogs expressed as kg active substance have only been calculated for the products authorised for use in animals. The sales of that subset represent around 95% of the total sales for dogs. The total sales of veterinary antimicrobials for oral use in dogs was 1 182 kg in 2011 which is 9% of the total sales of veterinary antimicrobials.

As described in SVARM 2008, the emergence of infections with multiresistant methicillin resistant *Staphylococcus pseudintermedius* and methicillin resistant *S. aureus* triggered a number of national and local initiatives. This has most likely led to changes in prescribers' behaviour, which in turn explains the downward trends in sales of antimicrobials for dogs.

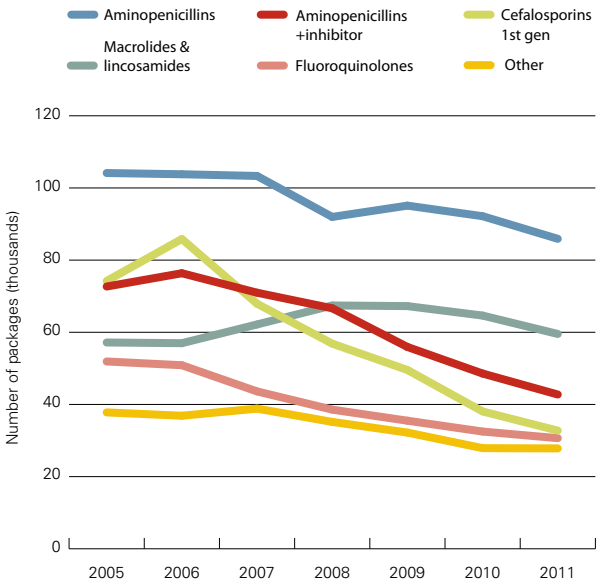
Farmed fish

The occurrence of bacterial disease in farmed fish is influenced by water temperatures in summer and the amounts prescribed may therefore vary between years. In 2011, a total of 49 kg was prescribed for in feed medication corresponding to 4 g per ton fish produced. The average annual sales 2002-2010 was 26 kg. Almost all treatments were for flavobacteriosis, and florfenicol was the most commonly used substance (42 kg). In addition, 6 kg of oxitetracycline and 1 kg of oxolinic acid were prescribed. Previously, furunculosis and cold water vibriosis were more common but today effective vaccination strategies are widely applied.

TABLE AC IV. Sales of antimicrobial drugs per category of animals in 2009-2011 given as percent of total sales in kg active substance[1].

Antimicrobial	Companion animals			Food producing animals, horses, other or unknown		
	2009	2010	2011	2009	2010	2011
Tetracyclines	8.4	9.3	7.2	91.6	90.7	92.8
Penicillin G & V	4.4	1.1	2.7	95.6	98.9	97.3
Aminopenicillins	63.3	69.7	75.6	36.7	30.3	24.4
Cephalosporins	97.2	96.6	97.2	2.8	3.4	2.8
Aminoglycosides & polymyxins	16.4	5.7	5.0	83.6	94.3	95.0
Sulphonamides	12.7	2.5	10.9	87.3	97.5	89.1
Trimethoprim	3.6	2.6	2.3	96.4	97.4	97.7
Macrolides & lincosamides	23.1	34.3	39.0	76.9	65.7	61.0
Fluoroquinolones	30.2	26.5	30.4	69.8	73.5	69.6
Pleuromutilins	0.3	0.0	0.2	99.7	100.0	99.8

[1]Data are from the Swedish Board of Agriculture's report on usage of veterinary medicines (www.jordbruksverket.se; in Swedish), includes antimicrobials authorized for animals and for humans sold for use in animals.



FIGUE AC III. Sales of antimicrobials for oral use in dogs (QJ01, QA07 and J01) expressed as number of packages (thousands).

Trends in sales of antimicrobials for pigs in Sweden

IN SWEDEN, veterinary medicinal products must be dispensed by pharmacies. All pharmacies deliver data on sales of veterinary medicinal products, including target animal species as given on the prescription, to a government owned company (Apotekens Service). In almost all commercial pig production herds, the owner has a contract with one veterinarian. In such circumstances, the veterinarian is allowed to delegate treatments of specified indications to the animal caretaker. This system is widely applied, and almost all antimicrobials for treatment of individual animals on pig farms are acquired by veterinary prescription from the pharmacies. Antimicrobials may also be mixed in feed or water, and in such cases the prescription will be handled by the pharmacy.

To study trends in sales of antimicrobials for pigs, the sales of antimicrobial products (ATCvet codes QJ01 and QA07AB) with pig specified on the prescriptions for the years 2006-2010 were extracted. In addition, all sales for unknown species of products authorized for pigs and formulated for in feed or water medication were included. Year 2011 was excluded because the figures for some antimicrobial classes are somewhat incomplete with regard to products sold with special license. To correct for changes in animal numbers, data were expressed as mg active substance per population correction unit (PCU) of pigs (an estimate of kg live weight of slaughter pigs and sows) (EMA 2011).

The sales expressed as kg active substance in 2006 and the change (%) from 2006 to 2010 are given in Table and in Figure the sales expressed as mg active substance/PCU are shown. Irrespective of unit of measurement, the sales of products for use in individual pigs, mainly injectables, increased when measured during the study period. In particular, use of benzylpenicillin increased. The sales of tetracyclines, macrolides and pleuromutilins for medication of groups of pigs decreased. A shift from medication of groups of animals via feed or water towards medication of individual clinically diseased animals, preferably with narrow spectrum antibiotics such as penicillin, is well in line with the rational and prudent use of antimicrobials.

TABLE. Sales of antimicrobials for individual and group medication of pigs in 2006 (kg active substance) and change 2006 to 2010 (%)

Antimicrobial class	Individual medication, 2006	Change (%)	Group medication, 2006	Change (%)
Tetracyclines	54.7	13%	796.3	-39%
Penicillin G	1004.6	31%		
Aminopenicillins	88.8	0%	0.0	[a]
Aminoglycosides, polymyxins	102.9	-3%	170.4	-44%
Trimethoprim & sulphonamides	415.8	17%		
Macrolides	134.5	-39%	764.0	-51%
Fluoroquinolones	20.6	-17%		
Pleuromutilins	34.5	-53%	419.5	-63%
Total	*1856.3*	*17%*	*2150.1*	*-45%*

[a]Aminopenicillins for group medication were not used in 2006, but have been sold with special license from 2008.

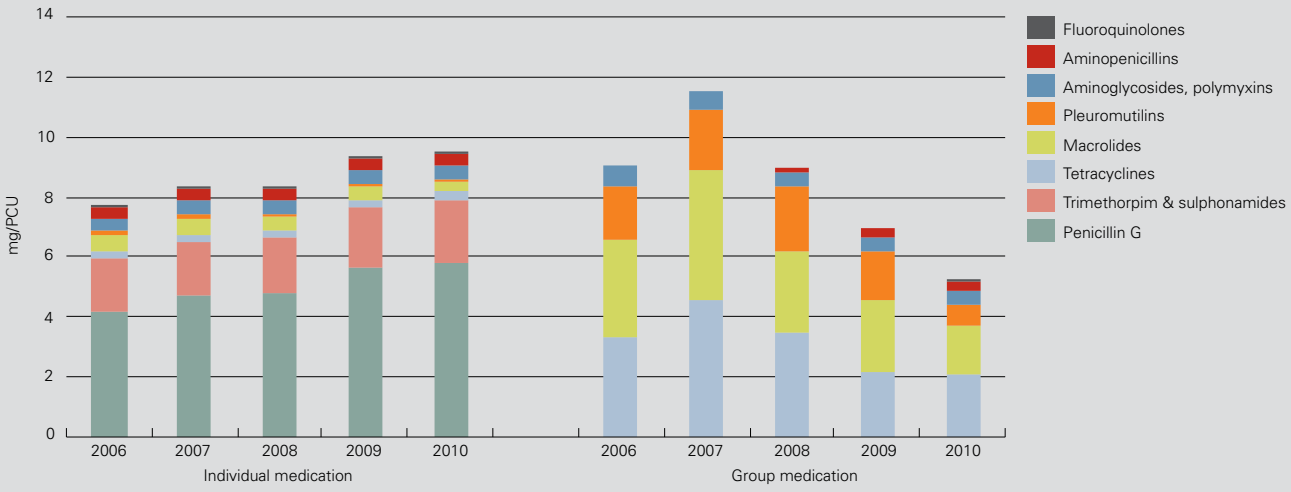


Figure. Sales of antimicrobials for individual and group medication of pigs expressed as mg/PCU.

Zoonotic bacteria

ZOONOSES ARE DISEASES and infections that can be naturally transmitted between animals and man. Antimicrobial resistance in zoonotic bacteria such as *Salmonella*, *Campylobacter* and methicillin resistant *Staphylococcus aureus* (MRSA) from animals is therefore of direct public health concern. Data regarding these bacteria from Swedish animals are presented here. More information on infections with zoonotic bacteria in Sweden is presented in the yearly report *Surveillance of zoonotic and other animal disease agents in Sweden*, available at www.sva.se.

Salmonella

Isolates included

Findings of *Salmonella* in animals are notifiable in Sweden and antimicrobial susceptibility is tested in one isolate from each warm-blooded animal species (wild and domesticated) involved in an incident. In incidents involving more than one serovar or phage type, one isolate of each serovar and phage type is tested. In SVARM 2011, isolates from incidents notified in 2011 are included but also isolates from incidents previously notified but still under restrictions. In addition, isolates obtained in the salmonella surveillance programme from samples collected at slaughter are included. For details on methodology see Appendix 3.

Results and comments

The overall situation regarding *Salmonella* among Swedish animals is favourable. Occurrence of *Salmonella* among food-producing animals is low and few incidents involve multiresistant strains.

All animals 2011

Altogether, 71 isolates were tested of which 42 were *S.* Typhimurium and six were of the monophasic serovars O 4,5:i:- or O 4:i:- (Table Salm I). The majority of isolates (72%) were susceptible to all antimicrobials tested but 20 isolates were resistant to at least one substance and seven isolates (10%) were resistant to three or more substances (Table Salm II).

The 20 resistant isolates were from 19 separate incidents of which 11 involved food-producing animals (Table Salm II). Of the eight incidents in cattle, four were notified already in 2010 but still under restrictions in 2011. Only one incident involved *S.* Typhimurium DT 104 with the common resistance phenotype: ampicillin, chloramphenicol, streptomycin, sulphonamide, and tetracycline.

Food-producing animals 2000-2011

From a public health perspective resistance in *Salmonella* from food-producing animals is of greater concern than resistance in isolates from wild animals or pets. In the period 2000-2011 isolates from the vast majority of notified incidents in food-producing animals were tested in SVARM, in total 541 isolates. Of these, 255 isolates (47%) were *S.* Typhimurium. Most isolates (40%) were from pigs, 29% were from cattle, 28% from poultry and 2% from sheep.

Distributions of MICs and occurrence of resistance among the isolates of *S.* Typhimurium are given in Table Salm VI. Fifty-nine (23%) isolates of *S.* Typhimurium were resistant to at least one antimicrobial and 19 isolates (7%) to three or more antimicrobial classes, i.e. they were multiresistant (Table Salm VII). Among serovars other than Typhimurium from food-producing animals, 11 isolates (4%) were multiresistant.

The 19 multiresistant isolates of *S.* Typhimurium were from 17 separate incidents of which 11 involved only cattle, three involved pigs and one incident involved both pigs and cattle. Of the remaining incidents one was in sheep and one in ducks in a hobby flock. Three incidents in 2004 involving cattle were epidemiologically linked through trade of calves. An epidemiological link is also suspected between four incidents 2007-2008 involving cattle, pigs and sheep. Links between the other incidents are unknown.

Monophasic *Salmonella*

Twelve incidents involving monophasic *Salmonella* subspecies I (O 4,5,12:i-/O 4,5:i:-/O 4:i:-) have been discovered since this type was first confirmed in Swedish animals in 2006. Five incidents involved cattle, three incidents pigs, one incident ducks, and one incident involved both cattle and poultry. Monophasic *Salmonella* has also been isolated from a dog and a wild bird. Epidemiological links between some of the incidents have been confirmed.

In eight incidents, isolates were resistant to ampicillin, streptomycin, sulphonamide and tetracycline but in one incident also isolates resistant only to tetracycline were found. In two incidents in pigs the isolates were resistant to streptomycin and sulphonamides. Finally, in one incident where *Salmonella* was isolated only from cattle carcasses sampled at slaughter and in one incident in a wild bird the isolates were susceptible to all antimicrobials tested.

TABLE SALM I. Number of *Salmonella enterica* tested for antimicrobial susceptibility, 2011.

Serovar	Cattle	Bison	Pigs	Sheep	Poultry	Ostriches	Horses	Dogs	Cats	Wild birds	Wild mammals	Total
S. Agona	1											1
S. Be					1							1
S. Brandenburg								1				1
S. Derby			1					1				2
S. Dublin	5											5
S. Enteritidis					1							1
S. Infantis			1									1
S. Mbandaka					1							1
S. Reading	2											2
S. Typhimurium, DT 104			1									1
S. Typhimurium, DT 110b						1						1
S. Typhimurium, DT 120	1		3									4
S. Typhimurium, DT 146	1											1
S. Typhimurium, DT 195			1									1
S. Typhimurium, DT 40									1			1
S. Typhimurium, DT 41	2											2
S. Typhimurium, NST										1		1
S. Typhimurium, NST 1:3	4	1			2		1					8
S. Typhimurium, NST 1:7									4			4
S. Typhimurium, NST 11:58	1						2					3
S. Typhimurium, NST 11:7 U277									1			1
S. Typhimurium, NST 6:1			1									1
S. Typhimurium, not phage typed	1							1	8	2	1	13
S. enterica, subsp. diarizonae (IIIb)	1			2								3
S. enterica (I), O -:r:1,5			1									1
S. enterica (I), O 4,5:-:1,5										1		1
S. enterica (I), O 4,5:i:-	3							1				4
S. enterica (I), O 4:i:-			1							1		2
S. enterica (I), O 4,5:-:5							1					1
S. enterica (I), O 6,7:d:-	2											2
Total	**24**	**1**	**10**	**2**	**5**	**1**	**4**	**4**	**14**	**5**	**1**	**71**
Percent of total	34%	1%	14%	3%	7%	1%	6%	6%	20%	7%	1%	

TABLE SALM II. MICs (mg/L) of *Salmonella enterica* resistant to at least one antimicrobial, 2011. Shaded fields indicate resistance.

Animal species	Serovar	Am	Ctx	Cm	Ff	Gm	Km	Ci	Nal	Sm	Su	Tc	Tm
Pig	S. Typhimurium DT 104	>64	0.25	256	32	1	4	0.06	4	128	>1024	32	≤0.25
Cattle	S. Typhimurium DT 120	>64	≤0.06	4	4	0.5	2	0.03	8	256	>1024	1	≤0.25
Dog	S. Typhimurium, not phage typed	>64	0.12	4	4	1	2	0.06	4	>256	>1024	2	≤0.25
Cattle	S. Typhimurium NST 11:58	1	≤0.06	4	4	1	2	0.03	4	16	>1024	2	>32
Horse	S. Typhimurium NST 11:58	1	≤0.06	4	4	1	4	0.03	4	16	1024	2	>32
Horse	S. Typhimurium NST 11:58	1	0.12	4	4	1	4	0.03	4	16	>1024	2	>32
Cattle	S. Typhimurium DT 146	1	0.12	4	4	1	2	0.03	4	16	>1024	2	>32
Cat	S. Typhimurium NST 1:7	1	0.12	4	≤2	0.5	2	0.03	4	32	64	2	0.5
Cattle	S. Typhimurium NST 1:3	1	≤0.06	≤2	≤2	0.5	2	0.03	4	32	64	1	≤0.25
Cat	S. Typhimurium, not phage typed	1	0.12	4	4	0.5	2	0.06	4	32	128	2	0.5
Cat	S. Typhimurium, not phage typed	1	≤0.06	4	4	0.5	4	0.06	4	32	128	2	0.5
Cattle	S. Typhimurium, not phage typed	1	0.12	4	4	2	2	0.06	4	>256	>1024	>64	≤0.25
Dog	S. enterica (I) O 4,5:i:-	>64	0.12	4	4	1	2	0.06	4	256	>1024	>64	≤0.25
Cattle	S. enterica (I) O 4,5:i:-	>64	0.12	4	4	1	2	0.06	8	256	>1024	>64	≤0.25
Cattle	S. enterica (I) O 4,5:i:-	1	≤0.06	4	4	0.5	4	0.06	4	8	128	>64	≤0.25
Pig	S. enterica (I) O 4:i:-	1	≤0.06	4	4	1	2	0.03	4	128	>1024	2	≤0.25
Pig	S. enterica (I) O -:r:1,5	1	0.25	8	8	1	4	0.25	256	16	128	2	0.5
Pig	S. Infantis	1	0.12	4	4	1	4	0.25	256	16	32	2	≤0.25
Cattle	S. Dublin	≤0.5	≤0.06	≤2	4	0.5	2	0.03	8	32	64	1	0.5
Dog	S. Derby	1	0.12	4	8	1	4	0.06	4	>256	1024	64	>32

TABLE SALM III. Distribution of MICs and resistance (%) in *Salmonella enterica* (n=71) from all animals, 2011.

Antimicrobial	Resistance %	Distribution (%) of MICs (mg/L)																		
		≤0.008	0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	>1024
Ampicillin	7							11.3	81.7							7.0				
Cefotaxime	0				43.7	52.1	4.2													
Chloramphenicol	1									18.3	71.8	8.5					1.4			
Ciprofloxacin	3		2.8	56.3	38.0		2.8													
Florfenicol	1									22.5	64.8	11.3		1.4						
Gentamicin	0						1.4	49.3	46.5	2.8										
Kanamycin	0								4.2	63.4	32.4									
Nalidixic acid	3									2.8	84.5	9.9					2.8			
Streptomycin	18									2.8	2.8	14.1	62.0	7.0		2.8	4.2	4.2		
Sulphonamide	17													5.6	38.0	36.6	2.8		2.8	14.1
Tetracycline	8								28.2	63.4				1.4	1.4	5.6				
Trimethoprim	7						54.9	35.2	2.8						7.0					

TABLE SALM IV. Distribution of MICs and resistance (%) in *Salmonella* Typhimurium (n=42) from all animals, 2011.

Antimicrobial	Resistance %	Distribution (%) of MICs (mg/L)																		
		≤0.008	0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	>1024
Ampicillin	7							7.1	85.7							7.1				
Cefotaxime	0				40.5	57.1	2.4													
Chloramphenicol	2									14.3	78.6	4.8					2.4			
Ciprofloxacin	0			61.9	38.1															
Florfenicol	2									26.2	66.7	4.8		2.4						
Gentamicin	0							47.6	47.6	4.8										
Kanamycin	0								2.4	57.1	40.5									
Nalidixic acid	0									2.4	88.1	9.5								
Streptomycin	19											9.5	71.4	9.5		2.4	2.4	4.8		
Sulphonamide	19														31.0	45.2	4.8		2.4	16.7
Tetracycline	5								26.2	69.0				2.4		2.4				
Trimethoprim	10						50.0	38.1	2.4						9.5					

TABLE SALM V. Resistance (%) and source of isolates for *Salmonella* Typhimurium from all animals, 1978-2011.

Antimicrobial	Cut-off value (mg/L)	Resistance (%)								
		1978-88[a] (n=125)	1989-99 (n=317)	2000–05 (n=291)	2006 (n=52)	2007 (n=71)	2008 (n=63)	2009 (n=67)	2010 (n=43)	2011 (n=42)
Ampicillin	>8	2	6	5	15	7	11	3	2	7
Cefotaxime	>0.5	-	-	0	0	0	0	0	0	0
Ceftiofur	>2	-	-	0	0	-	-	-	-	-
Chloramphenicol	>16	4[b]	5[b]	5	2	1	8	3	0	2
Ciprofloxacin	>0.06	-	-	0	0	0	3	1	0	0
Enrofloxacin	>0.25	-	1	<1	-	-	-	-	-	-
Florfenicol	>16	-	-	3	2	1	8	3	0	2
Gentamicin	>2	-	0[b]	2	0	0	0	0	0	0
Kanamycin	>16	-	-	0	0	0	0	0	0	0
Nalidixic acid	>16	-	-	2	0	0	2	1	0	0
Neomycin	>4	0[b]	1[b]	1	-	-	-	-	-	-
Streptomycin	>16	74	15	25	13	3	29	7	5	19
Sulphonamide	>256	-	-	5	13	6	11	7	9	19
Tetracycline	>8	13	6	5	10	3	10	3	5	5
Trimethoprim	>2	-	-	<1	0	0	0	4	5	10
Trim-sulpha	>0.5/9.5	0	3	5	-	-	-	-	-	-
Percent of isolates from:										
Cattle, sheep, pigs, poultry		100	46	30	40	53	70	49	70	47
Horses, cats, dogs			29	54	36	17	16	31	23	43
Wildlife			25	16	24	30	14	19	7	10

[a] 1988 includes isolates to September, isolates from October-December 1988 given under 1989; [b] Cut-off value for resistance >8 mg/L.

TABLE SALM VI. Distribution of MICs and resistance (%) in *Salmonella* Typhimurium (n=255) from food-producing animals, 2000-2011.

Antimicrobial	Resistance %	Distribution (%) of MICs (mg/L)																		
		≤0.008	0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	>1024
Ampicillin	9							4.3	71.4	14.1	1.2				9.0					
Cefotaxime[a]	0				31.6	62.0	6.4													
Ceftiofur[b]	0							29.0	68.0	3.0										
Chloramphenicol	5									12.5	78.8	3.5				0.8	4.3			
Ciprofloxacin[c]	<1			62.6	36.8			0.6												
Enrofloxacin[d]	0				54.3	42.0	3.7													
Florfenicol	5										91.8	3.1	0.4	4.7						
Gentamicin	2							17.3	71.4	9.8	1.6									
Kanamycin[c]	0									31.1	65.5	2.9	0.6							
Nalidixic acid	<1									1.6	78.0	14.9	4.7	0.4			0.4			
Streptomycin	20										0.4	17.6	62.4	11.4	2.4	2.4	2.4	1.2		
Sulphonamide	10														51.8	31.8	6.3			10.2
Tetracycline	7								37.3	50.6	5.1		1.6	1.2	2.0	2.4				
Trimethoprim	<1						42.0	51.4	5.9						0.8					

[a] 187 isolates tested; [b] 100 isolates tested; [c] 174 isolates tested; [d] 81 isolates tested.

TABLE SALM VII. Resistance phenotypes of *Salmonella* Typhimurium (n=255) from incidents in food-producing animals, 2000-2011. All isolates were tested for susceptibility to ampicillin, ceftiofur/cefotaxime, enrofloxacin/ciprofloxacin, florfenicol, gentamicin, chloramphenicol, nalidixic acid, streptomycin, sulphametoxazole, tetracycline, and trimethoprim.

Resistance phenotype	Animal species	Phage type																					
		1	7	9	10	12	15A	39	40	41	99	104	110b	120	125	126	146	193	195	U277	NT	NST	Not typed	Total
AmFfCmNalSmSuTcCi	Pigs											1											1
AmFfCmSmSuTc	Cattle											5		1								1	7
AmFfCmSmSuTc	Pigs											2										1	3
AmFfCmSmSuTc	Sheep											1											1
AmCmSmSuTc	Cattle											1											1
AmSmSuTc	Cattle													1							2		3
AmSmSuTc	Poultry																				1		1
AmSmSu	Cattle													1									1
SmSuTc	Cattle																					1	1
AmSu	Cattle											2											2
AmSu	Pigs											1											1
GmSm	Cattle									1													1
GmSm	Pigs								1														1
GmSm	Poultry									1													1
SmSu	Poultry						2																2
SuTm	Cattle																1					1	2
Am	Poultry																				2		2
Gm	Poultry																				1		1
Nal	Pigs					1																	1
Sm	Cattle											1		1		1					4		7
Sm	Pigs								4	3		1		1							1	4	1	15
Sm	Poultry									1												3		4
Susceptible	Cattle	4			2		1	1	1	6				5	1	1					1	21	6	50
Susceptible	Pigs	1	1			2			33	5	1	1		8					1	1	2	17	8	81
Susceptible	Sheep	1																					3	4
Susceptible	Poultry	1		1		1			4	1			1	2				1	1	1	4	41	2	61
Number of isolates		**7**	**1**	**1**	**2**	**4**	**3**	**1**	**43**	**18**	**1**	**16**	**1**	**20**	**1**	**2**	**1**	**1**	**2**	**2**	**11**	**95**	**22**	**255**
percent of total		2	<1	<1	<1	2	1	<1	17	7	<1	6	<1	8	<1	<1	<1	<1	<1	<1	4	37	9	

Campylobacter

Isolates included

Campylobacter were isolated from samples of colon content from slaughter pigs collected at abattoirs for isolation of indicator bacteria. Isolates were identified as *Campylobacter jejuni* or *Campylobacter coli* by PCR (Denis et al., 1999). For details on methodology and sampling strategy, see Appendix 3.

Results and comments

Campylobacter were isolated from 85 (72%) of 118 samples cultured. The majority of isolates, 83, were *C. coli* and only two were *C. jejuni*. The isolation frequency is similar to previous studies in SVARM.

There was no resistance recorded against erythromycin, gentamicin or tetracycline (Table Camp). Resistance to ciprofloxacin, nalidixic acid, or streptomycin was common and occurred in 37, 37 and 61% of the isolates respectively. Most isolates were resistant only to a single group of antimicrobials but 21 isolates were resistant to both quinolones and streptomycin. The two isolates of *C. jejuni* were susceptible to all antimicrobials tested.

A tendency of increasing resistance to quinolones (ciprofloxacin and nalidixic acid) was recorded (Table Camp). Neither quinolones nor fluoroquinolones are authorised or used for treatment of groups of pigs via feed or water in Sweden. Over the last five years, the yearly sales of injectable fluoroquinolones for pigs were 20 kg or less, corresponding to 4-7 mg/slaughtered pig. Fluoroquinolones are probably mostly used in piglets and sows and to a lesser extent in fattening pigs older than 12 weeks. Selection for quinolone resistance in *Campylobacter* therefore probably occurs in younger pigs and/or sows before pigs are moved to the finishing stage. The high prevalence (39%) of quinolone resistance in *Campylobacter* spp. from piglets <12 weeks old reported in SVARM 2006 supports this hypothesis.

Occurrence of streptomycin resistance in *C. coli* is remarkably high (61%) but since only data from two years for Swedish isolates are available trends in resistance cannot be evaluated. A high prevalence of streptomycin resistance in *C. coli* from pigs and cattle is reported also from other countries (EFSA, 2007).

Streptomycin resistance in *Campylobacter* spp. 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 59% of the streptomycin resistant isolates were resistant only to this antimicrobial. However, similar *aadA2* encoding class 1 integrons, encoding streptomycin/spectinomycin resistance, have been identified in *Campylobacter*, *Escherichia coli* and *Salmonella* (O'Halloran et al., 2004). Accordingly, streptomycin resistance could be a marker for the presence of a transferable resistance element and the issue deserves further study.

TABLE CAMP. Distribution of MICs and resistance (%) in *Campylobacter coli* from slaughter pigs 2011. Data on resistance for 1999, 2003, 2005 and 2008 are given for comparison.

Substance	1999 (n= 91)	2003 (n=100)	2005 (n=97)	2008 (n=97)	2011 (n=83)	Distribution (%) of MICs (mg/L)											
						≤0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Ciprofloxacin	30[a]	17[a]	24[a]	30	37	18.1	28.9	14.5	1.2				20.5	16.9			
Erythromycin	1	0	0	1	0				26.5	37.3	32.5	3.6					
Gentamicin	0	-	0	0	0				12.0	83.1	4.8						
Nalidixic acid	30	17	24	29	37					1.2		7.2	31.3	19.3	3.6		37.3
Streptomycin	-	-	-	57	61					1.2	7.2	30.1	3.6		2.4	32.5	22.9
Tetracycline	4	3	4	2	0		14.5	43.4	37.3	4.8							

[a] Enrofloxacin tested.

Methicillin resistant *Staphylococcus aureus* (MRSA)

Isolates included

In Sweden, MRSA in animals was first verified in 2006 and was made notifiable in 2008. During 2011, MRSA was isolated from infection sites in two horses and one cat. Up to and including 2011 a total of 45 cases in animals have been confirmed at SVA (Table MRSA).

Most cases are detected in passive surveillance when animals with clinical infections are sampled and isolates of *S. aureus* with resistance to oxacillin are further analysed with confirmatory tests. Samples from animals with suspected MRSA infection or colonisation are selectively enriched in order to increase the sensitivity. Screening studies for active surveillance of MRSA have been performed with selective methods in pigs and horses and without selective methods in dogs and dairy cattle in different years.

Results and comments

Dogs and cats

During 2011, MRSA was isolated from one cat with skin infection. Altogether, MRSA has been confirmed in 18 dogs and 5 cats in Sweden since 2006, when the first detection in animals was made. Most isolates are from wound infections, mainly post operative wounds. Eighteen of the isolates were of *spa*-type t032, two of t002, one of t127, one of t020 and one of t022. All isolates were negative for the PVL-gene (coding for Panton Valentine Leukocidin toxin).

Horses

During 2011, two horses were diagnosed with MRSA-infections. Altogether, MRSA has been isolated from 17 horses in Sweden. Most isolates are from clinical cases with post operative wound infections. Screening studies have been performed twice in horses in Sweden. In a study in 2007, MRSA was found in one sample and in a study in 2010, no MRSA was found.

Most cases of clinical MRSA-infections were horses with post operative wound infections connected to two equine hospitals. One contact horse outside the hospitals was revealed as carrier without signs of infection. Of the horses identified in 2011, one had a skin infection and had no known contact with any of the equine hospitals. The isolate from that horse had a susceptibility pattern different from all the other horse isolates. Fifteen of the isolates were of *spa*-type t011, belonging to the livestock-associated MRSA clonal complex (CC)398, and two of *spa*-type t064. All isolates were PVL-negative.

Cattle

During 2011, MRSA was confirmed from four milk samples from dairy cows. This was the first detection of MRSA in cattle in Sweden. The isolates had the divergent *mecA* homologue, $mecA_{LGA251}$, reported in MRSA from bovine milk samples and humans (Garcia-Alvares et al. 2011). Isolates with this novel *mecA* gene will most likely be suspected as methicillin resistant by susceptibility testing, but, since $mecA_{LGA251}$ is only 70% identical at the DNA level to *mecA*, they will not be confirmed as MRSA with conventional confirmatory methods.

Screening studies for MRSA in milk from Swedish dairy cattle have been performed in 2001, 2002-2003, 2005, 2008-2009 and 2010-2011. During 2010-2011, 311 isolates of beta-lactamase producing *S. aureus* isolated from milk samples were investigated for methicillin resistance. In none of these studies was MRSA originally detected. However, with the knowledge of the novel *mecA* gene available, isolates with increased MIC values for oxacillin were examined with a new confirmatory method during the autumn of 2011. This led to the identification of the four MRSA isolates with $mecA_{LGA251}$ originating from three milk samples taken in 2010 and one in 2011. The isolates belonged to *spa*-type t524, ST130 and *spa*-type t9111, ST425 and were PVL-negative.

Pigs

Screening studies for MRSA in pigs have been performed four times in Sweden. During 2006-2007, fattening pigs were screened by culture of nasal swabs. None of the samples were positive. In 2008, a baseline study was performed in the European Union. Holdings with breeding pigs were screened for MRSA by culture of dust using harmonized methodology. Overall, MRSA was confirmed in 27% of the holdings in the EU, but from none of the 208 Swedish holdings sampled.

MRSA was isolated from pigs in Sweden for the first time in the summer of 2010, when fattening pigs were sampled by nasal swabs at slaughter. One out of 191 samples was positive in this screening study. The isolate belonged to *spa*-type t011 and CC398 and was PVL-negative.

In 2011, 53 nucleus and multiplying herds, which constitutes the top of the Swedish breeding pyramid, were sampled. Weaned pigs 5-12 weeks old from each herd (6 pigs per pen from 15 pens) were sampled by rubbing the skin behind one ear with a sterile compress. MRSA was not detected in any of the samples. The results from the screening studies indicate that Sweden has a favourable situation concerning MRSA in the pig population.

Public health aspects

Zoonotic transmission of MRSA occurs by direct or indirect contacts, making farmers, animal owners, veterinarians and other persons in close contact with animals the population at risk. Reported cases of MRSA in animals are still few in Sweden but the situation may easily change. Sweden is still a country with a comparatively low prevalence of human MRSA infection (SWEDRES 2011) and therefore measures should be taken to prevent a situation where animals constitute a reservoir for MRSA spreading to humans and into human healthcare.

MRSA in food-producing animals is reported globally, mostly in pigs but the prevalence is high also among veal calves and broilers and MRSA also occurs among dairy cows. The livestock-associated MRSA CC398 dominates and can be a major contributor to the overall human MRSA burden in countries with a low prevalence of human MRSA infections but is of less significance in countries where human infections are more common (EFSA, 2009).

In Sweden, PVL-negative MRSA of *spa*-types correlating to CC398 (i.e. t011, t108, t034 and t571) was documented in 31 humans in 2006-2011, of which 9 cases were from 2011 (SWEDRES 2011). In total, ten of the isolates were of *spa*-type t011 which is the dominating type among MRSA from pigs in Europe but also the most common *spa*-type among isolates from Swedish horses. MRSA with $mecA_{LGA251}$ from humans and dairy cows was reported internationally in 2011. This variant of MRSA was detected in 15 human cases in 2011 and in milk samples from four dairy cows. Three of the cows were sampled in 2010 and one cow in 2011. *Spa*-type t9111 was found in two of the human cases and in one of the samples from cows.

MRSA isolated from dogs and cats often belong to the same *spa*-types as in humans, supporting the view that humans often are a source of MRSA in small companion animals (EFSA 2009, CVMP, 2009). Most *spa*-types found in Swedish dogs and cats are common among MRSA from humans in Sweden. *Spa*-type t032 is by far the most common type among Swedish dogs and cats and it was present among the ten most common *spa*-types in humans 2007-2010 (SWEDRES 2011). *Spa*-types t032 and t002 were the most common types among human isolates of MRSA in 2007 and 2008, respectively.

The spread of MRSA among animals and between animals and man could be prevented by improved biosecurity and infection control. Basic hygiene measures such as hand washing and disinfection is of key importance. Continuous communication of relevant information and recommendations on practical measures are important strategies against MRSA.

TABLE MRSA. MICs of methicillin resistant *Staphylococcus aureus* from Swedish animals up to and including 2011. All isolates were positive for the *mecA* or *mecA*$_{LGA251}$ and *nuc* genes by molecular methods. Shaded areas indicate MIC above EUCAST cut-off values for the wild-type population.

Animal species	Year	Clinical background	Antimicrobial													Spa-type
			Ox[a]	Fox	Pc	Ct	Cl	Em	Tc	Fu	Gm	Km	Ci	Tp	Cm	
Dog	2006	post-op wound	>16	>16	>4	8	≤0.25	0.5	≤0.5	0.5	≤0.5	2	>4	1	8	t032
Dog	2006	post-op wound	>16	>16	>4	8	≤0.25	0.5	≤0.5	0.5	≤0.5	2	>4	1	8	t032
Dog	2006	post-op wound	>16	8	>4	>8	≤0.25	0.5	≤0.5	0.25	1	4	>4	2	8	t032
Dog	2007	post-op wound	>16	>16	>4	>8	≤0.25	0.5	≤0.5	0.5	≤0.5	4	>4	2	8	t032
Dog	2007	abscess	>16	>16	>4	>8	≤0.25	0.5	≤0.5	0.5	≤0.5	2	>4	1	8	t032
Dog	2007	post-op wound	>16	>16	>4	>8	0.5	0.5	2	-	1	2	>4	2	4	t032
Dog	2007	post-op wound	>16	16	>4	8	≤0.25	0.5	≤0.5	0.25	≤0.5	2	>4	1	8	t032
Dog	2007	unknown	>16	16	>4	>8	≤0.25	0.5	≤0.5	0.25	≤0.5	4	>4	2	8	t032
Dog	2008	wound	>16	>16	>4	>8	≤0.25	1	≤0.5	0.25	1	2	>4	2	8	t032
Dog	2008	unknown	>16	>16	>4	>8	≤0.25	≤0.25	≤0.5	0.5	1	2	>4	1	8	t032
Dog	2008	unknown	>16	>16	>4	>8	≤0.25	1	≤0.5	0.25	1	2	>4	2	8	t032
Dog	2008	unknown	>16	>16	>4	>8	0.5	>32	≤0.5	0.5	32	>32	>4	>32	16	t127
Dog	2009	post-op wound	8	>16	>4	>8	≤0.25	0.5	≤0.5	0.25	≤0.5	2	>4	2	8	t032
Dog	2009	wound	>16	>16	>4	>8	0.5	1	1	0.5	1	4	>4	4	16	t032
Dog	2010	wound	>16	>16	>4	>8	>32	>32	≤0.5	0.5	1	>32	>4	2	16	t002
Dog	2010	ear	8		>4	>8	≤0.25	0.5	≤0.5	0.5	≤0.5	2	>4	1	8	t032
Dog	2010	unknown	>16	16	>4	8	≤0.25	>32	≤0.5	0.5	≤0.5	2	>4	8	4	t020
Dog	2010	skin	16	16	>4	1	≤0.25	≤0.25	≤0.5	8	1	2	0.5	2	8	t002
Cat	2009	urine	>16	>16	>4	>8	≤0.25	0.5	≤0.5	0.25	≤0.5	0.5	>4	4	4	t032
Cat	2009	unknown	>16	>16	>4	>8	≤0.25	0.5	≤0.5	0.5	1	1	>4	2	8	t032
Cat	2010	ear	>16		>4	>8	≤0.25	0.5	≤0.5	1	≤0.5	2	>4	1	8	t032
Cat	2010	nose	>16	16	>4	>8	≤0.25	≤0.25	≤0.5	0.25	≤0.5	1	>4	1	8	t032
Cat	2011	skin infection	>16	>16	>4	>8	≤0.25	≤0.25	≤0.5	0.25	≤0.5	2	>4	1	8	t022
Horse	2007	screening	>16		>4	1	≤0.25	0.5	64	0.5	>64	>32	1	>32	8	t011
Horse	2008	post-op wound	>16	>16	>4	1	≤0.25	0.5	32	0.5	64	>32	1	>32	8	t011
Horse	2008	post-op wound	>16	>16	>4	2	≤0.25	1	32	1	>64	>32	1	>32	8	t011
Horse	2008	post-op wound	16	>16	>4	2	≤0.25	1	32	0.5	>64	>32	0.5	>32	8	t011
Horse	2008	post-op wound	>16	>16	>4	2	≤0.25	0.5	32	0.25	>64	>32	0.5	>32	8	t011
Horse	2008	screening	>16	16	>4	2	≤0.25	1	32	0.5	64	>32	0.5	>32	8	t011
Horse	2008	post-op wound	>16	8	>4	2	≤0.25	1	64	1	>64	>32	1	>32	16	t011
Horse	2008	post-op wound	2	>16	4	4	≤0.25	≤0.25	32	0.12	4	32	0.25	>32	4	t011
Horse	2009	wound	16	>16	>4	>8	≤0.25	0.5	64	0.25	16	>32	0.25	>32	8	t011
Horse	2009	post-op wound	16	>16	4	1	≤0.25	0.5	32	0.25	64	>32	1	>32	8	t011
Horse	2010	post-op wound	>16	>16	>4	8	0.5	2	64	1	>64	>32	1	>32	16	t011
Horse	2010	post-op wound	>16	>16	>4	4	≤0.25	1	32	0.5	>64	>32	0.5	>32	8	t064
Horse	2010	post-op wound	>16	>16	>4	8	≤0.25	0.5	64	0.25	64	>32	0.25	>32	8	t011
Horse	2010	wound	>16	>16	>4	4	≤0.25	0.5	32	0.5	>64	>32	0.25	>32	8	t011
Horse	2010	post-op wound	>16	>16	>4	2	≤0.25	1	32	0.5	16	>32	0.25	>32	8	t064
Horse	2011	post-op wound	16	>16	>4	1	≤0.25	≤0.25	32	0.12	32	>32	0.25	>32	4	t011
Horse	2011	skin infection	>16	>16	>4	2	≤0.25	≤0.25	64	0.5	≤0.5	4	0.25	1	8	t011
Pig	2010	snout	>16	>16	>4	>8	0.5	1	64	0.5	>64	>32	0.25	>32	16	t011
Cow	2010	milk	4	16	2	1	≤0.25	≤0.25	≤0.5	0.25	≤0.5	2	0.5	2	8	t524
Cow	2010	milk	4	16	1	1	≤0.25	0.5	≤0.5	0.5	≤0.5	2	0.25	1	4	t524
Cow	2010	milk	16	>16	>4	4	≤0.25	0.5	≤0.5	0.25	≤0.5	2	0.5	2	8	t524
Cow	2011	milk	2	>16	2	2	≤0.25	0.5	≤0.5	0.12	≤0.5	4	0.25	1	8	t9111

[a] tested with 2% NaCl.

Escherichia coli with ESBL or transferrable AmpC-type resistance in meat obtained from the Swedish market

ENTEROBACTERIACEAE producing extended-spectrum betalactamases (ESBL) or transferable AmpC betalactamases (pAmpC) is a rapidly emerging public health problem. These bacteria produce enzymes that hydrolyse antibiotics belonging to the betalactam group, including third generation cephalosporins, which are important antimicrobial agents in human medicine. The presence of ESBL- and pAmpC- producing *E. coli* is increasingly reported in humans and in food-producing animals, hence, a food borne transmission may be a possible link between the two populations (EFSA, 2011).

During 2009 to 2011 a project financed by the Swedish Civil Contingencies Agency (MSB) was run in collaboration between the National Veterinary Institute (SVA), the National Food Agency (SLV) and the Swedish Institute for Communicable Disease Control (SMI). This project aimed to provide data required for identifying the extent to which food serves as a source of human exposure to ESBL and/or pAmpC-producing bacteria for use in future risk management strategies. The results have been published in a report by Egervärn et al. (2011). Below is a short summary of the results.

Methodology

The prevalence of ESBL and/or pAmpC-producing *E. coli* was investigated in 518 samples of imported meat from cattle, pigs and broilers and in 100 samples of Swedish broiler meat. The latter samples were included due to the recent report of ESBL- and pAmpC-producing *E. coli* in Swedish broilers within the Swedish monitoring programme SVARM (SVARM 2010). Samples of the imported meat were collected at retail stores and outlets from June 2009 to June 2011, while the Swedish broiler meat samples were collected at slaughter-houses during ten weeks in autumn 2010. ESBL and/or pAmpC-producing *E. coli* were isolated from meat after selective culture with cefotaxime (1 mg/L) and the isolates were characterised phenotypically and by different molecular methods in accordance with the recommendations by EFSA (EFSA, 2011). To investigate the potential link between meat-associated ESBLs and pAmpCs and those found in patients in Sweden, ESBL- and pAmpC genes identified in *E. coli* from meat were compared with gene data from clinical ESBL- and pAmpC-producing *E. coli* isolates reported within the national surveillance programme SWEDRES in 2010.

Results and comments

Depending on the country of origin for the meat products ESBL- and pAmpC-producing *E. coli* were found in 0-8% of imported beef samples, 2-13% of imported pork samples and 15-95% of broiler meat samples available on the Swedish market. The highest prevalence was in South American broiler meat (95%), followed by European broiler meat (61%) and Danish broiler meat (15%). ESBL- and pAmpC-producing *E. coli* were found in 44% of the Swedish broiler meat samples tested. Thus, ESBL- and pAmpC-producing bacteria were frequently found in broiler meat, even in countries such as Sweden and Denmark with no use of cephalosporins in broiler production. In Sweden the occurrence of resistant bacteria is suspected to be due to spread from imported breeding stock into Swedish broiler production (SVARM 2010). The most prevalent ESBL gene among human clinical *E. coli* in Sweden was $bla_{\text{CTX-M-15}}$. It was found in 1% of the bacteria isolated from meat. The overall overlap between gene variants in bacteria isolated from meat and from Swedish patients was small, indicating that meat is probably only a limited source of ESBL- and pAmpC genes in human medicine. Further studies are needed, including a more detailed comparison of ESBL- and pAmpC genes/plasmids and *E. coli* isolates from meat and patients, to assess the potential public health risk of these bacteria in food.

Indicator bacteria

IN 2011 INDICATOR bacteria from slaughter pigs and from pig meat was monitored. Isolates tested were *Escherichia coli* and enterococci randomly selected from cultures of intestinal content and meat. In addition, all samples were screened for *E. coli* resistant to third generation cephalosporins by selective culture on media supplemented with cefotaxime. For details on methodology see Appendix 3.

Escherichia coli

Pigs

Isolates of *Escherichia coli* were obtained from 167 (91%) of 184 samples cultured. The majority of isolates (72%) were susceptible to all antimicrobials tested but 46 isolates (28%) were resistant to at least one substance (Table EC I). Resistance to sulphonamides (17%) or streptomycin (16%) were the most common traits.

Twenty-two isolates (13%) were resistant to three or more antimicrobials (Table EC I). Phenotypes of these isolates are presented in Table EC III and associations between resistance traits in Table EC IV.

Of the randomly selected isolates one was resistant to cefotaxime (MIC of 2 mg/L). Transferable genes coding for extended spectrum beta-lactamases were not found when the isolate was tested by molecular methods and resistance is likely caused by mutational hyperproduction of AmpC beta-lactamases.

On screening for resistance to third generation cephalosporins, *E. coli* resistant to cefotaxime (MIC of 2-8 mg/L) were isolated from nine samples. Six isolates were of the AmpC type but transferable genes for resistance to extended spectrum beta-lactamases were not found and resistance in these isolates is likely caused by mutational hyperproduction of AmpC beta-lactamases. Three isolates however had genes coding for enzymes of the CTX-M-3, CTX-M-15 or TEM-52 groups. For more details and comments see Highlight "*Escherichia coli* with ESBL- or transferrable AmpC-type resistance in production animals".

Pig meat

Escherichia coli was isolated from 20 (20%) of 100 samples cultured. The majority (70%) of isolates was susceptible to all antimicrobials tested but six isolates (30%) were resistant to at least one substance (Table EC I and II). Resistance to ampicillin was the most common trait (30%). Two isolates (10%) were resistant to three or more antimicrobials. Both these isolates were resistant to ampicillin, streptomycin, sulphonamide and trimethoprim and one of the isolates also to kanamycin.

Two isolates were resistant to ciprofloxacin with MIC 0.12 mg/L but susceptible to nalidixic acid, MIC 4-8 mg/L. This phenotype indicates resistance of *qnr*-type. No sample yielded *E. coli* resistant to third generation cephalosporins on culture on cefotaxime supplemented media.

Comments

Levels of resistance in *E. coli* from pigs and pig meat are low in an international perspective. For some antimicrobials levels of resistance have been stable over the years studied wheras resistance to other substances appears to have increased (Fig EC I). Notably resistance to ampicillin, sulphonamide or trimethoprim in *E. coli* from pigs have gradually increased from 3-7% in year 2000 to 11-17% in 2011. A similar tendency is observed in *E. coli* from diagnostic submissions (Table Pig I, Animal Pathogens). These three antimicrobials are used for treatment of pigs and resistance is likely a consequence of this. Direct selection is however probably augmented by co-selection since the three resistance traits often are linked and frequently occur in multiresistant isolates (Table EC III). Use of one of the antimicrobials thereby imposes a selection pressure also for resistance to the others.

The potential of co-selection is illustrated by chloramphenicol resistance. Although this antimicrobial has not been used for pigs in Sweden for more than twenty five years chloramphenicol resistance is more prevalent in 2011 (4%) than it was in 2000 (<1%). Chloramphenicol resistance is only observed in combination with other traits (Table EC IV), notably sulphonamide resistance, and is likely retained by use of other antimicrobials in pigs.

ESBL resistance was verified in *E. coli* from three pigs after selective culture on cefotaxime supplemented media. Apparantly such isolates are still uncommon in pigs in Sweden but the findings indicate an impaired situation since no sample was found positive for *E. coli* with ESBL resistance in 2008. For more details and analysis see Highlight "*Escherichia coli* with ESBL or transferrable AmpC-type resistance in production animals".

Altogether, 100 samples of pig meat collected at cutting plants were cultured for *E. coli* but only 20 isolates were obtained. The isolation frequency was low also in the study of pig meat in 2008. The low prevalence of *E. coli* on pig meat indicates a low level of contamination and a good hygienic quality but from the perspective of resistance monitoring the small number of isolates studied is worrisome since conclusions on trends in resistance cannot be made.

Isolates of *E. coli* from pig meat had similar resistance phenotypes as isolates from pigs indicating contamination by intestinal content from pigs. However, two isolates had a *qnr*-phenotype which is rarely found in *E. coli* from pigs in Sweden (Thyselius et al., 2007). This could signify another source of contamination than intestinal content from pigs. Notably, *E. coli* with transferable resistance to third generation cephalosporins were not obtained from pig meat even after selective culture.

TABLE EC I. Resistance (%) and multiresistance (%) for *Escherichia coli* from slaughter pigs and pig meat, 2011. Data for other animals from previous SVARM-reports given for comparison.

Antimicrobial	Cut-off value (mg/L)	Resistance (%) (95% confidence interval inside brackets)							
		Pigs	Pig meat	Broilers	Broiler meat	Horses	Calves	Sheep	Dogs
		2011 n=167	2011 n=20	2010 n=181	2010 n=77	2010-11 n=274	2009 n=223	2006-09 n=115	2006 n=257
Ampicillin	>8	13 (8.4-19.3)	30 (11.9-54.3)	6 (3.1-10.6)	10 (4.6-19.4)	2 (0.4-3.7)	<1 (0.0-2.5)	2 (0.2-6.1)	5 (3.0-9.0)
Cefotaxime	>0.25	<1 (0.0-3.3)	0 (0.0-16.8)	1 (0.1-3.9)	0 (0.0-4.7)	0 (0.0-1.3)	0 (0.0-1.6)	0 (0.0-3.2)	<1 (0.0-2.1)
Chloramph.	>16	4 (1.7-8.4)	0 (0.0-16.8)	0 (0.0-2.0)	1 (0.0-7.0)	<1 (0.0-2.0)	0 (0.0-1.6)	0 (0.0-3.2)	<1 (0.1-2.9)
Ciprofloxacin	>0.06	2 (0.7-6.0)	10 (1.2—31.7)	13 (8.2-18.4)	6 (2.1-14.5)	<1 (0.0-2.0)	0 (0.0-1.6)	<1 (0.0-4.8)	2 (0.6-4.5)
Colistin	>2	0 (0.0-2.2)	0 (0.0-16.8)	0 (0.0-2.0)	0 (0.0-4.7)	<1 (0.1-2.6)	-	-	-
Florfenicol	>16	0 (0.0-2.2)	0 (0.0-16.8)	0 (0.0-2.0)	0 (0.0-4.7)	0 (0.0-1.3)	0 (0.0-1.6)	0 (0.0-3.2)	0 (0.0-1.4)
Gentamicin	>2	1 (0.1-4.3)	0 (0.0-16.8)	0 (0.0-2.0)	0 (0.0-4.7)	<1 (0.1-2.6)	0 (0.0-1.6)	3 (0.5-7.4)	<1 (0.0-2.1)
Kanamycin	>8	1 (0.1-4.3)	5 (0.1-24.9)	4 (1.9-8.5)	1 (0.0-7.0)	4 (2.3-7.5)	<1 (0.0-2.5)	2 (0.2-6.1)	2 (0.9-5.0)
Nalidixic acid	>16	2 (0.7-6.0)	0 (0.0-16.8)	13 (8.2-18.4)	6 (2.1-14.5)	<1 (0.0-2.0)	0 (0.0-1.6)	0 (0.0-3.2)	2 (0.6-4.5)
Streptomycin	>16	16 (10.9-22.6)	10 (1.2—31.7)	7 (3.5.11.3)	4 (0.8-11.0)	13 (9.1-17.3)	4 (2.2-8.1)	3 (0.5-7.4)	7 (4.2-10.8)
Sulphonamide	>64	17 (11.4-23.3)	10 (1.2—31.7)	7 (3.5.11.3)	17 (9.3-27.1)	15 (10.9-19.7)	2 (0.5-4.5)	7 (3.1-13.2)	13.2 (9.3-18.0)
Tetracycline	>8	8 (4.7-13.7)	0 (0.0-16.8)	8 (4.3-12.6)	8 (2.9-16.2)	2 (0.6-4.2)	2 (0.5-4.5)	<1 (0.0-4.8)	2 (0.9-5.0)
Trimethoprim	>2	11 (7.0-17.2)	10 (1.2—31.7)	3 (1.2-7.1)	1 (0.0-7.0)	16 (11.9-20.9)	<1 (0.0-2.5)	2 (0.2-6.1)	4 (1.9-7.0)
Multiresistance[a]									
Susceptible to all		72	70	72	65	81	95	88	82
Resistant to 1		9	10	19	27	4	3	9	10
Resistant to 2		5	5	2	5	3	<1	2	4
Resistant to 3		3	5	3	1	9	<1	1	2
Resistant to >3		10	10	3	1	3	<1	1	2

[a] Ciprofloxacin and nalidixic acid considered as one substance.

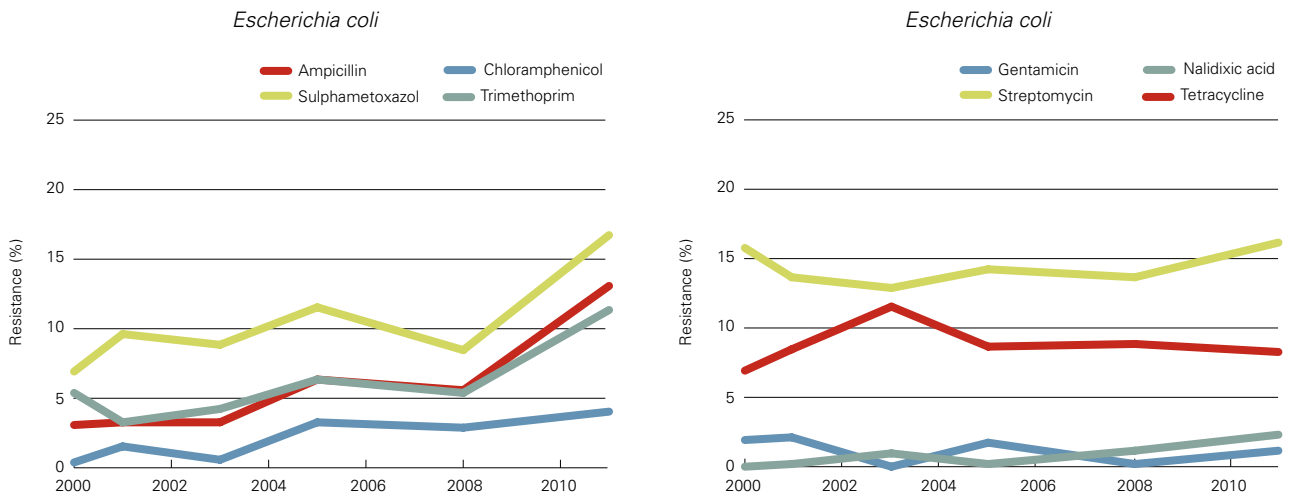


FIGURE EC I. Percent resistance in *Escherichia coli* from pigs 2000-2011.

TABLE EC II. Distribution of MICs and resistance (%) in *Escherichia coli* from intestinal content from pigs (n=167) and from pig meat (n=20), 2011.

			Distribution (%) **of MICs** (mg/L)																	
Antimicrobial	**Source**	**Resistance** %	**≤0.008**	**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	Pigs	13								12.6	56.3	18.0		0.6				12.6			
	Pig meat	30								5.0	35.0	30.0		10.0	10.0			10.0			
Cefotaxime	Pigs	<1			7.2	73.7	18.0	0.6			0.6										
	Pig meat	0			10.0	70.0	20.0														
Chloramph.	Pigs	4									9.0	73.1	13.8		1.8	2.4					
	Pig meat	0									25.0	45.0	25.0	5.0							
Ciprofloxacin	Pigs	2		1.2	80.2	16.2		1.2	0.6		0.6										
	Pig meat	10		5.0	60.0	25.0	10.0														
Colistin	Pigs	0							69.5	29.9	0.6										
	Pig meat	0							45.0	55.0											
Florfenicol	Pigs	0										50.3	47.9	1.8							
	Pig meat	0										55.0	35.0	10.0							
Gentamicin	Pigs	1						7.2	75.4	15.6	0.6	1.2									
	Pig meat	0						15.0	45.0	30.0	10.0										
Kanamycin	Pigs	1											98.8		1.2						
	Pig meat	5											95.0		5.0						
Nalidixic acid	Pigs	2								0.6	37.1	58.1	1.8				1.8	0.6			
	Pig meat	0									40.0	55.0	5.0								
Streptomycin	Pigs	16									3.6	44.3	31.7	4.2	2.4	6.6	3.6	3.0	0.6		
	Pig meat	10									10.0	45.0	20.0	15.0	5.0				5.0		
Sulphonamide	Pigs	17											15.0	40.7	24.0	3.6				0.6	16.2
	Pig meat	10											15.0	60.0	15.0						10.0
Tetracycline	Pigs	8								34.1	57.5				4.2	2.4	1.2	0.6			
	Pig meat	0								20.0	75.0	5.0									
Trimethoprim	Pigs	11					3.6	26.3	55.1	3.0	0.6			0.6	10.8						
	Pig meat	10						50.0	30.0	10.0					10.0						
			≤0.008	**0.016**	**0.03**	**0.06**	**0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**256**	**512**	**1024**	**>1024**

TABLE EC III. Phenotypes of multiresistant *Escherichia coli* from pigs (intestinal content), 2000-2011. "R" in shaded fields indicates resistance. Data from previous SVARM reports are included.

2000 (n=260)	2001 (n=308)	2003 (n=303)	2005 (n=390)	2008 (n=349)	2011 (n=167)	Sum (n=1777)	Resistance phenotypes									
							Su	Sm	Am	Tc	Tm	Cm	Km	Gm	Nal	Ctx
			1	1		2	R	R	R	R	R	R				
					1	1	R	R	R	R					R	R
					1	1	R	R	R	R	R		R		R	
1		1		1		3	R	R	R	R						
2	1	1	4	2	2	12	R	R	R	R	R					
	2		1			3	R	R	R			R				
	2			2	1	5	R	R	R		R	R				
	4		5	2		11	R	R	R							
				1		1	R	R	R				R			
3	1	2	3	5	6	20	R	R	R		R					
					1	1	R	R	R		R		R			
				1		1	R	R	R		R	R				
					1	1	R	R		R	R				R	
2	3	5	3			13	R	R		R						
		2	2	4		8	R	R		R	R					
1	1		3	1		6	R	R				R				
3	2	2	2		3	12	R	R			R					
				1	1	2	R		R	R		R				
			2			2	R		R	R	R	R				
				2	2	4	R		R			R				
		1	4	2	3	10	R		R		R	R				
			1			1	R				R	R				
				2		2	R				R				R	
		1				1		R	R						R	
		1				1		R		R	R					
				1		1		R					R	R		
		1				1			R	R					R	
12 5%	**16** 5%	**17** 6%	**31** 9%	**28** 8%	**22** 13%	**126** 7%	**Number of isolates** (percent of all isolates)									

TABLE EC IV. Association between resistance traits in *Escherichia coli* from intestinal content of pigs 2000-2011. For each antimicrobial the first row gives prevalence of resistance to other antimicrobials in susceptible isolates (S) and the second row prevalence in resistant isolates (R). All antimicrobials were not tested each year and therefore all combinations of resistance traits can not be calculated.

Single substance susceptibility		**Cross resistance** (%)									
		n	**Am**	**Cm**	**Ff**	**Gm**	**Nal**	**Sm**	**Su**	**Tc**	**Tm**
Ampicillin	S	1682	0.0	0.6	0.1	1.3	0.5	11.4	5.9	7.8	2.6
	R	95	100	29.5	0.0	0.0	4.2	64.2	83.2	28.4	59.0
Apramycin	S	788	3.1	0.9	0.0	1.5	0.3	14.1	8.9	9.4	4.3
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Cefotaxime	S	905	7.3	3.3	0.1	1.1	0.9	14.4	11.3	8.6	7.0
	R	1	100	0.0	0.0	0.0	100	100	100	100	0.0
Ceftiofur	S	1261	4.2	1.7	0.0	1.5	0.4	14.1	9.5	9.0	4.9
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Chloramp.	S	1739	3.9	0.0	0.1	1.3	0.8	13.5	8.1	8.7	4.5
	R	38	73.7	100	0.0	0.0	0.0	47.4	97.4	15.8	55.3
Ciprofloxacin	S	508	7.9	3.4	0.2	0.6	0.0	14.2	10.4	8.1	6.7
	R	8	25.0	0.0	0.0	0.0	100	37.5	62.5	50.0	50.0
Colistin	S	167	13.2	4.2	0.0	1.2	2.4	16.2	16.8	8.4	11.4
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Enrofloxacin	S	1256	4.1	1.7	0.0	1.5	0.0	14.1	9.6	8.9	4.9
	R	5	40.0	0.0	0.0	0.0	100	20.0	0.0	20.0	20.0
Florfenicol	S	1776	5.4	2.1	0.0	1.2	0.7	14.3	10.0	8.9	5.6
	R	1	0.0	0.0	100	0.0	0.0	0.0	0.0	0.0	0.0
Gentamicin	S	1755	5.4	2.2	0.1	0.0	0.7	14.1	10.1	9.0	5.7
	R	22	0.0	0.0	0.0	100	0.0	27.3	0.0	0.0	0.0
Kanamycin	S	510	7.7	3.3	0.2	0.4	1.4	13.9	10.8	8.6	7.1
	R	6	50.0	0.0	0.0	16.7	16.7	66.7	50.0	16.7	33.3
Nalidixic acid	S	1764	5.2	2.2	0.1	1.3	0.0	14.1	9.8	8.7	5.4
	R	13	30.8	0.0	0.0	0.0	100	30.8	38.5	38.5	38.5
Neomycin	S	1261	4.2	1.7	0.0	1.5	0.4	14.1	9.5	9.0	4.9
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Streptomycin	S	1524	2.2	1.3	0.1	1.1	0.6	0.0	3.3	5.1	2.0
	R	253	24.1	7.1	0.0	2.4	1.6	100	50.6	31.6	27.3
Sulphamethox.	S	1599	1.0	0.1	0.1	1.4	0.5	7.8	0.0	6.8	1.3
	R	178	44.4	20.8	0.0	0.0	2.8	71.9	100	27.5	44.4
Tetracycline	S	1619	4.2	2.0	0.1	1.4	0.5	10.7	8.0	0.0	4.5
	R	158	17.1	3.8	0.0	0.0	3.2	50.6	31.0	100	17.7
Trimethoprim	S	1677	2.3	1.0	0.1	1.3	0.5	11.0	5.9	7.8	0.0
	R	100	56.0	21.0	0.0	0.0	5.0	69.0	79.0	28.0	100

Escherichia coli with ESBL or transferrable AmpC-type resistance in production animals

ENTEROBACTERIACEAE producing extended-spectrum beta-lactamases (ESBL) or transferable AmpC beta lactamases (pAmpC) is a rapidly emerging public health problem (EFSA 2011). By producing hydrolyzing enzymes, these bacteria are resistant to antibiotics belonging to the betalactam group, including third-generation cephalosporins, which are important therapeutics in human medicine. The presence of ESBL- and pAmpC-producing *Escherichia coli* is increasingly reported in humans and in food-producing animals.

In most monitoring programmes in the EU, including the Swedish programme SVARM, data on prevalence of resistance in *E. coli*, are based on data from randomly selected colonies from non-selective cultures. In addition, in SVARM, healthy food animals and food are screened for ESBL- and pAmpC-producing *E. coli* by culture on media supplemented with cefotaxime. The results of all the screenings are summarized in Table I.

Data from 2011

Methodology

During 2011, 184 samples of intestinal content from slaughter pigs and 100 samples of pig meat were screened for *Escherichia coli* resistant to third generation cephalosporins. In addition, 100 samples of caecal content from broilers were screened.
The screening was performed by culturing the samples on MacConkey agar with 1 mg/L cefotaxime. Suspected ESBL- and/or pAmpC-producing *E. coli* were selected for testing of susceptibility to different antimicrobials by microdilution and tested for genotype by PCR. The specific gene variants for all the isolates from pigs and a selection of the isolates from broilers were determined by sequencing. Detailed description of the sampling strategies and laboratory methods used are given in Appendix 3, SVARM 2011.

Results

Pigs and pig meat

Escherichia coli with transferable cefotaxime resistance were isolated from 3 samples (1.6%) of intestinal content from pigs but not from any of the samples from pig meat. The genes confirmed in the three isolates were $bla_{CTX\text{-}M\text{-}3}$, $bla_{CTX\text{-}M\text{-}15}$ and $bla_{TEM\text{-}52}$, respectively (Table II). The isolates all had different antibiograms and one of them was only resistant to beta-lactams (Table II). In addition, in six of the samples of intestinal content from pigs, *E. coli* with AmpC type resistance was found but transferable genes were not detected. Resistance in these isolates is likely caused by mutational hyperproduction of AmpC beta-lactamases.

Broilers

From 54 samples (54%) of intestinal content from broilers, *E. coli* with transferable cefotaxime resistance were isolated. Of these, 3 were of the CTX-M-1 group and 51 of the CIT group. The isolates could be grouped in 14 different phenotypes based on antibiogram and genotype (Table III). Sequencing to identify the resistance gene in a selection of the isolates confirmed presence of the $bla_{CTX\text{-}M\text{-}1}$ or the $bla_{CMY\text{-}2}$ gene, respectively, depending on the group (Table III). In addition, in 3 of the samples of intestinal content from broilers, *E. coli* with AmpC type resistance was found but transferable genes were not detected. Resistance in these isolates is likely caused by mutational hyperproduction of AmpC beta-lactamases.

Comments

During 2011, ESBL-producing *E. coli* was isolated for the first time from pigs in Sweden. Among broilers, the prevalence of ESBL- and pAmpC- producing *E. coli* was even higher in 2011 than in 2010. However, in both pigs and broilers the proportion of *E. coli* in the intestinal flora that is ESBL- or pAmpC-producing seems to be low since such bacteria is only rarely detected when samples are cultured on media without cefotaxime.

The situation in Sweden regarding ESBL- and pAmpC-producing *E. coli* in farm animals is favorable compared to many other countries. This is probably a reflection of the continuous work with disease prevention and prudent antimicrobial use in Sweden. That a large proportion of broilers in Sweden are carrying ESBL- or pAmpC-producing *E. coli* is probably due to the continuous introduction of such bacteria with animals imported for breeding purpose (SVARM 2010). The imported day-old chickens are carrying ESBL- or pAmpC-producing *E. coli* already when they arrive to Sweden and these bacteria are subsequently spread down in the breeding pyramid.

Even if the situation in Swedish broiler production is worrisome, the overall situation regarding ESBL- and pAmpC-producing *E. coli* in production animals in Sweden is favourable. However, this could change if the production structures and/or the management routines are altered.

Public health aspects

The presence of ESBL- and pAmpC-producing *E. coli* in production animals in Sweden makes them a potential reservoir of both resistant bacteria and resistance genes. The importance of this reservoir is difficult to determine but likely lessened by the fact that only a small proportion of *E. coli* in colonized animals are ESBL- or pAmpC-producers. Furthermore, the only group of farm animals in Sweden where a large proportion of the animals are colonized are broilers. The most prevalent gene in isolates from broilers is $bla_{CMY\text{-}2}$ and although cases of human infections with *E. coli* carrying $bla_{CMY\text{-}2}$ have been reported it is not among the most prevalent genes (SWEDRES 2011). See also Highlight "*Escherichia coli* with ESBL or pAmpC in meat obtained from the Swedish market".

TABLE I. Number of samples with growth of *Escherichia coli* with transferable cefotaxime resistance on MacConkey agar with 1 mg/L cefotaxime and number of samples taken.

Year	Broilers	Broiler meat	Pigs	Pig meat	Fattened calves
2008			0:452	0:50	
2009					0:256
2010	68:200 (34%)	44:100 (44%)[a]			
2011	54:100 (54%)		3:184 (1.6%)	0:100	

[a] Not performed within SVARM. For further information see Highlight '*Escherichia coli* with ESBL or pAmpC in meat obtained from the Swedish market' or Egervärn et al. (2011).

TABLE II. Genotypes, resistance phenotypes and MICs of 3 isolates of *Escherichia coli* from pigs. White areas indicate MICs above EUCAST ECOFFs.

Genotype	Ctx	Am	Ci	Nal	Gm	Sm	Tc	Ff	Col	Su	Tm	Cm	Km
CTX-M-15	>2	>128	>1	>128	1	64	2	8	≤0.5	>1024	>16	32	>16
CTX-M-3	>2	>128	0.5	>128	1	256	2	<4	≤0.5	>1024	>16	4	≤8
TEM-52	>2	>128	0.03	2	1	8	2	≤4	≤0.5	32	0.5	4	≤8

TABLE III. Genotypes, resistance phenotypes and MICs of 54 isolates of *Escherichia coli* from broilers. White areas indicate MICs above EUCAST ECOFFs.

Genotype	n	Ctx	Am	Ci	Nal	Gm	Sm	Tc	Col	Ff	Cm	Km	Su	Tm
CMY-2	27	2->2	128->128	0.016-0.06	≤1-4	0.5-2	4-16	≤1-2	≤0.5-2	≤4-8	≤2-8	≤8	16-32	0.25-0.5
CMY-2	12	>2	64->128	0.06	2-4	0.5-2	4-8	≤1-2	≤0.5-1	≤4-8	4-8	≤8	>1024	0.25-0.5
CMY-2	2	>2	128	0.06	4	0.5-1	64	2	≤0.5	8	4-8	≤8	>1024	0.25
CMY-2	2	>2	64	0.12	64	0.5-1	4-8	≤1-2	≤0.5	≤4	4	≤8	16	≤0.12
CMY-2	3	2->2	128->128	0.12	2-4	1-2	8-16	2	≤0.5-1	≤4-8	4-8	≤8	32	0.25-0.5
CMY-2	1	>2	>128	0.06	4	1	8	64	1	8	8	≤8	16	0.5
CMY-2	1	>2	128	0.12	4	0.5	4	2	≤0.5	8	8	≤8	>1024	0.25
CMY-2	1	>2	128	0.06	2	1	64	64	≤0.5	≤4	4	>16	>1024	0.25
CMY-2	1	>2	128	0.03	4	2	64	2	≤0.5	8	8	16	>1024	0.5
CTX-M-1	1	>2	>128	0.03	2	1	8	64	≤0.5	8	4	16	>1024	4
CTX-M-1	1	>2	>128	0.03	4	4	8	64	≤0.5	8	8	≤8	>1024	8
CTX-M-1	1	>2	>128	0.06	2	0.5	8	64	≤0.5	8	4	≤8	>1024	4

Enterococcus

Pigs

A total of 22 isolates of *Enterococcus faecalis* and 22 isolates of *E. faecium* were obtained from 198 samples cultured. In *E. faecalis* tetracycline resistance was the most frequent trait but resistance to erythromycin was also common (Table ENT I). These traits were among the most common also in *E. faecium* but resistance to streptomycin, kanamycin or bacitracin was equally frequent in this species (Table ENT II).

Resistance to tetracycline and erythromycin are often associated in isolates of *E. faecium* and *E. faecalis* (Table IV) and often occur in multiresistant isolates (Table ENT III). Multiresistance is however rare in both species (Table ENT I & II).

Pig meat

From 100 samples of pig meat, 29 isolates of *E. faecalis* and 1 isolate of *E. faecium* were obtained. Most isolates of *E. faecalis* were susceptible to all antimicrobials tested but two isolates (7%) were resistant to tetracycline and one isolate to streptomycin (3%) (Table ENT I). The isolate of *E. faecium* was resistant to virginiamycin (Table ENT II).

Comments

In isolates from pigs, levels of resistance are low in an international perspective and mostly of the same magnitude as in previous years (Fig ENT I). The data available do not indicate any untoward trends in resistance but valid conclusions are hindered by the limited number of isolates available for testing in 2011.

In both species of enterococci, resistance to tetracycline or erythromycin (macrolide) are the most prevalent traits. This is consistent with use of tetracyclines (doxycycline) and macrolides (tylosin) for group treatment of enteritis and respiratory disease in pigs. Resistance to tetracycline and erythromycin are often linked (Table ENT II &IV) and it is therefore likely that selection for these traits is augmented by co-selection.

Resistance to ampicillin, linezolid and vancomycin in enterococci from pigs was not observed in 2011 and resistance to streptogramins (virginiamycin) was rare (Table ENT I & II). This is in agreement with previous findings in SVARM. Notably resistance to ampicillin has been documented in only four isolates of enterococci from pigs in Sweden since 2000 and resistance to virginiamycin only in a limited number of *E. faecium*. Moreover, vancomycin resistant enterococci carrying the *vanA* or *vanB* genes have never been documented from pigs, neither in randomly selected isolates nor by culture in previous years of almost 2000 samples on media supplemented with vancomycin. These findings show that enterococci in pigs in Sweden are not important reservoirs of resistance to antimicrobials used for treatment of enterococcal infections in humans.

Resistance among *E. faecalis* from pig meat was much less prevalent than among isolates from intestinal content of pigs (Table ENT I). Notably the common occurrence of resistance to erythromycin, tetracycline or streptomycin in isolates from intestinal content was not reflected in isolates from pig meat. These findings are in agreement with the results of the monitoring in SVARM 2008 and indicate that *E. faecalis* contaminating meat mostly emanate from other sources than intestinal content from the slaughtered pigs.

Only one isolate of *E. faecium* was obtained from the 100 samples of pig meat. Likewise, in 2008 only a small number of isolates of *E. faecium* was obtained. Contamination of pig meat with this species is apparently less common than contamination with *E. faecalis*.

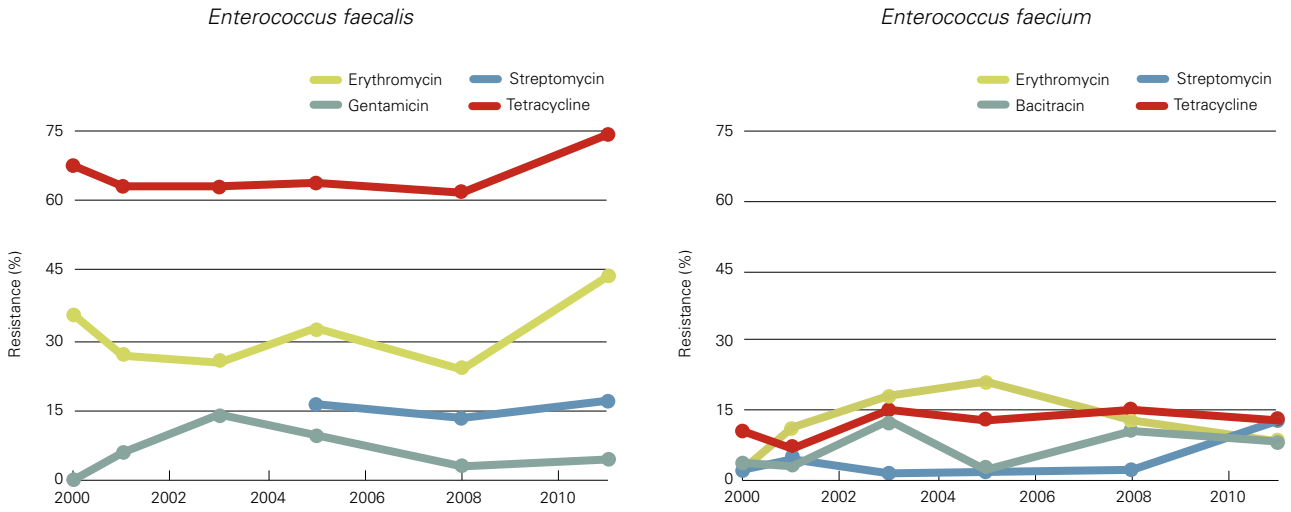


FIGURE ENT I. Percent resistance in *Enterococcus faecalis* and *Enterococcus faecium* from pigs 2000-2011.

TABLE ENT I. Resistance and multiresistance of *Enterococcus faecalis* from pigs and pig meat 2011. Data for other animals from previous SVARM-reports given for comparison.

Antimicrobial	Cut-off value (mg/L)	Resistance (%) (95% confidence interval in brackets)							
		Pigs	Pig meat	Broilers	Broiler meat	Horses	Calves	Sheep	Dogs
		2011 n=22	2011 n=29	2010 n=35	2010 n=81	2010-11 n=34	2009 n=10	2006-09 n=24	2006 n=135
Ampicillin	>4	0 (0.0-14.8)	0 (0.0-11.9)	0 (0.0-10.0)	0 (0.0-4.5)	0 (0.0-10.3)	0 (0.0-30.9)	0 (0.0-14.2)	<1 (0.0-4.1)
Bacitracin	>32	0 (0.0-14.8)	0 (0.0-11.9)	14 (4.8-30.3)	15 (7.9-24.4)	0 (0.0-10.3)	0 (0.0-30.9)	0 (0.0-14.2)	1 (0.2-5.2)
Chloramph.	>32	0 (0.0-14.8)	0 (0.0-11.9)	0 (0.0-10.0)	0 (0.0-4.5)	18 (6.8-34.5)	0 (0.0-30.9)	0 (0.0-14.2)	7 (3.1-12.3)
Erythromycin	>4	43 (23.2-65.5)	0 (8.4-58.1)	31 (16.9-49.3)	23 (14.8-34.2)	21 (8.7-37.9)	0 (0.0-30.9)	0 (0.0-14.2)	14 (8.7-21.1)
Gentamicin	>32	4 (0.1-21.9)	0 (0.0-11.9)	0 (0.0-10.0)	0 (0.0-4.5)	21 (8.7-37.9)	0 (0.0-30.9)	0 (0.0-14.2)	<1 (0.0-4.1)
Kanamycin	>1024	4 (0.1-21.9)	0 (0.0-11.9)	3 (0.1-14.9)	0 (0.0-4.5)	21 (8.7-37.9)	0 (0.0-30.9)	0 (0.0-14.2)	4 (1.6-9.4)
Linezolid	>4	0 (0.0-14.8)	0 (0.0-11.9)	0 (0.0-10.0)	0 (0.0-4.5)	0 (0.0-10.3)	0 (0.0-30.9)	0 (0.0-14.2)	0 (0.0-2.7)
Narasin	>2	0 (0.0-14.8)	0 (0.0-11.9)	37 (21.5-55.1)	19 (10.8-28.7)	0 (0.0-10.3)	0 (0.0-30.9)	0 (0.0-14.2)	1 (0.2-5.2)
Streptomycin	>512	17 (5.0-38.8)	3 (0.1-17.8)	0 (0.0-10.0)	4 (0.8-10.4)	9 (1.9-23.7)	0 (0.0-30.9)	4 (0.1-21.1)	9 (4.7-15.0)
Tetracycline	>4	74 (51.6-89.8)	7 (0.8-22.8)	31 (16.9-49.3)	37 (26.6-48.5)	44 (27.2-62.1)	30 (6.7-65.2)	8 (1.0-27.0)	32 (24.1-40.4)
Vancomycin	>4	0 (0.0-14.8)	0 (0.0-11.9)	0 (0.0-10.0)	0 (0.0-4.5)	0 (0.0-10.3)	0 (0.0-30.9)	0 (0.0-14.2)	0 (0.0-2.7)
Virginiamycin	>32	0 (0.0-14.8)	0 (0.0-11.9	0 (0.0-10.0)	0 (0.0-4.5)	0 (0.0-10.3)	0 (0.0-30.9)	0 (0.0-14.2)	0 (0.0-2.7)
Multiresistance (%)									
Susceptible to all above		17	90	31	30	56	70	92	25
Resistant to 1		35	10	34	43	24	30	4	38
Resistant to 2		43		23	27			4	27
Resistant to 3				9					2
Resistant to >3		4		3		21			7

TABLE ENT II. Resistance and multiresistance of *Enterococcus faecium* from pigs and pig meat 2011. Data for other animals from previous SVARM-reports given for comparison.

Antimicrobial	Cut-off value (mg/L)	Resistance (%) (95% confidence interval in brackets)							
		Pigs	Pig meat	Broilers	Broiler meat	Horses	Calves	Sheep	Dogs
		2011 n=22	2011 n=1	2010 n=136	2010 n=17	2010-11 n=27	2009 n=24	2006-09 n=15	2006 n=29
Ampicillin	>4	0 (0.0-14.8)	0 -	2 (0.5-6.3)	0 (0.0-19.5)	15 (4.2-33.7)	0 (0.0-14.2)	0 (0.0-21.8)	0 (0.0-11.9)
Bacitracin	>32	9 (1.1-28.0)	0 -	15 (9.8-22.6)	18 (3.8-43.4)	0 (0-12.8)	4 (0.1-21.1)	0 (0.0-21.8)	3 (0.1.17.8)
Chloramph.	>32	0 (0.0-14.8)	0 -	0 (0.0-2.7)	0 (0.0-19.5)	0 (0-12.8)	0 (0.0-14.2)	0 (0.0-21.8)	0 (0.0-11.9)
Erythromycin	>4	9 (1.1-28.0)	0 -	13 (8.0-20.1)	6 (0.1-28.7)	0 (0-12.8)	4 (0.1-21.1)	0 (0.0-21.8)	28 (12.7-47.2)
Gentamicin	>32	0 (0.0-14.8)	0 -	0 (0.0-2.7)	0 (0.0-19.5)	0 (0-12.8)	0 (0.0-14.2)	0 (0.0-21.8)	0 (0.0-11.9)
Kanamycin	>1024	9 (1.1-28.0)	0 -	0 (0.0-2.7)	0 (0.0-19.5)	0 (0-12.8)	0 (0.0-14.2)	0 (0.0-21.8)	0 (0.0-11.9)
Linezolid	>4	0 (0.0-14.8)	0 -	0 (0.0-2.7)	0 (0.0-19.5)	0 (0-12.8)	0 (0.0-14.2)	0 (0.0-21.8)	0 (0.0-11.9)
Narasin	>4	0 (0.0-14.8)	0 -	49 (39.9-57.2)	41 (18.4-67.1)	0 (0-12.8)	0 (0.0-14.2)	0 (0.0-21.8)	7 (0.8-22.8)
Streptomycin	>128	13 (2.8-33.6)	0 -	0 (0.0-2.7)	0 (0.0-19.5)	7 (0.9-24.3)	0 (0.0-14.2)	7 (0.2-32.0)	0 (0.0-11.9)
Tetracycline	>4	13 (2.8-33.6)	0 -	12 (7.5-19.3)	0 (0.0-19.5)	4 (0.1-19.0)	0 (0.0-14.2)	7 (0.2-32.0)	17 (5.8-35.8)
Vancomycin	>4	0 (0.0-14.8)	0 -	0 (0.0-2.7)	0 (0.0-19.5)	0 (0-12.8)	0 (0.0-14.2)	0 (0.0-21.8)	0 (0.0-11.9)
Virginiamycin	>4	4 (0.1-21.9)	100 -	5 (2.1-10.3)	6 (0.1-28.7)	4 (0.1-19.0)	0 (0.0-14.2)	0 (0.0-21.8)	0 (0.0-11.9)
Multiresistance (%)									
Susceptible to all above		74		35	47	74	92	87	62
Resistant to 1		13	100	45	35	22	8	13	30
Resistant to 2		4		21	18	4			6
Resistant to 3				2					
Resistant to >3		9		1					2

TABLE ENT III. Phenotypes of multiresistant *Enterococcus faecalis* and *Enterococcus faecium* from pigs (intestinal content), 2000-2011. "R" in shaded fields indicates resistance. Data from previous SVARM-reports are included.

E. faecalis

Year		Resistance pattern							
2000-08 n=318	2011 n=22	Tc	Em	Gm	Am	Sm	Cm	Km	Na
1		R	R	R	R				
1		R	R	R					R
8		R	R	R					
1		R	R	R		R	R	R	
1	1	R	R	R		R		R	
2		R	R						R
2		R	R			R			
2		R	R			R	R		
1		R			R				R
19 (5%)	**1** (5%)	**Number of isolates** (percent of all isolates)							

E. faecium

Year		Resistance pattern							
2000-08 n=311	2011 n=22	Tc	Em	Vi	Sm	Am	Cm	Ba	Gm
1		R	R	R			R		
1		R	R	R	R				
1		R	R	R					
1		R	R		R	R			
	2	R	R		R				
4		R	R					R	
1			R	R	R				
1				R	R				R
10 (3%)	**2** (9%)	**Number of isolates** (percent of all isolates)							

TABLE ENT IV. Association between resistance traits in *Enterococcus faecalis* and in *Enterococcus faecium* from pigs (intestinal content) 2000-11. For each antimicrobial the first row gives prevalence of resistance to other antimicrobials in susceptible isolates (S) and the second row prevalence in resistant isolates (R). All antimicrobials were not tested each year and all combinations of resistance traits can therefore not be calculated.

E. faecalis

Single substance susceptibility		n	Cross resistance (%)								
			Am	Ba	Em	Gm	Na	Sm	Tc	Va	Vi
Ampicillin	S	339	0.0	0.3	29.2	6.2	0.9	19.8	64.3	0.3	0.0
	R	2	100	0.0	50.0	50.0	50.0	50.0	100	0.0	0.0
Avilamycin	S	244	0.8	0.0	29.1	7.4	1.6	22.1	63.9	0.4	0.0
	R	6	0.0	16.7	50.0	16.7	0.0	16.7	83.3	0.0	0.0
Bacitracin	S	340	0.6	0.0	29.1	6.5	1.2	20.0	64.7	0.3	0.0
	R	1	0.0	100	100	0.0	0.0	0.0	0.0	0.0	0.0
Chloramph.	S	221	0.0	0.5	25.3	5.4	0.5	16.3	62.0	0.5	0.0
	R	12	0.0	0.0	83.3	58.3	0.0	58.3	100	0.0	0.0
Erythromycin	S	241	0.4	0.0	0.0	2.1	0.4	16.6	55.2	0.4	0.0
	R	100	1.0	1.0	100	17.0	3.0	28.0	87.0	0.0	0.0
Flavomycin	S	206	0.5	0.0	30.1	7.8	1.5	22.8	67.5	0.5	0.0
	R	9	11.1	0.0	11.1	0.0	11.1	0.0	33.3	0.0	0.0
Gentamicin	S	319	0.3	0.3	26.0	0.0	0.9	16.3	62.7	0.3	0.0
	R	22	4.5	0.0	77.3	100	4.5	72.7	90.9	0.0	0.0
Kanamycin	S	88	0.0	0.0	26.1	0.0	0.0	11.4	63.6	0.0	0.0
	R	3	0.0	0.0	100	100	0.0	100	100	0.0	0.0
Linezolid	S	91	0.0	0.0	28.6	3.3	0.0	14.3	64.8	0.0	0.0
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Narasin	S	337	0.3	0.3	28.8	6.2	0.0	19.6	64.1	0.3	0.0
	R	4	25.0	0.0	75.0	25.0	100	50.0	100	0.0	0.0
Streptomycin	S	273	0.4	0.4	26.4	2.2	0.7	0.0	66.7	0.4	0.0
	R	68	1.5	0.0	41.2	23.5	2.9	100	55.9	0.0	0.0
Tetracycline	S	121	0.0	0.8	10.7	1.7	0.0	24.8	0.0	0.8	0.0
	R	220	0.9	0.0	39.5	9.1	1.8	17.3	100	0.0	0.0
Vancomycin	S	340	0.6	0.3	29.4	6.5	1.2	20.0	64.7	0.0	0.0
	R	1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	100	0.0
Virginiamycin	S	341	0.6	0.3	29.3	6.5	1.2	19.9	64.5	0.3	0.0
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

E. faecium

	n	Cross resistance (%)								
		Am	Ba	Em	Gm	Na	Sm	Tc	Va	Vi
S	332	0.0	6.3	12.7	0.6	0.3	3.0	11.1	0.0	9.9
R	2	100	0.0	50.0	0.0	0.0	50.0	50.0	0.0	0.0
S	271	0.7	5.5	13.3	0.7	0.4	2.6	10.7	0.0	11.8
R	1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S	313	0.6	0.0	11.5	0.6	0.3	3.5	10.2	0.0	9.9
R	21	0.0	100	33.3	0.0	0.0	0.0	28.6	0.0	9.5
S	179	0.0	8.9	16.2	0.6	0.0	2.8	14.0	0.0	4.5
R	1	0.0	0.0	100	100	0.0	0.0	100	0.0	100
S	291	0.3	4.8	0.0	0.3	0.3	1.7	9.6	0.0	9.3
R	43	2.3	16.3	100	2.3	0.0	14.0	23.3	0.0	14.0
S	255	0.8	5.9	12.5	0.8	0.4	2.7	10.6	0.0	11.4
R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S	332	0.6	6.3	12.7	0.0	0.3	3.0	11.1	0.0	9.3
R	2	0.0	0.0	50.0	100	0.0	50.0	50.0	0.0	100
S	60	0.0	10.0	8.3	0.0	0.0	3.3	11.7	0.0	1.7
R	2	0.0	0.0	100	0.0	0.0	100	100	0.0	0.0
S	62	0.0	9.7	11.3	0.0	0.0	6.5	14.5	0.0	1.6
R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S	333	0.6	6.3	12.9	0.6	0.0	3.3	11.4	0.0	9.9
R	1	0.0	0.0	0.0	0.0	100	0.0	0.0	0.0	0.0
S	323	0.3	6.5	11.5	0.3	0.3	0.0	10.5	0.0	8.4
R	11	9.1	0.0	54.5	9.1	0.0	100	36.4	0.0	54.5
S	296	0.3	5.1	11.1	0.3	0.3	2.4	0.0	0.0	9.1
R	38	2.6	15.8	26.3	2.6	0.0	10.5	100	0.0	15.8
S	334	0.6	6.3	12.9	0.6	0.3	3.3	11.4	0.0	9.9
R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S	301	0.7	6.3	12.3	0.0	0.3	1.7	10.6	0.0	0.0
R	33	0.0	6.1	18.2	6.1	0.0	18.2	18.2	0.0	100

TABLE ENT V. Distribution of MICs and resistance (%) in *Enterococcus faecalis* from pigs (n=22) and pig meat (n=29), 2011.

Antimicrobial	Source	Resistance %	Distribution (%) of MICs (mg/L)															
			≤0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	2048	>2048
Ampicillin	Pigs	0			4.3	82.6	13.0											
	Pig meat	0				86.2	13.8											
Bacitracin[a]	Pigs	0								100								
	Pig meat	0								100								
Chloramphenicol	Pigs	0						17.4	78.3	4.3								
	Pig meat	0						31.0	69.0									
Erythromycin	Pigs	43			8.7	34.8	13.0						43.5					
	Pig meat	0			6.9	24.1	62.1	6.9										
Gentamicin	Pigs	4							30.4	65.2					4.3			
	Pig meat	0							69.0	31.0								
Kanamycin	Pigs	4												95.7				4.3
	Pig meat	0												100				
Linezolid	Pigs	0				8.7	78.3	13.0										
	Pig meat	0				3.4	89.7	6.9										
Narasin	Pigs	0	13.0	34.8	52.2													
	Pig meat	0	31.0	58.6	10.3													
Streptomycin	Pigs	17										21.7	60.9				17.4	
	Pig meat	3										55.2	37.9	3.4			3.4	
Tetracycline	Pigs	74			13.0	13.0					30.4	43.5						
	Pig meat	7			24.1	65.5	3.4					6.9						
Vancomycin	Pigs	0				39.1	52.2	8.7										
	Pig meat	0				13.8	79.3	6.9										
Virginiamycin	Pigs	0						4.3		73.9	21.7							
	Pig meat	0							6.9	93.1								
			≤0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	2048	>2048

[a] MIC in U/mL, see Appendix 3 for details.

TABLE ENT VI. Distribution of MICs and resistance (%) in *Enterococcus faecium* from pigs (n=22), 2011.

Antimicrobial	Source	Resistance %	Distribution (%) of MICs (mg/L)															
			≤0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	2048	>2048
Ampicillin	Pigs	0				56.5	26.1	17.4										
Bacitracin[a]	Pigs	9								82.6	8.7			8.7				
Chloramphenicol	Pigs	0						39.1	60.9									
Erythromycin	Pigs	9			30.4	26.1	13.0	21.7					8.7					
Gentamicin	Pigs	0						4.3	69.6	26.1								
Kanamycin	Pigs	9												82.6	8.7			8.7
Linezolid	Pigs	0				8.7	47.8	43.5										
Narasin	Pigs	0		13.0	60.9	26.1												
Streptomycin	Pigs	13									17.4	69.6					13.0	
Tetracycline	Pigs	13			73.9	13.0						8.7	4.3					
Vancomycin	Pigs	0				82.6	8.7	8.7										
Virginiamycin	Pigs	4			17.4	13.0	17.4	47.8		4.3								
			≤0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	2048	>2048

[a] MIC in U/mL, see Appendix 3 for details.

Vancomycin resistant enterococci (VRE) in Swedish broiler production – a summary

VANCOMYCIN RESISTANT ENTEROCOCCI (VRE) are an important cause of nosocomial infections in humans. Presence of VRE in farm animals constitute a reservoir of resistance that can spread to humans via the food-chain. The existence of VRE among farm animals is due to earlier selection by extensive use of the vancomycin analog avoparcin for growth promotion. In Sweden, the use of avoparcin ceased before the middle of the 1980s, and a decade later it ceased in the whole of the European Union as a consequence of the Commission Directive 97/6/EC. Once the use of avoparcin was discontinued, the prevalence of VRE among farm animals in Europe decreased. However, VRE are still present among farm animals and by spread via food products they could potentially have a negative impact on public health.

Among randomly selected enterococci from Swedish broilers, VRE are only isolated on rare occasions. For example, within the SVARM programme, VRE have only been isolated four times since 2000, although 1850 samples from broilers have been cultured. Contrary, using selective methods by culture on media containing vancomycin an increase in the occurrence of VRE among broilers in Sweden since 2000 is visible. This increase has occurred in the absence of an obvious selective pressure as avoparcin has not been used since 1984. However, since 2005 the number of broilers colonized with VRE has decreased and seems to have stabilized (Figure VRE).

To increase the knowledge about the epidemiology of VRE in Swedish broiler production and thereby hopefully find ways to reduce the occurrence, a PhD project was initiated in 2007 and completed in 2011. Below are the major findings from the project summarised. The complete thesis is available at http://pub.epsilon.slu.se/8125/.

All VRE isolated from broilers in Sweden are *Enterococcus faecium* with a plasmid located *vanA* gene (Nilsson et al., 2009b; Nilsson et al., 2012). The majority of the isolates has the same resistance phenotype including decreased susceptibility to narasin and low level resistance to erythromycin (Nilsson et al., 2009b). Further investigations have shown that the increased occurrence is caused by the spread of one predominant clone which is of multilocus sequence type (MLST) 310 (Nilsson et al., 2009b). Clones with other sequence types and/or resistance phenotypes do however exist (Nilsson et al., 2009b; Nilsson et al., 2012).

To understand why one clone dominates, both genotypic and phenotypic characterizations of the different clones were made. This has not provided evidence to why the occurrence of VRE among Swedish broilers has increased or why one clone dominates. The vancomycin resistance is for example easily transferrable from many of the clones (Nilsson et al., 2012). Contrary, plasmid addiction systems are most likely not involved in the retention of the *vanA* gene as such systems are nearly absent among VRE from broilers in Sweden (Nilsson et al., 2012).

From some of the VRE clones, decreased susceptibility to the ionophore narasin was co-transferred with the vancomycin resistance (Nilsson et al., 2012). Thereby the use of narasin for coccidial prophylaxis could contribute to retention of the *vanA* gene. The traits are probably located close to each other, so when retaining the decreased susceptibility to narasin, the enterococci also retain the *vanA* gene. This theory is so far only a speculation and needs to be further investigated.

It has been shown that broilers are colonized with VRE persisting in the broiler houses (Nilsson et al., 2009a). However, differences in occurrence of VRE among farms indicate that a reduction could be possible if the factor(s) causing these differences could be identified. Attempts to identify differences in management routines between farms contaminated and not contaminated with VRE was unsuccessful (Jansson et al., to be published). Also the possibility that the bacteria have a reduced susceptibility to commonly used disinfectants was investigated *in vitro* but a sufficient reduction in the amount of bacteria was achieved with all tested products (Nilsson, 2011). Hence, resistance to disinfectants does not seem to be the reason for persistence of VRE at farms. Instead, the reasons could be difficulties to apply to the disinfection protocols and procedures rather than in the protocols *per se*. For example, the practical difficulties in cleaning the houses adequately can lead to quenching of the disinfectant by remaining biological substances. Also difficulties in applying the disinfectant at various locations within the houses could contribute to the unsuccessful disinfection results.

Due to the results of the *in vitro* studies, the effect on VRE of a method that combines steam and formaldehyde, originally developed to disinfect layer houses from *Salmonella*, was tested (Nilsson, 2011). A reduction in the contamination of the broiler houses was then achieved. Hopefully, this could in the future be used to reduce the occurrence of VRE on farms and subsequently in the whole Swedish broiler production.

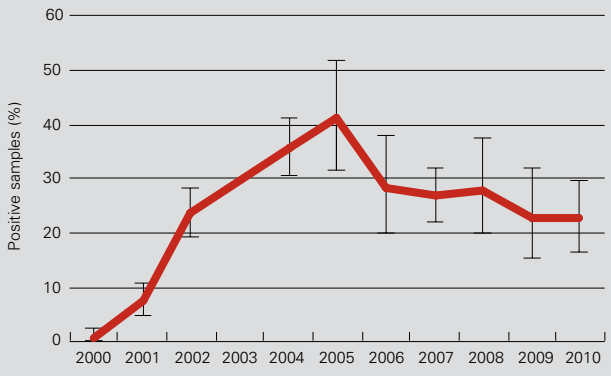


FIGURE. Proportion of Swedish broilers colonized with VRE from 2000-2010. Number of samples each year was between 100 and 350. 95% confidence intervals indicated.

Animal pathogens

ISOLATES TESTED are from clinical submission of samples to SVA if not otherwise stated. For many samples, information on the indications for sampling is not available but the vast majority of submissions are likely from diseased animals. Therefore, data are probably biased towards samples from treated animals or from herds where antimicrobial treatments are common. Any assessment of trends is based on the assumption that this bias is inherent throughout the observation period.

In SVARM, isolates are, when possible, classified as susceptible or resistant by epidemiological cut-off values issued by EUCAST (see Guidance for readers and Appendix 3 for details). This classifies isolates with acquired reduced susceptibility as resistant, which is relevant for monitoring purposes, but it should be understood that this not always implies clinical resistance.

Pigs

Escherichia coli

Isolates of *Escherichia coli* from years 1992-2011 are from clinical submissions of samples from the gastro-intestinal tract (intestinal content, faecal samples or mesenteric lymph nodes), while data from 1989-1991 include all *E. coli* isolated from pigs, irrespective of material type.

Before the first of October 2007, all *E. coli* isolates from the gastro-intestinal tract were susceptibility tested. After that date, the criteria for susceptibility testing were changed and in general only *E. coli* isolates that harbour genes coding for virulence factors are tested for susceptibility. The presence of genes coding for the following proteins are determined by PCR: enterotoxin (LT), heat-stabile enterotoxin a and b (STa and STb), verocytotoxin (VT2e) and adhesionsfactors F4, F5, F6, F18 and F41. Isolates with at least one of these genes were susceptibility tested.

As in previous years, resistance to ampicillin, streptomycin, tetracycline or trimethoprim-sulphonamides in *E. coli* was most commonly occurring in 2011 but resistance to ceftiofur was not detected (Table Pig I). In the 70s and 80s, prevalence of *E. coli* resistant to ampicillin was around 7% (Franklin, 1976; Franklin, 1984). From the late 90s, prevalence of ampicillin resistance rose gradually, but after 2004 the figures have stabilised around 20%. Multiresistance occurred in 25% of the isolates compare to 15% in 2010, 19% in 2009 and 14% in 2008. The combination with resistance to ampicillin, streptomycin and trimethoprim-sulphonamides was the most common trait, occurring in 30% of the multiresistant isolates. Ten percent of all the isolates were resistant to four or more antimicrobials and two percent were resistant to five or more. One isolate was resistant to ampicillin, enrofloxacin, streptomycin, trimethoprim-sulphonamides and tetracycline. There is no product authorised on the Swedish market for the indication intestinal infections in pigs that can be presumed to have clinical effect on *E. coli* with this resistance profile.

Brachyspira hyodysenteriae

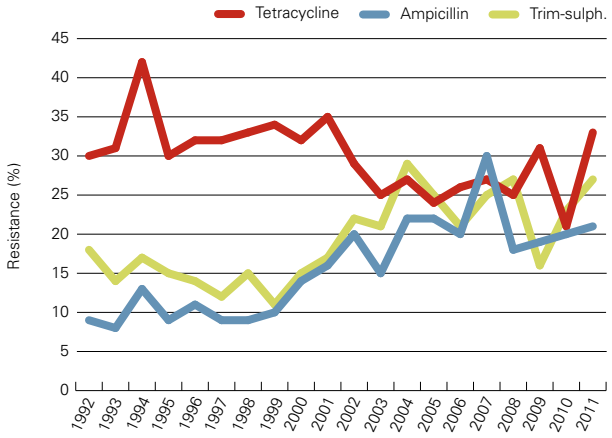
Isolates of B*rachyspira hyodysenteriae* are from clinical submissions of faecal samples from pigs.

All isolates were susceptible to tiamulin (Table Pig II). In the late 80s, susceptibility of *B. hyodysenteriae* was tested with an agar dilution technique, and 20% of the isolates were resistant

TABLE PIG I. Resistance (%) in *Escherichia coli* from pigs 1989-2011 and distribution of MICs for isolates from 2011. Isolates are from clinical submissions of faecal samples or samples taken post mortem from the gastro-intestinal tract.

Antimicrobial	Resistance (%)									Distribution (%) of MICs (mg/L)									
	1989-91 n=248	1992-94 n=431	1995-97 n=1244	1998-00 n=1074	2001-03 n=935	2004-06 n=1009	2007-09 n=278	2010 n=94	2011 n=91	≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	6	10	9	11	17	22	21	20	21				2.2	39.6	31.9	5.5	20.9		
Ceftiofur	-	-	-	-	<1[g]	<1	0	0	0		63.7	30.8	5.5						
Enrofloxacin[a]	1[f]	7	5	6	8	9	7	6	6	94.5		4.4		1.1					
Florfenicol	-	-	-	-	<1[g]	<1	0	0	0					4.4	53.8	39.6	2.2		
Gentamicin[b]	1	1	<1	1	4	1	<1	0	1					95.6	3.3	1.1			
Neomycin	17	14	9	6	5	4	6	1	3						93.4	3.3			3.3
Streptomycin[c]	44	44	32	30	36	36	35	28	37						41.8	16.5	4.4	9.9	27.5
Tetracycline	28	35	31	33	30	26	26	21	33				20.9	36.3	9.9		33.0		
Trim-Sulph.[d,e]	17	15	13	14	19	25	20	23	27			70.3	2.2			27.5			

[a] Cut-off value >0.25 mg/L until 2001; [b] Cut-off value >8 mg/L until 2002; [c] Cut-off value >32 mg/L until 2001; [d] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphametoxazole); [e] Cut-off value >4 mg/L until 2001; [f] 227 isolates tested; [g] 688 isolates tested.



F IGURE PIG. Resistance (%) to ampicillin, tetracycline and trimethoprim-sulphametoxazole in *Escherichia coli* from pigs 1992-2011.

to tylosin (Gunnarsson et al., 1991). In 2001, the figure had increased dramatically to around 80% and has since then been over 70% (Table Pig II).

The last four years isolates were susceptibility tested also for tylvalosin, a macrolide authorised for treatment of swine dysentery in the European Union. No cut-off value for resistance to tylvalosin is available but Karlsson et al. (2004) showed a correlation between the MICs of tylosin and tylvalosin indicating that macrolide resistance caused by structural changes of ribosomal RNA also affects the binding of tylvalosin. Since 2005 isolates have been susceptibility tested for doxycycline and valnemulin. Cut-off values are not available for these substances either.

Ongoing compilation and analysis of antimicrobial susceptibility data from isolates of *B. hyodysenteriae* from Sweden 1990-2010 (data not shown) will, hopefully, result in the proposal of epidemiological cut-off values for the substances tested at SVA. During 1990-2003, a slow increase in the number of isolates with decreased susceptibility for tiamulin was seen. This increase can only be detected if the material is divided in subpopulations from different time periods. After 2003, this increase has ceased. A slow decrease in susceptibility can easily be missed if monitoring is not continuously performed.

In Sweden, a programme for control of swine dysentery was launched in 2000. The programme has three strategies; testing of nucleus and multiplying herds for *B. hyodysenteriae* twice a year, eradication of the bacteria in infected herds and tracing the source of infection. It is imperative that all herds where treatment failure is suspected are thoroughly investigated. Since only macrolides and pleuromutilins are authorised for treatment of swine dysentery in pigs it is important to monitor resistance development in *B. hyodysenteriae*. The number of samples taken and isolates available for susceptibility testing has decreased during the years. However, this can probably be explained by a successful reduction of swine dysentery. This is supported by the marked decline in sales figures for tiamulin (see section "Use of antimicrobials").

TABLE PIG II. Resistance (%) in *Brachyspira hyodysenteriae* from pigs 2001-2003 and 2005-2011 and distribution of MICs for isolates from 2005-2011. Isolates are from clinical submissions of faecal samples.

Antimicrobial	Resistance (%)				Distribution (%) of MICs (mg/L)												
	2001 n=75	2002 n=109	2003 n=100	2005-11 n=132	≤0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	>128
Doxycycline	-	-	-	ND[a]			16.7	63.6	6.8	6.8	6.1							
Tiamulin	0	0	0	0		31.8	46.2	11.4	8.3	2.3								
Tylosin	83	73	89	74							0.8	12.1	12.1	1.5			2.3	71.2
Tylvalosin	-	-	-	ND[a,b]				1.8	9.1	23.6	3.6	16.3	25.5	14.5	1.8	3.6		
Valnemulin	-	-	-	ND[a]	79.5	12.1	2.3	3.8	2.3									

[a] ND=not determined because no cut-off value is available; [b]55 isolates tested.

TABLE PIG III. Resistance (%) in *Brachyspira pilosicoli* from pigs 2002-2003 and 2005-2011 and distribution of MICs for isolates from 2005-2011. Isolates are from clinical submissions of faecal samples.

Antimicrobial	Resistance (%)		Distribution (%) of MICs (mg/L)													
	2002-03 n=93	2005-11 n=247	≤0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	>128
Doxycycline	-	ND[b]			38.1	49.4	4.0	2.8	5.3	0.4						
Tiamulin	14	12		29.6	29.1	13.0	8.5	6.5	1.6		2.0	9.7				
Tylosin	50[a]	62							5.3	17.8	10.9	3.6	4.5	3.6	5.3	49.0
Tylvalosin	-	ND[b,c]					8.3	15.5	31.0	6.0	2.4	2.4	19.0	15.5		
Valnemulin	-	ND[b]	43.7	21.9	6.1	9.3	6.1	4.9	2.0	1.6	4.5					

[a] 86 isolates tested; [b] ND=not determined because no cut-off value is available; [c] 84 isolates tested.

Brachyspira pilosicoli

Isolates of *Brachyspira pilosicoli* are from clinical submissions of faecal samples from pigs.

In 2001, the first isolates of *B. pilosicoli* resistant to tiamulin were confirmed in Sweden. These isolates were associated with treatment failure in a pig herd with spirochaetal diarrhoea (see SVARM 2003). Since then, tiamulin resistant strains have been isolated every year but there is no apparent increasing trend in prevalence of resistance (Table Pig III). The proportion of isolates resistant to tylosin has been around 60% during the last years (Table Pig III).

During 2008-2011, five isolates with high MICs of tiamulin, tylosin and tylvalosin were detected. Although such isolates may be susceptible to other antimicrobials, only tiamulin and tylosin are currently licensed for treatment of spirochaetal diarrhoea in pigs in Sweden. Since resistance occurs, susceptibility testing of *B. pilosicoli* from herds where tiamulin is to be used is of importance.

Actinobacillus pleuropneumoniae

Isolates of *Actinobacillus pleuropneumoniae* from 1992-2000 were isolated from the respiratory tract (nasal swabs and lung, including regional lymph nodes) but from 2005-2011 all isolates are from lungs sampled post mortem.

Since 2005, *A. pleuropneumoniae* has been susceptible to almost all antimicrobials tested (Table Pig IV). Pneumonia caused by *A. pleuropneumoniae* is an important disease in Swedish pig production and a high frequency of sampling and susceptibility testing is desirable if emerging resistance is to be detected early. The number of samples taken and isolates tested has been few over the years, but the sampling increased modestly when the surveillance programme SVARMpat was started in 2005. In 2011, intensified sampling from slaughtered pigs at abattoirs was performed within the SVARMpat programme which increased the number of isolates available for susceptibility testing considerably.

TABLE PIG IV. Resistance (%) in *Actinobacillus pleuropneumoniae* from pigs 1992-2000 and 2005-2011. Distribution of MICs for isolates from 2011. Isolates are from clinical submissions of samples from the respiratory tract or from post mortem investigations of lungs.

	Resistance (%)				**Distribution** (%) **of MICs** (mg/L)													
Antimicrobial	**1992-00** n=18	**2005-07** n=84	**2008-10** n=79	**2011** n=57	**≤0.016**	**0.03**	**0.06**	**0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**>128**
Ampicillin	6	0	0	0		1.8	1.8	36.8	36.8	22.8									
Cefotaxime	-	0	0	0	96.5	3.5													
Chloramph.	11	0	0	0								100							
Ciprofloxacin	6[a]	0	0	0		35.1	64.9												
Florfenicol	-	0	0	0									100						
Gentamicin	-	0	0	0								5.3	68.4	26.3					
Nalidixic acid	-	0	0	0							3.5	84.2	12.3						
Penicillin	6	0	0	0				14.0	61.4	24.6									
Streptomycin	-	0	1	2											14.0	84.2	1.8		
Tetracycline	11[b]	1	0	0							100								
Trimethoprim	-	0	0	0				43.9	40.4	14.0	1.8								

[a] Enrofloxacin tested, cut-off value 2 mg/L.; [b] cut-off value >8 mg/L.

TABLE PIG V. Resistance (%) in *Pasteurella* spp. from pigs 2000-2001 and 2005-2011. Distribution of MICs for isolates from 2008-2011. Isolates are from the respiratory tract, isolated from nasal swabs or from post mortem investigations of lungs.

	Resistance (%)			**Distribution** (%) **of MICs** (mg/L)															
Antimicrobial	**2000-01** n=75	**2005-07** n=38	**2008-11** n=76	**≤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	0	0								100								
Cefotaxime	-	0	0[b]				100												
Chloramph.	1	0	0[b]									100							
Ciprofloxacin	1[a]	0	0[b]	11.9	61.0	25.4	1.7												
Florfenicol	-	0	0[c]										100						
Gentamicin	4	0	0									69.7	26.3	3.9					
Nalidixic acid	-	0	0[b]								42.4	44.1	11.9		1.7				
Penicillin	0	0	0					19.7	68.4	11.8									
Streptomycin	4	0	4										3.9	36.8	38.2	17.1	3.9		
Tetracycline	1	0	0								97.4	2.6							
Trimethoprim	-	0	0[b]						69.5	28.8	1.7								

[a] Enrofloxacin tested, cut-off value 2 mg/L; [b] 59 isolates tested; [c] 72 isolates tested.

TABLE PIG VI. Resistance (%) in *Streptococcus equisimilis* from pigs 2009-2011. Isolates are from joints from nursing piglets with arthritis.

Antimicrobial	Resistance (%)	Distribution (%) of MICs (mg/L)												
	2009-11 n=82	≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Cephalothin	0		24.4	42.7	32.9									
Chloramph.	0					6.1	6.1	41.5	43.9	2.4				
Ciprofloxacin	NR		3.7	18.3	7.3	35.4	32.9	2.4						
Clindamycin	7				90.2	2.4			2.4	2.4			2.4	
Erythromycin	2				90.2	1.2	1.2	4.9					2.4	
Penicillin	0	92.7	7.3											
Tetracycline	23						1.2	17.1	41.5	17.1		8.5	14.6	
Trimethoprim	ND					3.7	26.8	46.3	20.7	1.2		1.2		

NR= Not relevant as the inherent susceptibility is above concentrations that can be obtained during therapy; ND=not determined because no cut-off value is available.

In order to show the distribution of the lower MIC values, the isolates from 2011 were susceptibility tested on panels with extended ranges compared to previous years for some of the substances.

Pasteurella spp.

Isolates of *Pasteurella* spp. are from nasal swabs collected within a control programme for atrophic rhinitis in nucleus and multiplying herds or from post mortem investigation of lungs. Isolates from the control programme are likely from healthy pigs, whereas isolates from post mortem investigations of lungs are most likely from pigs with respiratory problems.

Since 2005, *Pasteurella* spp has been susceptible to almost all antimicrobials tested (Table Pig V). In 2011, enrofloxacin was tested as a representative for quinolones instead of ciprofloxacin and nalidixic acid. Since only 17 isolates were available for susceptibility testing, distribution of MICs of enrofloxacin is not included in Table Pig V. However, resistance to enrofloxacin was not detected and almost all isolates had MICs of ≤0.12.

Streptococcus equisimilis

During 2009-2011, bacteriological sampling was performed from 130 nursing piglets with arthritis. Two affected joints per pig were sampled at post mortem investigation. *Streptococcus equisimilis* (beta-hemolytic, Lancefield group C) was the most common bacterial species isolated.

In Sweden, penicillin is the substance of choice for treatment of arthritis in pigs. All isolates of *S. equisimilis* were susceptible to penicillin and there is no report of penicillin resistance in beta-hemolytic streptococci. Resistance to tetracycline was the most common trait occurring in 23% of the isolates.

Cattle

Escherichia coli

Isolates of *Escherichia coli* are from the gastro-intestinal tract of calves.

Over the last decades there has been an increase in resistance in *E. coli* from calves. During 2007-2011, resistance to tetracycline was the most common trait occurring in 64% of the isolates followed by streptomycin occurring in 49% and ampicillin in 33% (Table Cattle I). Twenty eight isolates (40%) were multiresistant, of which all were resistant to streptomycin and all but three to tetracycline.

Two isolates from 2010 had MIC (2 mg/L) above the cut-off value of ceftiofur. These two isolates were not available for further investigation. Since the MIC was just above the cut-off value, the results are probably due to methodological error, or the isolates express chromosomal AmpC.

Pasteurella spp.

Isolates from years 1997-2000 are from a field study on respiratory pathogens in calves presented in SVARM 2000 and isolates from 2005-2011 are isolated from clinical submissions of samples from calves with respiratory disease or from post-mortem investigations of lungs.

Antimicrobial resistance among isolates of *Pasteurella* spp. is rare (Table Cattle II) and penicillin is considered the substance of choice for treatment of pneumonia in calves in Sweden. One isolate in 2009 and one in 2010 had MICs above the cut-off value for ceftiofur. This is most likely not a true value, since the MICs of penicillin was 0.12 mg/L and 0.25 mg/L, respectively.

Isolates of beta-lactamase producing *Pasteurella* spp. were confirmed in Sweden from one herd in 2003. Since 2005, resistance to penicillin and tetracycline, the substances commonly used for treatment of respiratory disease in calves, has not been detected in *Pasteurella* spp. However, in 2010 an isolate of beta-lactamase producing *Mannheimia haemolytica* from a calf with pneumonia was confirmed after post mortem investigation of the lungs. The isolate was susceptible for tetracycline, quinolones and cefotaxime. The herd was known to have respiratory problems and a few months later an isolate of *M. haemolytica* with the same resistance pattern was isolated from another calf, indicating that this strain persisted in the herd.

Over the years, the number of isolates available for susceptibility testing has been low. However, the number of tested isolates increased in 2011 due to a study within the SVARMpat programme. Frequent sampling of calves with respiratory disorders and subsequent susceptibility testing is desirable if emerging resistance is to be detected early.

TABLE CATTLE I. Resistance (%) in *Escherichia coli* from cattle 1992-2002, 2004 and 2005-2011. Distribution of MICs for isolates from 2007-2011. Isolates are from diagnostic submissions of faecal samples or samples taken post mortem from the gastro-intestinal tract, except isolates from 2004 which are from a study of both healthy and diseased calves.

	Resistance (%)				**Distribution** (%) **of MICs** (mg/L)									
Antimicrobial	**1992-02** n=220	**2004** n=87[h]	**2005-06** n=63	**2007-11** n=70	**≤0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**>32**
Ampicillin	24	29	32	33				1.4	45.7	20.0		32.9		
Ceftiofur[a]	0[g]	0	0	3		27.1	65.7	4.3	2.9					
Enrofloxacin[b]	10	14	13	10	90.0	2.9	2.9		4.3					
Florfenicol	0[g]	0	0	1					4.3	28.6	64.3	1.4	1.4	
Gentamicin[c]	5	0	0	1					82.9	15.7			1.4	
Neomycin	8	7	13	24						70.0	5.7		7.1	17.1
Streptomycin[d]	42	48	54	49						5.7	25.7	20.0		48.6
Tetracycline	31	37	49	64				12.9	15.7	5.7	1.4	64.3		
Trim/Sulph.[e,f]	11	10	21	17			80.0	2.9			17.1			

[a] Cut-off value >2 mg/L until 2006; [b] Cut-off value >0.25 mg/L until 2004; [c] Cut-off value >8 mg/L until 2001; [d] Cut-off value >32 mg/L until 2006; [e] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphametoxazole); [f] Cut-off value >4 mg/L until 2006; [g] 16 isolates tested; [h] 1/3 of the isolates were from calves with diarrhoea.

TABLE CATTLE II. Resistance (%) in *Pasteurella* spp. from calves 1997-2000 and 2005-2011. Distribution of MICs for isolates from 2011. Isolates are from the respiratory tract, isolated from nasal swabs or from post mortem investigations of lungs.

Antimicrobial	Resistance (%)				Distribution (%) of MICs (mg/L)									
	1997-00 n=254	2005-07 n=27	2008-10 n=71	2011 n=80	≤0.06	0.12	0.25	0.5	1	2	4	8	16	>16
Ampicillin	1	0	0	0					100					
Ceftiofur	-	0	3[b]	0[d]			100							
Enrofloxacin	2	0	0[c]	0		92.5	7.5							
Florfenicol	-	0	0	0							100			
Penicillin	0	0	0	0		47.5	38.8	13.8						
Tetracycline	3	0	0	0					98.8	1.3				
Trim/Sulph.[a]	2	0	0	0				96.3	2.5	1.3				

[a] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphametoxazole); [b] 65 isolates tested; [c] 46 isolates tested; [d] 76 isolates tested.

Farmed fish

Isolates of *Aeromonas salmonicida* subsp. *achromogenes*, *Flavobacter columnare* and *Flavobacter psychrophilum* are from clinical submissions of farmed fish. Most isolates represent a unique batch of fish but occasional isolates are duplicates within the same batch. Antimicrobial susceptibility was tested by microdilution according recommendations by Alderman & Smith (2001). At SVA this methodology is used for routine testing of isolates from clinical submissions of fish.

This year data for 14 isolates of *A. salmonicida* subsp. *achromogenes*, 8 of *F. columnare* and 27 of *F. psychrophilum* were available. As in previous years the majority of the two former bacterial species are from brown trout whereas most isolates of *F. psychrophilum* are from rainbow trout. Data for 2011, 2010 and 2009 are compiled and presented as distributions of MICs in Table Fish I.

At present there are no accepted interpretative criteria for MIC data of bacteria from aquaculture. But evaluation of the distributions of MICs indicates the presence of isolates with reduced susceptibility, i.e. deviating high MICs, (Table Fish I). For example, MIC distributions for the quinolone nalidixic acid are bimodal in all three bacterial species. This indicates the presence of acquired resistance to quinolones. Likewise deviating high MICs of tetracycline in *Flavobacter*, and of florfenicol among *A. salmonicida* and *F. columnare*, indicate acquired resistance. Resistance to these antimicrobials is reasonable since there is a limited therapeutic use of florfenicol as well as of tetracycline and of the quinolone oxolinic acid in aquaculture in Sweden.

TABLE FISH I. Distribution of MICs for *Aeromonas salmonicida* subsp. *achromogenes, Flavobacter columnare* and *Flavobacter psychrophilum* from farmed fish, 2005-2011.

Bacterial species	Antimicrobial	Year	Number of isolates	Distribution (%) of MICs (mg/L)									
				≤0.25	0.5	1	2	4	8	16	32	64	>64
Aeromonas salmonicida subsp. *achromogenes*	Florfenicol	2009-11	45				97.8			2.2			
		2005-08	87				96.6	2.3	1.1				
	Nalidixic acid	2009-11	45		80.0	2.2					2.2	6.7	8.9
		2005-08	87		80.5	4.6				1.1	3.4	5.7	4.6
	Tetracycline	2009-11	45	80.0	13.3	4.4				2.2			
		2005-08	87	90.8	8.0			1.1					
Flavobacter columnare	Florfenicol	2009-11	23				100						
		2005-08	46				95.7	2.2			2.2		
	Nalidixic acid	2009-11	23		78.3	13.0	4.3	4.3					
		2005-08	46		73.9	13.0	4.3				2.2	2.2	4.3
	Tetracycline	2009-11	23	73.9	26.1								
		2005-08	46	84.8	6.5	4.3		2.2			2.2		
Flavobacter psychrophilum	Florfenicol	2009-11	72				98.6		1.4				
		2005-08	69				98.6	1.4					
	Nalidixic acid	2009-11	72				16.7	26.4	4.2	1.4	4.2	6.9	40.3
		2005-08	69		7.2		37.7	39.1		1.4	1.4		13.0
	Tetracycline	2009-11	72	37.5	9.7	22.2	6.9	19.4	4.2				
		2005-08	69	72.5	5.8	5.8	7.2	5.8	1.4	1.4			

SVARMpat

THE SVARMPAT PROGRAMME (Swedish Veterinary Antimicrobial Resistance Monitoring – farm animal pathogens) is a project in co-operation between the National Veterinary Institute (SVA) and the Swedish Animal Health Service that was launched in 2005. It is financed by the Swedish Board of Agriculture.

The purpose of SVARMpat is to reduce emergence and spread of antimicrobial resistance in pathogenic bacteria from food-producing animals. The work is performed by monitoring and documenting antimicrobial resistance, by activities that increase knowledge of antimicrobial resistance and prudent use of antimicrobials, and by communication of knowledge generated within the programme.

Studies with sampling of animals and susceptibility testing of defined pathogens are performed. The programme also encourages practitioners to submission of samples from clinical cases and post mortem investigations. Such continuous clinical submissions yield isolates of *Actinobacillus pleuropneumoniae* and *Brachyspira* spp. from pigs and *Pasteurella* spp. from cattle and pigs, and susceptibility testing is performed within SVARMpat.

Activities in SVARMpat 2011:

- **Screening for MRSA in milk samples** from cows was started in 2010 and is still ongoing. Isolates of beta-lactamase producing *Staphylococcus aureus* from routine submissions to SVA are investigated for methicillin resistance. During 2010-2011, 311 isolates were tested but MRSA was not initially detected. However, when MRSA with a divergent *mecA* homologue, $mecA_{LGA251}$, was reported, the results were re-evaluated and in subsequent studies performed outside SVARMpat, three isolates from 2010 and one from 2011 were confirmed to be MRSA with $mecA_{LGA251}$ (See "Zoonotic bacteria").
- ***Mycoplasma bovis* in calves with pneumonia.** During 2010-2011, nasal swabs were taken from calves with respiratory symptoms. Samples were also taken at post mortem investigation of lungs from calves with pneumonia. Altogether, about 300 samples were investigated and during the autumn of 2011, *M. bovis* was detected in samples from three herds. Susceptibility testing of *M. bovis* was not performed since the methodology is not available at SVA. Due to the lack of cell wall in *M. bovis*, penicillin is not effective for treatment. In herds with *M. bovis* as the known causative agent of pneumonia in calves, preventive animal health measures and treatment regimes must be carefully considered.
- ***Mycoplasma ovipneumoniae* in sheep with pneumonia.** During 2010-2011, samples were taken at post mortem investigation of lungs from sheep with pneumonia. Altogether, 71 samples were investigated and in 23 *M. ovipneumoniae* was detected.
- **Investigation of microbial aetiology of infectious arthritis in nursing piglets** and the antimicrobial susceptibility of these bacteria. One lame piglet per herd with more than 100 sows was euthanized and an autopsy was performed together with bacteriological sampling of two affected joints. The study started in 2009 and was completed in 2011. Altogether, 130 piglets were analysed. *Streptococcus equisimilis* dominated the bacteriological findings, followed by *Staphylococcus hyicus* and *E. coli*. All streptococci (See "Animal pathogens"), but less than half of the staphylococci were susceptible to penicillin.
- **Exudative epidermitis in piglets.** In an ongoing study, piglets with exudative epidermitis are sampled and isolated strains of *Staphylococcus hyicus* are susceptibility tested. During 2011, samples from one pig per herd in six herds were investigated with findings of *S. hyicus* in five of them. Both strains with and without penicillinase production were isolated, sometimes from the same pig. This indicates that penicillin may not always be effective for treatment.
- **Otitis media in pigs.** A study on pigs with "head tilt" was initiated. Affected pigs are euthanized and autopsy performed. Bacteriological samples are taken from the middle ear, nose and sometimes brain. The aim is to increase the knowledge on presumed microbial etiology to this problem.
- **The PhD project "Vancomycin resistant enterococci in Swedish broilers"** was partly financed by SVARMpat. In the project, the spread of vancomycin resistant enterococci (VRE) in Swedish broilers since 2000 was investigated. The aim was to elucidate the epidemiology of VRE in broilers and, if possible, to mitigate further spread and reduce the prevalence on farms where VRE already occur. See also SVARM 2008 for details. The project started in 2007 and was completed during 2011 (See "Vancomycin resistant enterococci (VRE) in Swedish broiler production – a summary).
- **ESBL-producing *E. coli* in broilers.** Ongoing investigations on occurrence and epidemiology of ESBL-producing *E. coli* in broilers are partly financed by SVARMpat. In collaboration with the Swedish poultry meat association and the Board of Agriculture, occurrence of ESBL-producing *E. coli* in breeding animals imported to Sweden is monitored. Furthermore, several studies aiming at finding ways to mitigate spread of such bacteria in broiler production have been initiated.

Horses

Escherichia coli

The isolates of *Escherichia coli* included are from the genital tract of mares. As in previous years, resistance to trimethoprim-sulphonamides or streptomycin are the most common resistance traits (Table Horse I).

Trimethoprim-sulphonamide resistance is probably a consequence of the frequent use of this antimicrobial combination in horses. Since the introduction of trimethoprim-sulphonamides on the Swedish market, as an oral formulation for horses in the late 80s, the prevalence of resistance in *E. coli* has increased from only 2% in years 1992-1994 to 17% in 2011.

Multiresistance occurred in 11% of the isolates, a higher figure than in 2010. A majority of the multiresistant isolates were resistant to ampicillin, streptomycin and trimethoprim-sulphonamides. None of the isolates were resistant to more than four substances.

Resistance to ceftiofur was more common than in previous years. In 2011, eight isolates had MICs higher than 1 mg/L. Seven of these isolates were tested for ESBL production of which five were positive. Four of these isolates were positive when PCR was used to detect the gene for CTX-M-1 and the fifth for SHV. Besides being ESBL-producing, these *E. coli* were also resistant to gentamicin and trimethoprim-sulphonamide. The CTX-M-1 positive isolates were also resistant to tetracycline.

A majority of the ESBL producing *E. coli* from animals in Sweden isolated from diagnostic submissions are from the genital tract of mares. Close monitoring of the situation is therefore strongly warranted. For more information on occurrence of ESBL or pAmpC in Sweden; see highlights: "*Enterobacteriaceae* producing extended spectrum beta-lactamases (ESBL) – isolates from diagnostic submissions", "*Escherichia coli* with ESBL- or transferrable AmpC-type resistance in production animals" and "*Escherichia coli* with ESBL or pAmpC in meat obtained from the Swedish market".

Streptococcus zooepidemicus

The isolates included are from the respiratory tract of horses. As in previous years, resistance in *Streptococcus zooepidemicus* is rare (Table Horse II). Occurrence of resistance to trimethoprim-sulphonamides has been high during the last 15 years, probably due to the common use of oral trimethoprim-sulphonamide in horses. However, in 2011 only 8% of the isolates were resistant to this combination. The isolates were uniformly susceptible to penicillin but had a low inherent susceptibility to fluoroquinolones and aminoglycosides (i.e. gentamicin, neomycin and streptomycin). MICs for these substances are above concentrations that can be obtained during systemic therapy with these antimicrobials.

Staphylococcus aureus

The isolates of *Staphylococcus aureus* are from skin samples, excluding wounds and abscesses. The number of resistant isolates of *S. aureus* has been stable during the last three years and resistance to penicillin dominate (Table Horse III). None of the isolates were multiresistant.

One isolate had MIC >1 mg/L for oxacillin and was tested by PCR for the presence of the *mecA*-gene and was positive, i.e. methicillin resistant. More information on methicillin resistant *S. aureus* (MRSA) isolated from horses in Sweden is presented in the chapter "Zoonotic bacteria".

TABLE HORSE I. Resistance (%) in *Escherichia coli* from horses 1992-2011 and distribution of MICs for isolates from 2011. Isolates are from clinical submissions of samples from the female genital tract.

	Resistance (%)								**Distribution** (%) **of MICs** (mg/L)									
Antimicrobial	**1992-94** n=48	**1995-97** n=216	**1998-00** n=222	**2001-03** n=457	**2004-06** n=473	**2007-09** n=657	**2010** n=236	**2011** n=174	**≤0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**>32**
Ampicillin	15	17	10	9	7	10	7	12				1.1	12.1	58.6	16.1	12.1		
Ceftiofur	-	-	-	<1	<1	2	<1	5		37.4	53.4	4.6	1.1	3.4				
Enrofloxacin[a]	8	3	3	2	4	2	5	4	96.0	3.4	0.6							
Florfenicol	-	-	-	0	0	<1	<1	0					7.5	40.8	51.1	0.6		
Gentamicin[b]	0	3	6	6	2	4	2	5					93.1	1.7		0.6	4.6	
Neomycin	4	5	5	3	4	2	1	2						94.3	3.4	0.6		1.7
Streptomycin[c]	31	24	21	23	21	21	15	20						25.3	44.8	9.8	2.3	17.8
Tetracycline	6	5	9	6	8	7	5	8				35.1	54.0	2.9		8.0		
Trim-Sulph.[d, e]	2	15	17	18	17	20	13	17			81.0	1.7			17.2			

[a] Cut-off value >0.25 mg/L until 2002; [b] Cut-off value >8 mg/L until 2002; [c] Cut-off value >16 mg/L until 2001¸ [d] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphametoxazole); [e] Cut-off value >4 mg/L until 2001.

TABLE HORSE II. Resistance (%) in *Streptococcus zooepidemicus* from horses 1992-2011 and distribution of MICs for isolates from 2011. Isolates are from clinical submissions of samples from the respiratory tract.

	Resistance (%)								**Distribution** (%) **of MICs** (mg/L)									
Antimicrobial	**1992-94** n=218	**1995-97** n=402	**1998-00** n=409	**2001-03** n=505	**2004-06** n=534	**2007-09** n=491	**2010** n=43	**2011** n=131	**≤0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**>32**
Ampicillin	0	<1	0	0	0	0	0	0				100						
Enrofloxacin	NR[a]	NR	NR	NR	NR	NR	NR	NR			0.8	48.9	50.4					
Florfenicol	-	-	-	1	<1	0	0	2					95.4	0.8	2.3	1.5		
Gentamicin	NR	NR	NR	NR	NR	NR	NR	NR					1.5	1.5	31.3	57.3	8.4	
Penicillin	0	<1	0	0	0	0	0	0	98.5	1.5								
Spiramycin	<1	1	0	1	<1	<1	0	0						99.2	0.8			
Tetracycline	4	3	4	5	3	3	7	4				51.1	33.6	9.2	2.3	3.8		
Trim-Sulph.[b]	1	11	57	36	42	18	7	8			82.4	6.1	2.3	0.8	8.4			

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

TABLE HORSE III. Resistance (%) in *Staphylococcus aureus* from horses 2007-2011 and distribution of MICs for isolates from 2011. Isolates are from clinical submissions of samples from skin.

	Resistance (%)					**Distribution** (%) **of MICs** (mg/L)								
Antimicrobial	**2007** n=113	**2008** n=99	**2009** n=96	**2010** n=131	**2011** n=135	**≤0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**>32**
Ceftiofur	0	2	2	<1	2		5.9	5.9	72.6	14.1	1.5				
Enrofloxacin	3	2	2	2	0	47.4	48.1	4.4							
Florfenicol	2	3	1	<1	0					4.4	84.4	11.1			
Gentamicin	9	7	6	4	5					95.6	1.5			3.0	
Oxacillin	-	-	2	<1	<1			97.8	1.5	0.7					
Penicillin[a]	26	36	36	21	20										
Spiramycin	1	0	0	0	0						80.7	16.3	3.0		
Streptomycin	12	14	9	5	4						62.2	28.1	5.2	0.7	3.7
Tetracycline	2	6	4	<1	3				97.0	2.2			0.7		
Trim-Sulph.[b]	4	5	3	2	4			96.3	1.5	0.7		1.5			

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

Dogs

Escherichia coli

Isolates of *Escherichia coli* are from samples of urine, submitted either as urine or as dip-slide cultures. In 2011, there were no changes in resistance levels compared to previous years (Table Dog I), and resistance to ampicillin was the most common trait.

The isolates were tested for susceptibility to cefotaxime as an indicator of ESBL production. The ten isolates with MIC of cefotaxime >0.5 mg/L were further tested and all were confirmed AmpC-producing. For more information on occurrence of ESBL or pAmpC in Sweden see highlights:"*Enterobacteriaceae* producing extended spectrum beta-lactamases (ESBL)–isolates from diagnostic submissions", "*Escherichia coli* with ESBL- or transferrable AmpC-type resistance in production animals" and "*Escherichia coli* with ESBL or pAmpC in meat obtained from the Swedish market".

Multiresistance occurred in 5% of the isolates and this figure is on the same level as last year. Of the multiresistant isolates, 56% were resistant to at least ampicillin, trimethoprim-sulphonamide and tetracycline. Only three *E. coli*-isolates were resistant to five or more antimicrobials i.e. <1% of all isolates.

Staphylococcus pseudintermedius

Isolates of *Staphylococcus pseudintermedius* included are from skin samples. In 2005, *S. pseudintermedius*, a novel staphylococcal species was described (Devriese et al., 2005). Further on Sasaki et al. (2007) and Bannoehr et al. (2007) reported that canine strains of *S. intermedius* should be classified as *S. pseudintermedius*. Therefore, it was proposed to report strains from dogs as *S. pseudintermedius*, unless genomic investigations prove that the strain belongs to another related species (Devriese et al., 2009). Consequently, resistance data on *S. intermedius* from previous SVARM reports should be regarded as resistance data on *S. pseudintermedius*.

As in previous years, the prevalence of resistance to penicillin due to production of beta-lactamases (penicillinase) in *S.*

TABLE DOG I. Resistance (%) in *Escherichia coli* from dogs 1992-2011 and distribution of MICs for isolates from 2011. Isolates are from clinical submissions of urinary tract samples.

Antimicrobial	Resistance (%)								Distribution (%) of MICs (mg/L)									
	1992-94 n=245	1995-97 n=296	1998-00 n=418	2001-03 n=621	2004-06 n=917	2007-09 n=1527	2010 n=803	2011 n=661	≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	18	18	18	18	19	15	14	16				1.0	42.9	38.4	1.8	16.0		
Cefotaxime	-	-	-	-	-	<1	2	2			98.2	0.3	1.5					
Enrofloxacin[a]	9	9	10	9	10	8	8	10	90.0	3.1	2.9	1.5	0.3	0.3	1.9			
Gentamicin[b]	2	1	2	2	1	1	1	<1					97.0	2.2	0.5		0.3	
Nitrofurantoin	3	3	1	2	2	1	1	<1								97.5	1.6	0.8
Polymyxin B	-	-	-	-	-	4	3	4					96.3	2.5	1.2			
Tetracycline	16	14	12	11	10	8	8	7				16.3	70.8	5.7	0.3	7.0		
Trim-Sulph[c].	9	8	11	13	15	9	5	8			91.0	1.4	0.3	0.3	7.1			

[a] Cut-off value >0.25 mg/L until 2002; [b] Cut-off value >8 mg/L until 2001; [c] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphametoxazole) and cut-off value >4 mg/L until 2001.

pseudintermedius is high, 84% (Table Dog II). Already in the late 70s, 70% of *S. pseudintermedius* were resistant to penicillin (Franklin, 1978) and during the last two decades, the resistance frequency has been around 80-90%. Besides penicillin, resistance to clindamycin, erythromycin, fusidic acid or tetracycline was common in 2011, as in previous years.

At SVA, all isolates of *S. pseudintermedius* with oxacillin MIC >0.5 mg/L are examined for *mecA* gene with PCR (see Appendix 3 for details). In this material 8 isolates (2%) had MICs above this breakpoint and in seven of these the *mecA* gene was detected. The CLSI breakpoint for *S. pseudintermedius* (>0.25 mg/L) is not applicable on this data because of the oxacillin range in the microdilution panels used. For further information on MRSP, see highlight on "Methicillin resistant *S. pseudintermedius*".

Multiresistance occurred in 36% of the isolates. Twenty seven isolates (7%) were resistant to five or more antimicrobials and a third of these were MRSP. Resistance to penicillin, clindamycin and erythromycin was the most common phenotype, occurring in 66% of multiresistant isolates. Almost a third of these were also resistant to tetracycline. Macrolide resistance in *S. pseudintermedius* is commonly mediated by *erm*-genes, and if these genes are constitutively expressed, the bacteria will be resistant also to lincosamides (clindamycin) and streptogramin B. In this material, 77% of isolates resistant to erythromycin were also resistant to clindamycin. Resistance to enrofloxacin occurred mainly in multiresistant phenotypes.

In this material, there is a high probability of bias towards dogs with recurrent skin infections, previously treated with antimicrobials which could explain the high levels of resistance. A prospective study by Holm et al., (2002) showed higher levels of multiresistance among isolates from recurrent compared to those from first-time pyoderma. Pyoderma is a common cause for dog owners to seek veterinary consulta-

TABLE DOG II. Resistance (%) in *Staphylococcus pseudintermedius* from dogs 1992-2011 and distribution of MICs for isolates from 2011. Isolates are from clinical submissions of samples from skin.

Antimicrobial	Resistance (%)								Distribution (%) of MICs (mg/L)									
	1992-94 n=304	1995-97 n=322	1998-00 n=433	2001-03 n=382	2004-06 n=374	2007-09 n=859	2010 n=444	2011 n=388	≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Cephalothin	<1	<1	0	1	1	3	4	2					97.7	0.3	2.1			
Clindamycin	12	20	21	18	19	23	26	24				74.7		1.0	24.2			
Enrofloxacin	-	-	-	2[e]	2	5	6	6	60.3	30.2	3.9	3.1	0.8		1.8			
Erythromycin[a]	21	28	27	24	26	28	30	30			69.3	0.3			30.4			
Fusidic acid	9	14	20	20	25	24	20	24					74.7	1.8	23.5			
Gentamicin	<1	<1	<1	0	1	3	3	2					96.9	0.8	1.5	0.8		
Nitrofurantoin	1	1	<1	1	<1	<1	2	1								98.2	0.5	1.3
Oxacillin	1	2	1	2	2	1	4	2			97.7	0.3	2.1					
Penicillin[b]	79	80	80	80	84	87	86	84										
Tetracycline	24	12	28	25[g]	32	30	31	26				72.7	1.3	0.3		25.8		
Trim-Sulph[c]	1	2	1	3	6	5	6	6			69.1	24.5	0.5	0.8	5.2			

[a]Cut-off value >4 mg/L until 2001; [b] Denotes betalactamase production; [c] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphamethoxazole).

tion and this condition is often treated with clindamycin or cephalosporins. Fortunately, sales of antimicrobials for dogs continue to decline (See 'Use of antimicrobials'). To control the resistance situation in *S. pseudintermedius*, a prudent use of antimicrobials together with an effective infection control programme is of highest priority.

Pseudomonas aeruginosa

Isolates of *Pseudomonas aeruginosa* are from samples from the external ear canal. This bacterial species is considered clinically resistant to e.g. trimethoprim-sulphonamides, tetracyclines and aminopenicillins (including combinations with clavulanic acid). Fluoroquinolones, gentamicin and polymyxin B, are substances often used to treat pseudomonal ear infections in dogs and, the susceptibility data of these substances are, therefore, presented in Table Dog III. All isolates were susceptible to polymyxin B. However, resistance to gentamicin or enrofloxacin occurred and one isolate was resistant to both substances.

In addition, the maximum plasma concentration (C_{max}) of the fluoroquinolones currently licensed for use in dogs in Sweden, after oral treatment at the label dosage, ranges from 1.5-2.5 mg/L. To have beneficial effect of treatment, the C_{max} to MIC ratio should preferably be >4 (Walker & Dowling, 2006). It is clear that the ratio will not be reached in most infection sites after systemic administration even for the more susceptible isolates.

TABLE DOG III. Resistance (%) in *Pseudomonas aeruginosa* from dogs years 2002-2003, 2009-2011, and distribution of MICs for isolates from 2011. Isolates are from clinical submissions of samples from the ear canal of dogs.

Antimicrobial	**Resistance** (%)				**Distribution** (%) **of MICs** (mg/L)									
	2002-03 n=234	**2009** n=261	**2010** n=313	**2011** n=353	**≤0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**>32**
Enrofloxacin	NA[a]	25	20	12	1.4	1.7	11.3	48.7	24.6	6.5	5.7			
Gentamicin	9	5	2	2					81.3	12.5	4.2	1.1	0.8	
Polymyxin B	-	0	0	0					96.5	3.5				

[a]NA= not applicable because of the range of enrofloxacin concentrations tested.

Methicillin resistant *Staphylococcus pseudintermedius* (MRSP)

THE FIRST METHICILLIN RESISTANT *S. pseudintermedius* (MRSP) isolated in Sweden was from a healthy dog in a screening for methicillin resistant *S. aureus* in 2006 and since 2008, methicillin resistant coagulase positive staphylococci are notifiable in Sweden. On suspicion of MRSP, diagnostic laboratories are advised to send the isolates to the National Veterinary Institute (SVA) for confirmation by PCR of the presence of *mecA* gene.

The number of MRSP isolates notified to the Board of Agriculture in Sweden since 2008 is shown in Figure. Data for 2006-2007 in the figure, before MRSP was notifiable, correspond to the number of isolates sent to SVA and confirmed *mecA*-positive. MRSP have mostly been isolated from dogs but also from a few cats and two horses. The notified numbers have declined during the last two years but if there is a true reduction in the number of animals infected with MRSP is uncertain.

In 2011, 60 MRSP isolates were confirmed at SVA: 59 dogs and one cat. In 26% of the cases, MRSP were isolated from skin samples, 21% were isolated from wounds and the rest originated from miscellaneous sampling sites. Of the isolates from skin and wounds, 29 were randomly selected for further analyses. A majority of the 29 isolates (26) belonged to *spa*-type t02 and carried staphylococcal chromosomal cassette (SCC) *mec* II-III. One isolated belonged to *spa*-type t29 with SCC*mec* II-III while the other two isolates were non-typeable with *spa*-typing and had SCC*mec* II-III and a non-typeable SCC*mec*, respectively. Pulsed field gel electrophoresis (PFGE) analysis of 20 isolates of the 29 revealed that isolates in Sweden are related and that they display a high relatedness with the European clone ST71-J-t02-II-III described by Perreten and co-workers (2010).

Of the 29 isolates from 2011 tested further 12 (41%) were susceptible to chloramphenicol, tetracycline and fusidic acid, eight were susceptible to chloramphenicol, tetracycline, fusidic acid and gentamicin while three isolates were susceptible to tetracycline, fusidic acid and gentamicin. The other six isolates displayed varied antibiograms but they were all multiresistant.

In 2006 and 2007, most of the MRSP isolates had a characteristic antibiogram, being susceptible only to two of the substances in Sweden licensed for use in dogs i.e.: fusidic acid and tetracycline (SVARM 2007). In 2008, the first isolates resistant to tetracycline were detected. In 2011, of the 29 isolates tested further, two isolates were resistant to tetracycline and three were resistant to fusidic acid. One isolate was resistant to both these substances but on the other hand susceptible to fluoroquinolones.

Since the first cases of MRSP, there have been active discussions among veterinarians on how to prevent further spread and how to correctly use antimicrobials. For instance, in many animal clinics and hospitals, infection control programmes have been implemented with focus on strict hand hygiene routines. Also, veterinarians, with special interest in dermatology have agreed on an antimicrobial policy for treatment of dogs with dermatological disorders.

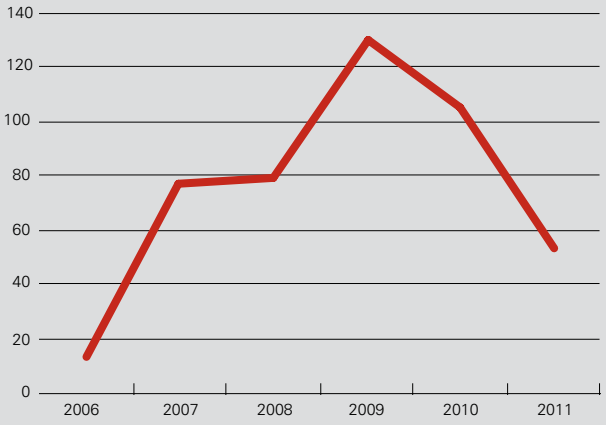


FIGURE. The number of cases of methicillin resistant *Staphylococcus pseudintermedius* notified to the Swedish Board of Agriculture 2008-2011. Data for 2006-2007 represent isolates that were sent to SVA and confirmed *mecA* positive.

Cats

Escherichia coli

Isolates of *Escherichia coli* are from samples of urine, submitted either as urine or as dip-slide cultures. Resistance to ampicillin was the most common trait (Table Cat I).

In 2011, 3% of the isolates were multiresistant and this figure is on the same level as last year. The most common resistance traits among the multiresistant isolates were; ampicillin, trimethoprim-sulphonamides and tetracycline which occurred in 44% of these isolates. None of the isolates were resistant to five or more antimicrobials.

One isolate had a MIC >1 mg/L of cefotaxime and was confirmed as ESBL-producing. For more information on occurrence of ESBL or pAmpC in Sweden see highlights:"*Enterobacteriaceae* producing extended spectrum beta-lactamases (ESBL) – isolates from diagnostic submissions", "*Escherichia coli* with ESBL- or transferrable AmpC-type resistance in production animals" and "*Escherichia coli* with ESBL or pAmpC in meat obtained from the Swedish market".

Cats with symptoms from the urinary tract are often treated with aminopenicillins or fluoroquinolones. This year, six isolates were resistant to both these antimicrobials, i.e. about 1.5% of all isolates. However, bacterial urinary tract infections are rare in cats and other causative agents or underlying causes have to be investigated prior to antimicrobial treatment.

Beta-hemolytic streptococci

The most commonly isolated species of beta-hemolytic streptococci in cats is *Streptococcus canis* (Lancefield group G). This is true both for healthy cats and cats with signs of infection. Streptococci isolated from clinical samples from cats submitted to SVA are not identified to species level and therefore antimicrobial susceptibility data for the group beta-hemolytic streptococci are presented (Table Cat II). In cats *S. canis* can cause a variety of infections such as metritis, mastitis, skin infections and septicemia in kittens. The isolates of beta-hemolytic streptococci included are from infections in various organs of cats for example the ears, the upper airways and the urogenital tract.

True penicillin resistance has never been reported for any beta-hemolytic streptococci. Recently, however, decreased susceptibility in *S. agalactiae* (Lancefield group B) has been associated to mutations causing amino acid substitutions in penicillin binding protein 2X (Kimura et al., 2008). Nonetheless these are very rare isolates and if reduced susceptibility to penicillin is recorded in any beta-hemolytic streptococci a renewed species identification and susceptibility test should be performed. One of the isolates included was penicillin resistant (MIC >1 mg/L) and the resistance phenotype indicates that this can most likely be explained by an enterococcal species mistakenly identified as a beta-hemolytic streptococci. Because the isolate was not saved this could not be verified. If this isolate is discounted all isolates were susceptible to beta-lactam antibiotics and only one isolate was resistant to trimethoprim-sulphametoxazole. Clindamycin resistance was recorded in 14% of the isolates. All of these were also resistant to erythromycin and with the exception of one isolate also to tetracycline. Such coupled resistance in *Streptococcus* spp. is typically caused by *erm* and *tet* genes carried together on transposons. The highest occurrence of resistance was to tetracycline (32%).

Beta-hemolytic streptococci have a low inherent susceptibility to fluoroquinolones and aminoglycosides and it can be observed that MICs are above concentrations that can be obtained during systemic therapy with these antimicrobials.

TABLE CAT I. Resistance (%) in *Escherichia coli* from cats 1992-2011 and distribution of MICs for isolates from 2011. Isolates are from clinical submissions of urine samples.

Antimicrobial	Resistance (%)							Distribution (%) of MICs (mg/L)									
	1992-94 n=61	1998-00 n=74	2001-03 n=135	2004-06 n=224	2007-09 n=546	2010 n=236	2011 n=273	≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	26	34	27	22	18	17	17				3.3	51.6	26.7	1.5	16.8		
Cefotaxime	-	-	-	-	3	1	2			98.2	1.5	0.4					
Enrofloxacin[a]	5	8	13	7	7	8	5	95.2	1.5	1.5	0.7	1.1					
Gentamicin[b]	0	3	-	-	1	<1	0					99.3	0.7				
Nitrofurantoin	2	2	1	3	1	1	3								96.0	1.5	2.6
Polymyxin B	-	-	-	-	6	3	4					96.0	2.9	1.1			
Tetracycline	28	16	16	14	8	6	8				23.8	64.5	3.7	0.4	7.7		
Trim-Sulph.[c]	7	10	15	7	5	4	3			96.3	0.4	0.7	0.4	2.2			

[a] Cut-off value >0.25 (mg/L) until 2002; [b] Cut-off value >8 mg/L until 2001; [c] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim-sulphamethoxazole), cut-off value >4 mg/L until 2001.

TABLE CAT II. Resistance (%) in beta-hemolytic streptococci from cats 2007-2011 and distribution of MICs for isolates from 2011. Isolates are from clinical submissions of samples from cats.

Antimicrobial	**Resistance** (%)	**Distribution** (%) **of MICs** (mg/L)									
	2007-11 n=184	**≤0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**>32**
Ampicillin	0				100						
Clindamycin	14				85.9			14.1			
Enrofloxacin	NR	1.6	0.5	21.2	65.8	10.9					
Erythromycin	15			81.5	1.1	1.1	1.1	15.2			
Gentamicin	NR					12.0	47.3	34.2	6.5		
Nitrofurantoin	2								96.7	1.6	1.6
Penicillin	<1	96.8	2.7			0.5					
Tetracycline	32				23.9	35.3	8.2	1.1	31.5		
Trim/Sulph.[a]	1			96.2	2.7			1.1			

[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.

Enterobacteriaceae producing extended spectrum beta-lactamases (ESBL) – isolates from diagnostic submissions

THIS HIGHLIGHT SUMMARISES information on ESBL producing bacterial isolates from diagnostic submissions. The isolates were referred to the Section of Antibiotics at SVA from other laboratories because of phenotypic resistance to third generation cephalosporins. The number of confirmed ESBL producing bacteria per year and animal species is shown in Table ESBL below.

In 2011, 14 isolates (from 13 horses) resistant to third generation cephalosporins were sent to SVA. All were confirmed phenotypically to be ESBL-producing; nine Escherichia coli and five *Enterobacter* spp. Of these, one *E. coli* isolate and two *Enterobacter cloacae* isolates produced both ESBL and AmpC. From one horse, both ESBL-producing *E. coli* and *Enterobacter* spp. were isolated. In six horses, the ESBL-producing bacteria originated from wound samples, five isolates were from the female genital tract and the remaining three isolates were from eyes and of unknown origin. All isolates were resistant to trimethoprim, sulphonamide and gentamicin. Resistance to tetracycline was found in 13 of the isolates and three isolates were resistant to fluoroquinolones. All isolates were susceptible to colistin and to florfenicol if the epidemiological cut-off (>16 mg/L) for *E. coli* is used to define resistance also in *Enterobacter* spp.

From dogs, 22 isolates resistant to third generation cephalosporins were sent to SVA during 2011 and nine of them were confirmed being phenotypically ESBL-producing (7 *E. coli*, 1 *Enterobacter cloacae*, and 1 *Enterobacter aerogenes*) and two isolates of *E. coli* were AmpC-producing (CMY-2).

Four of the ESBL-producing isolates originated from urine samples, two were of unknown origin while the others were isolated from various sites: furuncle, eye, vagina and peritoneum. Eight isolates were resistant to fluoroquinolones, five to trimethoprim and six to sulphonamides. One isolate of *Enterobacter cloacae* was resistant to gentamicin and chloramphenicol if the clinical breakpoint of >8 mg/L is used for the latter substance. All isolates were susceptible to colistin.
During 2011, one isolate of ESBL-producing *Klebsiella pneumoniae* was isolated from an abscess in a cat. This isolate was resistant to fluoroquinolones, tetracycline, trimethoprim and sulphonamide and was susceptible to gentamicin, chloramphenicol and colistin.

Routine diagnostic laboratories are advised to submit isolates of *Enterobacteriaceae* phenotypically resistant to third generation cephalosporins to the Section of Antibiotics at SVA, where confirmatory phenotypic and genotypic tests for ESBL and AmpC are performed (See Appendix 3). In a clinical condition where the patient needs to be treated with antimicrobials, multiresistant *Enterobacteriaceae* pose a challenge for the veterinarian, especially in horses, since the number of antimicrobials licensed is limited. Increased awareness of the need for infection control and antimicrobial stewardship is essential to minimize the spread of these resistant bacteria.

TABLE ESBL. Number of extended spectrum beta-lactamases (ESBL) producing *Enterobacteriaceae* isolated from diagnostic submissions from animals during 2008-2011.

Animal species	Bacterial species	2008	2009	2010	2011
Cats	*Enterobacter* spp.				
	Escherichia coli			2	
	Klebsiella oxytoca			1	
	Klebsiella pneumoniae				1
Dogs	*Enterobacter* spp.		1	2	2
	Escherichia coli	1		1	7
	Klebsiella pneumoniae		1		
Horses	*Enterobacter* spp.		1	3	5
	Escherichia coli	2	3	7	9
	Klebsiella pneumoniae		1	1	
	Escherichia hermanii			1	

Appendix 1: Demographic data

AGRICULTURAL STATISTICS are provided by Statistics Sweden in collaboration with the Board of Agriculture and published annually as a Yearbook of Agricultural Statistics and continuously as Statistical Messages (SM). The Yearbook and Statistical Messages are available on the Internet via the websites for Statistics Sweden (www.scb.se) or the Board of Agriculture (www.sjv.se).

Annual figures on number of animals and holdings are given in Table AP1 I & II, and on numbers and volumes of animals slaughtered in Table AP1 III & IV. Details on methodology as well as comments on the data can be found in the respective data sources.

Briefly, the total number of dairy cows, pigs and laying hens has decreased notably over the last three decades concomitantly with an increase in herd size. In the same period, the number of beef cows, sheep and chickens reared for slaughtered has increased. Data on horses are not available all years but since 2004 the number of horses has increased substantially.

TABLE AP1 I. Number of livestock and horses (in thousands) 1980-2011 (Yearbook of Agricultural Statistics Sweden 2001 & 2011 and Statistical Message JO 20 SM 1102 & JO 24 SM 1101).

Animal Species	1980[a]	1985[a]	1990	1995	2000	2005	2009	2010	2011
Cattle									
Dairy cows	656	646	576	482	428	393	357	348	346
Beef cows	71	59	75	157	167	177	192	197	196
Other cattle >1 year	614	570	544	596	589	527	502	512	495
Calves <1 year	595	563	524	542	500	508	488	479	475
Total, cattle	1 935	1 837	1 718	1 777	1 684	1 605	1 538	1 537	1 512
Sheep									
Ewes & rams	161	173	162	195	198	222	254	273	297
Lambs	231	252	244	266	234	249	287	292	326
Total, sheep	392	425	406	462	432	471	540	565	623
Pigs									
Boars & sows	290	260	230	245	206	188	160	156	153
Fattening pigs >20 kg [b]	1 254	1 127	1 025	1 300	1 146	1 085	943	937	901
Piglets <20kg [c]	1 170	1 113	1 009	769	566	539	426	427	429
Total, pigs	2 714	2 500	2 264	2 313	1 918	1 811	1 529	1 520	1 483
Laying hens									
Hens	5 937	6 548	6 392	6 100	5 670	5 065	5 261	6 061	6 376
Chickens reared for laying	2 636	2 159	2 176	1 812	1 654	1 697	1 898	1 647	1 828
Total, hens	8 573	8 708	8 568	7 912	7 324	6 762	7 159	7 707	8 204
Turkeys									
Total, turkeys						122		130	
Horses									
Total, horses						283[d]		363	

[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 AP1 II. Number of holdings with animals of different types, 1980-2009 (Yearbook of Agricultural Statistics, Sweden 2001 & 2011 and Statistical Message JO 20 SM 1102 & JO 24 SM 1101).

Animal Species	1980	1985	1990	1995	2000	2005	2009	2010	2011
Cattle									
Dairy cows	44 143	35 063	25 921	17 743	12 676	8 548	6 020	5 619	5 260
Beef cows	12 436	10 310	10 883	17 069	13 861	12 821	11 922	12 190	11 809
Other cattle >1 year	63 179	52 652	42 696	39 160	30 457	24 808	20 330	20 295	19 107
Calves <1 year	62 314	52 001	41 986	36 542	27 733	22 888	18 965	18 494	17 721
Total holdings with cattle	70 503	58 872	47 292	41 990	32 063	26 179	21 733	21 586	20 503
Sheep	10 238	10 595	9 749	10 037	8 089	7 653	8 245	8 657	9 449
Pigs	26 122	19 937	14 301	10 753	4 809	2 794	2027	1 695	1 515
Laying hens	23 603	17 531	12 900	9 593	5 678	4 916	3 306	3 703	3 827
Chickens reared for laying	5 093	2 714	1 875	1 405	715	634	573	487	733
Broilers						234	183	181	202
Turkeys						383		102	
Horses						56 000[a]		78 000	

[a] Data from 2004.

TABLE AP1 III. Number of animals slaughtered (in thousands) at slaughterhouses, 1980-2009. (Yearbook of Agricultural Statistics, Sweden 1981, 1986, 1991 & 2009 and Statistical Message JO 48 SM 1203).

Animal Species	1980	1985	1990	1995	2000	2005	2009	2010	2011
Cattle									
Cattle >1 year	574	584	523	502	490	433	430	425	429
Calves < 1 year	130	152	70	30	39	33	29	27	27
Total, cattle	704	736	593	532	529	466	459	453	456
Sheep	302	328	280	189	202	206	255	255	262
Pigs	4 153	4 283	3 653	3 743	3 251	3 160	2 956	2 936	2 845
Broilers	40 466[a]	36 410[a]	38 577[a]	61 313	68 617	73 458	73 504	78 507	78 182
Turkeys							477	495	574

[a] Data supplied by the National Food Administration.

TABLE AP1 IV. Quantity of livestock slaughtered (in 1000 tonnes) at slaughterhouses, 1990-2009 (Yearbook of Agricultural Statistics, Sweden 1991 & 2009 and Statistical Message JO 48 SM 1202).

Animal Species	1990	1995	2000	2004	2005	2009	2010	2011
Cattle								
Cattle >1 year	139.5	140.1	145.4	137.8	131.4	135.4	133.5	133.5
Calves < 1 year	6.8	3.2	4.4	4.6	4.5	4.6	4.3	4.4
Total, cattle	146.3	143.3	149.8	142.4	135.9	140.0	137.8	138.2
Sheep	5.0	3.5	3.9	3.8	4.1	5.1	5.0	5.1
Pigs	293.1	308.8	277.0	294.5	275.1	261.7	263.5	256.1
Broilers	44.0[a]	73.6[a]	89.9	91.2	96.2	105.2	112.0	111.5
Turkeys						3.0	3.2	3.7

[a] Data supplied by the National Food Administration.

Appendix 2: Materials and methods, use of antimicrobials

Legal framework and distribution of medicines

Marketing of drugs in Sweden is regulated by the Medicinal products act, which applies both to human and veterinary medicinal products (VMPs). 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 veterinary medicinal products for a certain condition, the MPA can permit special license prescription for a VMP for a specified pharmacy and prescriber. VMPs have to be dispensed through pharmacies, which are supplied by drug wholesalers or manufacturers. Veterinarians are not allowed to sell VMPs but may deliver products to the animal care-taker in relation to examination of a case, however, for self cost (no profit). Veterinarians are not permitted to own a pharmacy.

Antimicrobial drugs for veterinary use, including medicated feed, may only be sold on prescription.

All pharmacies in Sweden are required to provide prescription statistics on a daily basis to an infrastructure company owned by the state: Apotekens Service. For VMPs, the animal species as given on the prescription is also recorded, unless the product is sold for use in veterinary practice. Apotekens Service maintains a database 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. The feed mills normally acquired the antimicrobial VMPs from a pharmacy. All quantities of VMPs used by feed mills are reported yearly to the Board of Agriculture as part of the feed control. Mixing of antimicrobials in feed may also take place on farms; provided that the Board of Agriculture has inspected and authorised the establishment for the purpose. In such cases, the premix is sold by a pharmacy following prescriptions from a veterinarian.

Data sources and inclusion criteria

Raw data on sales is obtained from Apotekens Service and represent the sales of antimicrobial VMPs sold by pharmacies. For the overall statistics (Table AC I-III), the data include all antimicrobial VMPs marketed in Sweden and sold for use in terrestrial animals in the ATCvet classes QA, QG and QJ. Previously, most antimicrobial VMPs sold with special license (products prescribed and sold on exemption from general Swedish market authorization) were also included. However, in 2011 it was noticed that the information on sales of products with special license was less complete than in previous years (see comments in chapter on use of antimicrobials). Medicinal products authorised for human use but prescribed for use in animals is not included in the overall statistics.

The ionophoric antibiotics are presently regulated as feed additives and not sold through pharmacies and are not included in the statistics from Apotekens Service. However, the Board of Agriculture collects figures on sales of ionophores from the feed mills as a part of the feed control system. As the source differs, data on ionophores are given only in Table AC III.

Data for year 2011 published by the Board of Agriculture is used to present the repartition of the sales per category of animals (Table IV) (www.jordbruksverket.se). The data include VMPs in the same ATCvet classes as given above and in addition products authorised for human use but sold for use in animals for the corresponding classes are included. The attribution to species is done using data from electronic records of prescriptions from pharmacies. Efforts are made to assign the sales of products sold for use in veterinary practice to species or to a category of animals (companion or food producing animals) as far as possible, using information on e.g. which animal species a particular product is authorised for.

The electronic records on animal species as specified on the prescription are also used to obtain data on number of prescriptions and packages sold specifically for use in dogs. That dataset closely corresponds to what is called “out-patient use”.

The data coverage is assumed to be very high. In rare cases, premixes mixed in medicated feed may be delivered from feed mills without the sales being recorded by a pharmacy. Examination of the reports by all feed mills to the Board of Agriculture shows that this happened only once during 2005-2009 (a total quantity of 40 kg active substance). In addition, as mentioned some drugs sold on special licence have not been captured in 2011.

Analysis and reporting of data

Data are retrieved as number of packages sold per product presentation and per animal species, if recorded. Calculation to kg active substance is done based on product information obtained from the national product register of the MPA.

Data on sales of antimicrobials for animals has been analysed and reported by the SVA since 1980. SVA is responsible for monitoring antimicrobial resistance but not of use, but still monitors use to support work on its mandate to stimulate rational use of antimicrobials. Statistics on usage is published in English in the yearly reports of the Swedish Veterinary Antimicrobial Resistance Monitoring programme. Since 2005, the Board of Agriculture is responsible for statistics on use of certain veterinary medicinal products, including antimicrobials. Board of Agriculture publishes the results in Swedish in an electronic report on sales of certain drugs for animals. Data are reported by companion or production animals (including horses), and to the extent possible also by specific animal species.

Appendix 3: Materials and methods, resistance monitoring

Sampling strategy

Zoonotic bacteria

Salmonella

Salmonellosis in animals is a notifiable disease in Sweden and isolates from each notified incident must be confirmed at SVA. Data presented in SVARM are from susceptibility testing of these isolates. The summary for each year include one isolate of each serovar, and when appropriate phage-type, from each warm-blooded animal species in incidents notified. In addition, isolates from incidents previously notified and still under restrictions are included in the yearly statistics. Also included are isolates obtained in the salmonella surveillance programme from samples collected at slaughter (carcass swabs, neck skins and lymph nodes).

Campylobacter

Campylobacter from pigs were cultured from samples of colon content collected at abattoirs for isolation of indicator bacteria (see below). From the total number of samples collected about one fourth was selected for culture. The selection was made sequential but ensuring that cultured samples were distributed between abattoirs according to annual slaughter volume and evenly distributed over the sampling periods. Each isolate of *Campylobacter coli* or *C. jejuni* is from a unique herd.

Methicillin resistant *Staphylococcus aureus* (MRSA)

Findings of MRSA in animals are notifiable in Sweden and hitherto all isolates from notified incidents have been confirmed at SVA. For surveillance strategies see Zoonotic bacteria MRSA.

In the screening for MRSA in pigs in 2011, 53 nucleus and multiplying herds were sampled. In each herd, samples were taken in fifteen pens with weaned pigs, 5-12 weeks old. The pigs were sampled by rubbing the skin behind one ear with a sterile compress. The same compress was used on 6 pigs in one pen and analyzed at the lab as a pooled sample. The sampling was organized by the Swedish Animal Health Service (SvDHV) and all samples were cultured at SVA.

Indicator bacteria

Pigs

Indicator bacteria, *Escherichia coli* and *Enterococcus* spp. from intestinal content were isolated from colon content of healthy pigs. Samples were collected at slaughter under the supervision of the National Food Agency (SLV) at nine abattoirs that together processed more than 90% of the total number of pigs slaughtered in Sweden 2010.

At each abattoir, an equal number of samples were collected during each of two periods (March-May, September-November). 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 represents a unique herd. By these measures, bacterial isolates included are from randomly selected healthy pigs of Swedish herds. Each isolate of *Escherichia coli*, *Enterococcus faecalis* and *Enterococcus faecium* is from a unique herd.

Pig meat

Indicator bacteria from pig meat were isolated from samples collected at cutting plants. Samples were collected under the supervision of SLV at ten cutting plants each processing more than 100 tons of pig meat in 2010.

Each cutting plant collected ten samples of processed meat packed for retail. At each plant, two samples were collected weekly for five consecutive weeks starting in November 2011. Samples were kept frozen at -18°C before and during shipment to SVA for culture.

Broilers

Selective culture for *E. coli* resistant to third generation cephalosporins was performed on caecal content from healthy broilers sampled at slaughter. Samples cultured were from the Swedish Campylobacter programme in which whole caeca are collected from each batch of broilers slaughtered. From these samples, 100 were selected by convenience in June and November for culture. Each sample is from a unique flock but not always from a unique production site.

Animal pathogens

Isolates of animal pathogens included are from routine bacteriological examinations of clinical submissions or post-mortem examinations. Isolates of *Actinobacillus pleuropneumoniae* and *Streptococcus equisimilis* 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 *E. coli* from pigs are isolated from the gastrointestinal tract (gut content, faecal samples or mesenteric lymph nodes) 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* emanate from tissue samples from lungs sampled post mortem and isolates of *Pasteurella* spp. from cattle from the respiratory tract. Isolates of *S. equisimilis* are isolated from joints of piglets with arthritis sampled post mortem.

In horses, *E. coli* are isolated from the genital tract of mares, *Streptococcus zooepidemicus* from the respiratory tract and *S. aureus* from skin samples. In dogs, *E. coli* are isolated from samples of

urine, *S. pseudintermedius* from skin samples and *Pseudomonas aeruginosa* from samples in the external ear. *E. coli* from cats are isolated from samples of urine and beta-hemolytic streptococci are from infections in various organs for example the ears, the upper airways and the urogenital tract.

In farmed fish, *Aeromonas salmonicida* subsp. *achromogenes*, *Flavobacter columnare* and *Flavobacter psychrophilum* are from post mortem examination.

Isolation and identification of bacteria

Zoonotic bacteria

Salmonella

Salmonella were isolated and identified at the Dept. of Bacteriology, 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-EN 6579:2002/ Amd 1:2007). Confirmatory identification and serotyping of isolates was performed at the Dept. of Bacteriology, SVA according to the standard procedures of Kaufmann and White. The Dept. of Bacteriology, SVA is accredited for isolation, identification and serotyping of *Salmonella*.

Isolates of *Salmonella* Typhimurium and *S.* Enteritidis were phage-typed by the Swedish Institute for Infectious Disease Control (SMI), Stockholm using the Colindale scheme.

Campylobacter

Campylobacter spp. from pigs were isolated and identified at Dept. of Animal Health and Antimicrobial Strategies, SVA. Briefly, samples were cultured directly on Preston selective agar for thermophilic *Campylobacter* spp. and incubated at 42°C for 48h. Identification was based on colony morphology, microscopic appearance including motility and the production of oxidase and catalase. Additionally, all isolates of *C. coli* and *C. jejuni* were identified by PCR. A protocol from Denis et al. (1999) was followed except for the primer concentration for *mapA* and *ceuE* that was lowered to 0.24 µM. This PCR is used for species identification by the EURL campylobacter laboratory at SVA.

Methicillin resistant *Staphylococcus aureus* (MRSA)

In the screening of pigs for MRSA, samples were incubated overnight at 37°C in 30 ml Mueller-Hinton broth with 6.5% NaCl. From this pre-enrichment broth, 1 mL was inoculated into 9 mL trypton soy broth with 3.5 mg/L cefoxitin and 75 mg/L aztreonam and incubated overnight at 37°C. Of the selective broth 10 µL was spread on bovine-blood agar and on Oxoid MRSA Brilliance-agar. The plates were incubated at 37°C and inspected after overnight incubation and after 48 hours. Colonies of suspected MRSA were spread on bovine-blood agar plates with a cefoxitin disc and incubated overnight at 37°C. Isolates with suspected cefoxitin resistance (zone diameter < 10 mm) were confirmed with genotypic methods.

Indicator bacteria

Escherichia coli

Approximately 0.5 g of caecum content from pigs was diluted in 4.5 mL isotonic saline. After thorough mixing, 0.1 mL of this suspension was spread on MacConkey agar and MacConkey agar with cefotaxime 1mg/L and incubated overnight at 37°C. Twenty-five g of pig meat was stomached in 2 min with 225 mL BPW (Buffered Pepton Water). Thereafter 20 mL was transferred to 20 mL double concentrated MacConkey broth and incubated at 37°C for 18-24 h. From the pre-enrichment 100 µL was spread on MacConkey agar and incubated overnight at 37°C.

For selective culture for *E. coli* resistant to third generation cephalosporins in broilers, approximately 0.5 g of caecum content from was diluted in 4.5 mL isotonic saline. After thorough mixing, 0.1 mL of this suspension was spread on MacConkey agar with cefotaxime 1mg/L and incubated overnight at 37°C.

For species confirmation, one lactose positive colony with morphology typical for *E. coli* was sub-cultured onto 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. Colonies growing on MacConkey agar with cefotaxime were sub-cultured on horse-blood agar (5% v/v) and further tested for ESBL production.

Enterococci

Caecum content from pigs was diluted as described for *E. coli* (see above) and cultured on solid media without antibiotics. Diluted caecum content (0.1 mL) was spread onto Slanetz-Bartley (SlaBa) agar. The plates were incubated for 48 h at 37°C.

For isolation of enterococci from meat, 20 mL of the BPW from stomached pig meat (see above) was mixed with 20 mL double concentrated Enterococcosel broth, incubated at 37°C overnight. From the Enterococcosel broth 100 µL was cultured on SlaBa agar and incubated at 37°C for 48 h.

From cultures of caecal content from pigs and from pig meat two colonies, randomly chosen, were sub-cultured on bile-esculin agar and blood agar (37°C, 24 h). Colonies with morphology consistent with enterococci, and with a positive reaction on bile-esculin agar were identified to species level according to Devriese et al. (1993) by use of the following biochemical tests: mannitol, sorbitol, arabinose, saccharose, ribose, raffinose and methyl-alfa-D-glucopyranoside. Only isolates of *E. faecium* and *E. faecalis* were tested for antimicrobial susceptibility.

Animal pathogens

Most isolates of animal pathogens were isolated and identified with accredited methodology, following standard procedures at SVA. Some strains from calves and pigs were sent to SVA from other clinical laboratories. Bacteria from terrestrial animals were isolated at the Dept. of Bacteriology, and bacteria from fish at the Dept. of Animal Health and Antimicrobial Strategies.

Susceptibility testing

Microdilution

At SVA, the Dept. of Animal Health and Antimicrobial Strategies or the Dept. of Bacteriology perform antimicrobial susceptibility tests on bacteria from terrestrial animals, with accredited methodology, using dilution methods in cation adjusted Mueller-Hinton broth (CAMBH) (Difco). Tests are performed following the standards for microdilution of the Clinical and Laboratory Standards Institute (CLSI, 2008). The microdilution panels used, VetMIC, are produced at the Dept. of Vaccines and Blood products, SVA. 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 antimicrobial that inhibits bacterial growth.

The Dept. of Animal Health and Antimicrobial Strategies perform antimicrobial susceptibility tests on bacteria from fish, using the same methodology as described above but adapted for aquatic bacteria according to Alderman & Smith (2001), which e.g. implies incubation at 20°C for two days.

For susceptibility testing of *Brachyspira hyodysenteriae* and *Brachyspira pilosicoli*, a broth dilution method is used (Karlsson et al., 2003). The antimicrobials are dried in serial twofold dilutions in the 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). The trays were incubated in an anaerobic atmosphere at 37°C for four days on a shaker.

For susceptibility testing of *Campylobacter* spp. the CLSI standard M45-A2 for fastidious bacteria was followed (CLSI, 2010).

Screening for methicillin resistance in *S. aureus* from milk samples from cows was performed with microdilution according to CLSI (2008), testing oxacillin with 2% NaCl added to the broth, and oxacillin without added NaCl and cefoxitin.

Phenotypic confirmatory test for production of extended spectrum beta-lactamases (ESBLs) in *E. coli* was performed by the double disc diffusion test according to CLSI (2008).

Genotyping

Suspected isolates of *S. aureus* was confirmed by PCR identifying the *nuc* gene (Sasaki et al. 2010). Presence of the *mecA* gene in *S. aureus* and *S. pseudintermedius* was confirmed by PCR in isolates with a phenotype indicating methicillin resistance (Nilsson et al. 2005). To identify the *mecA* homologue $mecA_{LGA251}$ PCR was performed as described by García-Álvarez et al. (2011). If negative with the PCR by Nilsson et al. (2005) but positive by García-Álvarez et al. (2011) the isolates were determined to carry $mecA_{LGA251}$.

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. It was performed according to the method described by Harmsen et al. (2003) and the specific *spa* type was determined using BioNumerics® (Applied Maths).

Genotypic screening of ESBL and AmpC positive *E. coli* was performed with PCR for identification of plasmid-mediated AmpC and CTX-M mediated ESBL according to Perez-Perez & Hanson (2002) and Woodford et al. (2006).
The specific gene variants were determined by sequencing using in-house primers and Big-Dye™ v1.1. or submitted to Macro Gene Inc. (South Korea) for sequencing.

Quality assurance system

The Dept. of Animal Health and Antimicrobial Strategies and Dept. of Bacteriology are accredited according to SS-EN ISO/IEC 17025 by the Swedish Board for Accreditation and Conformity Assessment (SWEDAC) to perform antimicrobial susceptibility tests with microdilution methods. The Dept. of Bacteriology is also accredited for isolation and identification of animal pathogens and *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* CCUG15915 (analogue to ATCC 29213) 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 for animal pathogens. For testing of *Brachyspira*, the *B. hyodysenteriae* type strain $B78^T$ $ATCC\ 27164^T$ was used for quality control.

The Dept. of Animal Health and Antimicrobial Strategies participates in several proficiency tests for antimicrobial susceptibility testing. These are arranged either by the European Union Reference Laboratory - Antimicrobial resistance or as national studies. Likewise, the Dept. of Bacteriology participates in proficiency tests concerning isolation and identification of *Salmonella* spp. and general clinical veterinary bacteriology and susceptibility tests.

Data handling

Records on *Salmonella* and animal pathogens such as source of cultured sample, identification results, antimicrobial susceptibility etc. were registered in a database at SVA. Relevant data were extracted for evaluation and compilation. For indicator bacteria data was recorded in an Access database at the Dept. of Animal Health and Antimicrobial Strategies.

Calculations and analysis of data were performed in the computer programs Microsoft Access or Microsoft Excel.

Concerning confidence limits

When the prevalence of antimicrobial resistance is close to zero, e.g. when one out of 120 isolates is resistant, the question arises how to calculate the prevalence of resistance and its confidence intervals. In the example, the prevalence could be estimated to 0.83% while the 95% confidence interval is trickier. The normal approximation to the binomial distribution would give a lower confidence of -0.8% and an upper confidence limit of 2.5%. The lower limit is nonsensical and indicates the unsuitability of the normal approximation in this case.

One way out of the dilemma is to calculate the exact binomial confidence limits, which would be possible in some cases (small number of isolates). Another alternative is to run Monte-Carlo simulations based on the beta-distribution which is possible but quite laborious for a huge set of data since each prevalence estimate has to be simulated 10 000 times. Finally the relationship between the F-distribution, the beta-distribution and the binomial distribution can be used. This gives the formulae that enable calculations of the confidence interval (Rao, 1965). Using this approach, the confidence intervals in the example would be 0.021% and 4.6%.

In conclusion, the normal approximation to the binomial distribution might be unsuitable when the prevalence is close to 0% or close to 100% since the approximation might lead to confidence intervals lower than 0% or higher than 100%. Moreover, when the prevalence of resistance is less than 5% using the link between the F-distribution and the binomial distribution yield different confidence intervals compared to those obtained from the normal approximation and should accordingly be preferred.

Appendix 4: Cut-off values for resistance

FOR INTERPRETATION of results of susceptibility testing of zoonotic bacteria (*Salmonella* and *Campylobacter*) and indicator bacteria (*Escherichia coli* and enterococci) epidemiological cut-off values (ECOFF) issued by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) (http://www.escmid.org) were used. When no ECOFFs are issued by EUCAST, values based on MIC distributions obtained in the SVARM programme were used.

ECOFFs were used when available also for animal pathogens. When no ECOFFs were available, or the range of concentrations tested is inappropriate for a recommended value, values based on MIC distributions obtained in the SVARM programme were used. Clinical breakpoints issued by CLSI (2008) were also taken into consideration. Epidemiological cut-off values classify isolates with acquired reduced susceptibility as resistant, which is relevant for monitoring purposes, but it should be understood that this not always implies clinical resistance.

Bacitracin values in this report are given in units/mL. In an attempt to convert unit/mL to mg/L we discovered that there appears to be some confusion in the matter. The bacitracin compound used in SVARM is obtained from Sigma and meets the standards set by the United States Pharmacopoeia (USP), stating that one unit is equivalent to 26 µg of the US standard. However, according to the International Standard Preparations, one international unit is equivalent to 13.51 µg. On the other hand, if the bacitracin is of a very high degree of purity, though unstable, it correspond to 66 (-70) units/mg, that is, one unit is equivalent to approximately 15 µg. Feedingstuff grade of bacitracin correspond to 42-50 units/mg (one unit=20-24 µg) (Otten et al., 1975).

TABLE AP4. Cut-off values (mg/L) for resistance. Values in red are current (April 2012) EUCAST epidemiological cut-off values (ECOFFs), blue underlined values deviate from ECOFFs and for values in black, ECOFFs are not defined.

Antimicrobial	*Actinobacillus pleuropneumoniae*	*Brachyspira hyodysenteriae*	*Brachyspira pilosicoli*	*Campylobacter jejuni*	*Campylobacter coli*	*Enterococcus faecalis*	*Enterococcus faecium*	*Escherichia coli (indicator)*	*Escherichia coli (pathogen)*	*Pasteurella* spp.	*Pseudomonas aeruginosa*	*Salmonella enterica*	*Staphylococcus pseudintermedius*	*Staphylococcus aureus*	*Streptococcus* spp.
Ampicillin	>1			>8	>8	>4	>4	>8	>8	>1		>8			>8
Bacitracin[a]						>32	>32								
Cefotaxime	>0.06							>0.25	>0.5	>0.06		>0.5			
Cefoxitin														>4	
Ceftiofur								>1	>1	>0.25		>2		>2	
Cephalothin													>2	>1	>4
Chloramphenicol	>2					>32	>32	>16		>2		>16		>16	>8
Ciprofloxacin	>0.06			>1	>1			>0.06		>0.06		>0.06		>1	
Clindamycin													>4	>0.25	>2
Colistin								>2							
Enrofloxacin								>0.12	>0.12	>0.25	>2	>0.25	>0.5	>0.5	
Erythromycin				>4	>16	>4	>4						>1	>1	>4
Florfenicol	>16							>16	>16	>16		>16		>8	>8
Fusidic acid													>4	>0.5	
Gentamicin	>8			>1	>2	>32	>32	>2	>4	>8	>8	>2	>4	>2	
Kanamycin						>1024	>1024	>8				>16		>8	
Linezolid						>4	>4								
Nalidixic acid	>16			>16	>32			>16		>16		>16			
Narasin						>2	>4								
Neomycin									>8			>4			
Nitrofurantoin									>32				>32		>32
Oxacillin													>0.5	>1	
Penicillin	>1									>1			[c]	[c]	>1
Polymyxin B									>2		>4				
Spiramycin														>16	>16
Streptomycin	>32			>2	>4	>512	>128	>16	>16	>32		>16		>16	
Sulphametoxazole								>64				>256			
Tetracycline	>2			>2	>2	>4	>4	>8	>8	>2		>8	>8	>1	>8
Tiamulin		>2	>2												
Trimethoprim	>4							>2	>2	>4		>2		>2	
Trim & sulpha[b]									>1	>4		>0.5	>2	>0.5	>4
Tylosin		>16	>16												
Vancomycin						>4	>4								
Virginiamycin						>32	>4								

[a] MIC in U/mL; [b] Concentration of trimethoprim given, tested with sulphametoxazole in concentration ratio 1/20; [c] beta-lactamase production.

Appendix 5: Antimicrobials licensed

ANTIMICROBIALS LICENSED for use in veterinary medicine in Sweden year 2011 are listed in Table AP5. Only substances in pharmaceutical preparations for systemic, oral, intrauterine or intramammary use are included (ATCvet codes QJ, QG, QA and QP). Data from FASS VET. 2011. For explanation of ATCvet code, see Appendix 2.

Changes since 2010

- **New substances or indications**
  - Ceftiofur (QJ01D D90), injectable for use in pigs
- **Withdrawn substances or indications**
  - Spiramycin (QJ01F A02), injectable for use in cattle

TABLE AP5. Antimicrobials licensed for use in cattle, sheep, pigs, poultry, horses, dogs and cats in Sweden, 2011. Routes of administration indicated: O = oral; I = injection; U = intrauterine; M = intramammary.

Antimicrobial agent	ATCvet code	Animal species						
		Cattle	Sheep	Pigs	Poultry	Horses	Dogs	Cats
Tetracyclines								
Doxycycline	QJ01A A02			O			O	O
Oxytetracycline	QJ01A A06, QG01A A07	I O U	I U	I O U	O			
Beta-lactams, penicillins								
Ampicillin	QJ01C A01	O		O		O	O	O
Amoxicillin	QJ01C A04	I		I			I O	O
Amoxicillin/Clavulanic acid	QJ01C R02			I			I O	I O
Penicillin G, sodium	QJ01C E01	I		I		I		
Penicillin G, procaine	QJ01C E09/QJ51C E09	I M	I	I		I	I	I
Beta-lactams, cephalosporins								
Cephalexin	QJ01D B01						O	
Ceftiofur	QJ01D D90	I		I				
Cefovecin	QJ01D D91						I	I
Sulphonamides -Trimethoprim								
Sulphadiazine - Trimethoprim	QJ01E W10	I	I	I		I O		
Sulphadoxine - Trimethoprim	QJ01E W13	I		I		I		
Macrolides								
Tulathromycin	QJ01FA94	I		I				
Gamithromycin	QJ01FA95	I						
Tylosin	QJ01F A90	I		I O	O		I	I
Lincosamides								
Clindamycin	QJ01F F01						O	O
Aminoglycosides								
Gentamicin	QJ01G B03					I U	I	
Dihydrostreptomycin (DHS)	QA07A A90	O U	O U	O U		O U	O	O
Fluoroquinolones								
Danofloxacin	QJ01M A92	I						
Enrofloxacin	QJ01M A90	I		I	O		I O	I O
Marbofloxacin	QJ01M A93						O	O
Pleuromutilins								
Tiamulin	QJ01X X92			I O	O			
Valnemulin	QJ01X X94			O				
Combinations								
Penicillin G, procaine/DHS	QJ01R A01, QJ51R C23	I M	I	I		I	I	I
Penicillin G, benzatin/DHS	QJ51R C24	M						
Penicillin G, ester/Framycetin	QJ51R C25	M						

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Appendix 7: SVARM 2000-2011 - an overview

DATA ON ANTIMICROBIAL susceptibility for over 30 000 isolates of bacteria have been presented in SVARM since 2000. The annual number of isolates of different categories is presented below.

TABLE AP7 I. *Salmonella enterica*, number of isolates 2000-2011.

Source	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Warm-blooded animals	67	52	49	101	68	105	101	112	122	117	82	71
Cold-blooded animals										17		

TABLE AP7 II. *Campylobacter* spp., number of isolates 2000-2011.

Source	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Cattle		67					68					
Pigs		98		105		100	46		97			83
Broilers		50	100		100				38		100	
Raw meat		74										
Water		19										

TABLE AP7 III. Indicator *Escherichia coli*, number of isolates 2000-2011.

Source	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Cattle	293						314			223		
Pigs	260	308		303		390		342	349			167
Pig meat									19			20
Broilers	274	296	306		300			296			181	
Broiler meat											77	
Horses											274	
Dogs							257					
Willow grouse						19						
Wild boars		87										
Sheep									115			

TABLE AP7 IV. Indicator *Enterococcus faecalis* and *E. faecium* number of isolates 2000-2011 *(E. faecalis/E. faecium).*

Source	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Cattle	22/71						13/98			10/24		
Pigs	56/48	52/106		87/71		55/47			68/39			22/22
Pig meat									17/3			29
Broilers	24/151	49/204	57/189		48/163			28/197			35/136	
Broiler meat											81/17	
Horses											34/27	
Dogs							135/29					
Wild boars		12/35										
Sheep									24/15			

TABLE AP7 V. Isolates of animal pathogens, number in SVARM 2000-2011.

Animal species & bacterial species	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Cattle												
Escherichia coli (enteric)			220		87	39	24			40	15	15
Escherichia coli (udder)				169								
Klebsiella spp. (udder)				44			24					
Pasteurella spp.	254							27	32	14	25	80
Staphylococcus aureus (udder)		100	100			96			87			
Streptococcus dysgalactiae (udder)			100									
Streptococcus uberis (udder)			100									
Fusobacterium necrophorum										41		
Pigs												
Actinobacillus pleuropneumoniae	18							84	39	24	39	57
Brachyspira hyodysenteriae	50	75	109	100		31	26	23	15	24	9	7
Brachyspira pilosicoli				93		57	72	44	31	24	13	16
Escherichia coli (enteric)	399	82	340	340	386	325	298	93	83	102	94	91
Pasteurella spp.		75						38	25	24	10	17
Staphylococcus hyicus					20							
Streptococcus equisimilis												82
Poultry (laying hens)												
Escherichia coli (infection)								70				
Sheep												
Staphylococcus aureus (udder)								25				
Fusobacterium necrophorum										24		
Fish												
Aeromonas salmonicida subsp.*achrom.*								67	20	23	8	14
Flavobacter columnare								30	16	10	5	8
Flavobacter psychrophilum								42	27	24	21	27
Horses												
Actinobacillus spp.		40										
Escherichia coli (genital)	323	103	166	188	188	161	124	273	174	210	236	174
Rhodococcus equi	73	20			187							
Streptococcus zooepidemicus	301	174	163	150	185	175	174	180	159	152	43	311
Staphylococcus aureus										308	131	135
Dogs												
Escherichia coli (urinary)	185	183	204	234	247	304	366	425	503	599	803	666
Pasteurella multocida					231							
Pseudomonas aeruginosa				234						261	313	353
Staphylococcus pseudintermedius	145	156	133	102	159	126	89	220	258	381	444	388
Cats												
Escherichia coli (urinary)			46	52	55	74	95	131	170	245	236	
Beta-hemolytic streptococci												184

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