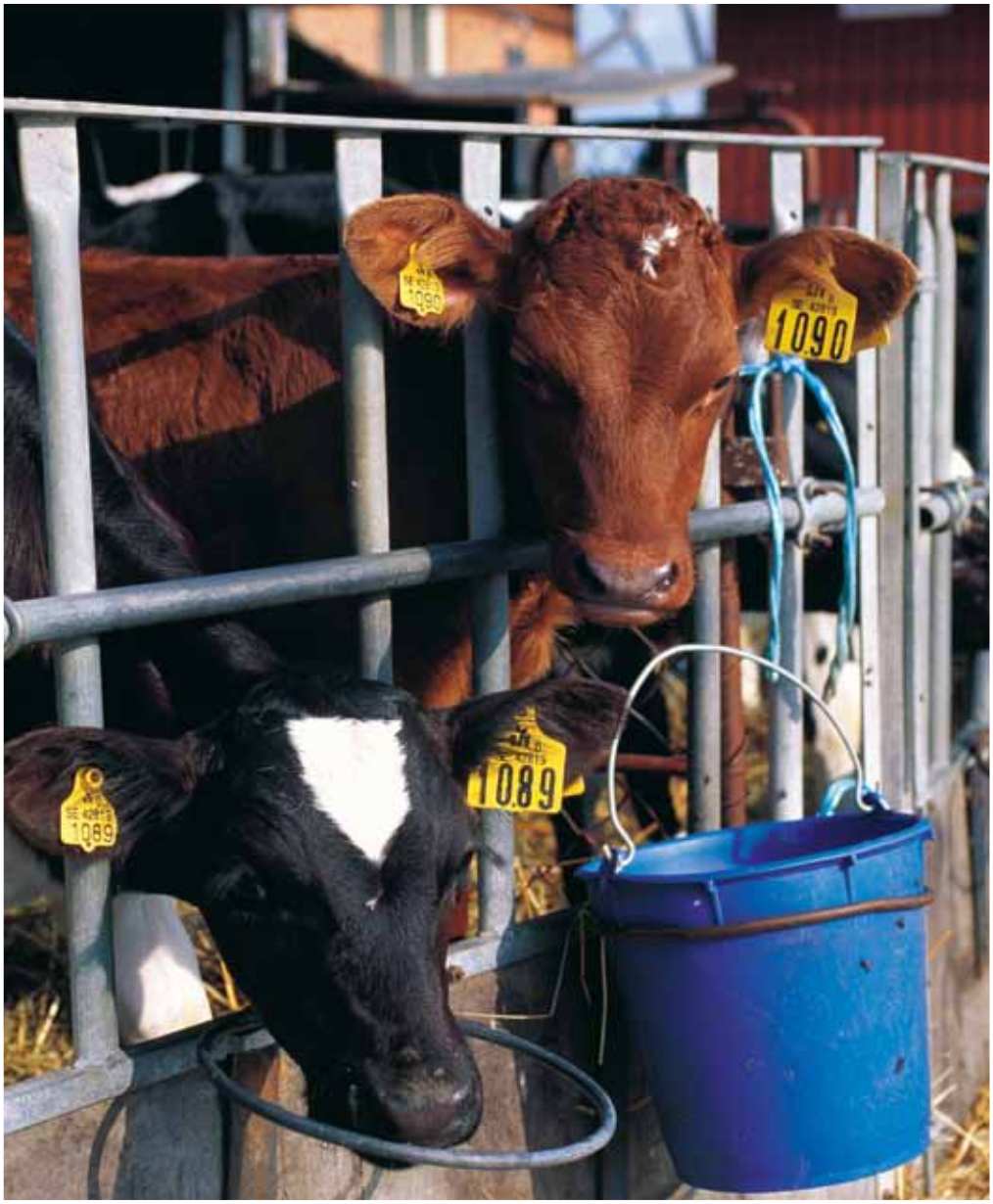
SVARM 2009

Swedish Veterinary Antimicrobial Resistance Monitoring



SVA

Swedish Veterinary Antimicrobial Resistance Monitoring 2009

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Preface

WELCOME to the tenth Swedish report combining results from the monitoring of antimicrobial resistance and antimicrobial usage in both veterinary and human medicine: SVARM and SWEDRES. These two reports are printed jointly to increase the awareness of trends in incidence of use and occurrence of antimicrobial resistance in the respective areas. Our hope is that the information is translated into action as needed.

In the ten years that have passed since the establishment of SVARM, the overall use of antimicrobials in veterinary medicine has decreased and the situation regarding resistance has for most monitored bacteria been stable. But several new challenges have appeared. A clone of vancomycin-resistant *Enterococcus faecium* (VRE) has spread among broiler farms, in the apparent absence of selective pressure. Methicillin-resistant *Staphlyococcus aureus* (MRSA) in animals are still not common but because of the zoonotic aspect, every case is scrutinized and its investigation and management requires close collaboration between human and veterinary medicine. Methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) have emerged as a serious veterinary therapeutic problem. Finally, this year the emergence of clinical infections in animals with enterobacteria producing extended spectrum beta-lactamases (ESBL) is highlighted.

The attention these acronyms have received within the veterinary profession and more generally through media has led to a generally increased awareness of the problems with antimicrobial resistance. Strama, the strategic programme against antimicrobial resistance in human medicine, and Strama VL, the corresponding function in the veterinary and food area, provide platforms for all interested parties to exchange information, analyze problems, pinpoint solutions and initiate prioritized activities. Thanks to the combined efforts of organizations and engaged individuals nationally and locally, the strategies have so far been comparatively successful in tackling the new challenges and generally in containing resistance.

The next ten years will undoubtedly bring new threats in addition to those we currently struggle with. National and international multidisciplinary collaboration is necessary to enhance our collective capacity to meet these challenges. Further improvement of the implementation of prudent use of antimicrobials and infection control will be needed both in veterinary and in human medicine. In a long term perspective, the need for antimicrobials must be reduced by further improving animal health. Only through the continued efforts of all parties concerned can we preserve the effectiveness of antimicrobials for treatment of current and future generations of animals and people.

Summary

THE 2009 REPORT FROM SVARM shows that the situation regarding antimicrobial resistance in bacteria of animal origin remains favourable from an international perspective. In the ten years since the SVARM-program started the situation has mostly been stable but there are examples of worrying and undesired trends. Methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) has emerged as an important pathogen in animal health care and Methicillin-resistant *Staphylococcus aureus* (MRSA) has found its way into populations of Swedish animals. Also a clone of vancomycin-resistant enterococci (VRE) has spread among broilers. These three examples illustrate that the situation can rapidly change in an unfavourable direction and emphasize the need to continuously monitor resistance and use of antimicrobials. But monitoring is only an adjunct to efforts aiming at improving prudent use, infection control and animal health, which are the three cornerstones for mitigating resistance.

The total amount of antimicrobials used for animals was 15 368 kg in 2009, which is the lowest figure in 30 years. The amount of antimicrobials for in-feed or in-water medication has decreased by 8% since 2006 and is today but 13% of the total sales. The sales of products for administration to individual animals have decreased by 10% since 2006. The sales of cephalosporins, mainly products for dogs, have decreased by 39% since 2006. The sales of antimicrobials for dogs have decreased by 14% since 2006, measured as total number of prescriptions dispensed. The downward trend in prescriptions for dogs is probably explained by ongoing national and local initiatives on hygiene and prescribing policies.

Methicillin-resistant *Staphylococcus aureus* (MRSA) were confirmed in two dogs, two cats and two horses in 2009. Since first reported in 2006, there have been 15 cases in dogs, 2 in cats and 12 in horses until the end of April 2010. So far MRSA has not been found in food producing animals in Sweden. Isolates from dogs and cats were of *spa*-types t032, t127, t002 all of which are common among MRSA from humans in Sweden. In contrast, all isolates from horses are of spa-type t011 which belong to the livestock associated MRSA CC398, common in several animal species in other countries but rare among humans in Sweden. Since there is a zoonotic aspect to MRSA in animals, the situation should be closely monitored. Also, routines and recommendations for prevention of spread, as well as for management of MRSA in animals, should be elaborated.

Salmonella is rare in Swedish animals and most incidents involve susceptible strains. In 2009, 91% of the strains were susceptible to all antimicrobials tested and only 4 of 74 strains from food producing animals and 2 of 24 strains from companion animals were multiresistant. Resistance to third generation cephalosporins was not observed. 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. This is emphasised by the three incidents this year of multiresistant monophasic Salmonella subspecies I, O 4,5,12;i- in cattle.

Resistance in indicator bacteria, i.e. *Escherichia coli* and *Enterococcus* spp. from the intestinal flora of healthy animals, are believed to reflect the antimicrobial selective pressure in an animal population. In indicator bacteria from fattened calves, studied this year, resistance was most rare. No isolate of *E. coli* was resistant to fluoroquinolones and transferable resistance to third generation cephalosporins was not observed although all samples were screened for this type of resistance. Likewise, resistance to vancomycin, linezolid or streptogramins was not observed in enterococci.

The findings, in agreement with previous studies in dairy cows and calves/yearlings, show that *E. coli* and *Enterococcus* in these categories of cattle is no significant reservoir of resistance genes and indicate a low selection pressure for resistance in Swedish cattle older than six months.

Vancomycin-resistant enterococci (VRE) among broilers, screened by culture on vancomycin supplemented media, gradually increased from less than one percent in 2000 to a peak of 41% of 99 samples cultured in 2005. The increase was caused by spread of a single clone of *E. faecium* carrying the *van*A gene. This year, VRE were isolated from 23% of 105 samples which is similar to the prevalence in 2006-2008 indicating that the spread has abated.

Escherichia coli from clinical submissions were often resistant to ampicillin, tetracycline or trimethoprim-sulphonamides, irrespective of source (pig, cattle, horse, dog or cat). Multiresistance commonly involved these substances, ranging from 4% in isolates from cats to 33% in isolates from cattle. In addition, resistance to enrofloxacin was common (12%) in *E. coli* from pigs with diarrhoea.

Since 2007, production of **extended spectrum beta-lactamases (ESBL)** have been confirmed in 14 isolates of *Enterobacteriaceae* from dogs, cats and horses. Beta-lactamases involved were of groups CTX-M-1 and SHV and in addition the isolates were multiresistant.

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

Resistance was rare in ***Actinobacillus pleuropneumoniae*** and in ***Pasteurella*** spp. from the respiratory tract of pigs as well as

in *Pasteurella* spp. from the respiratory tract of calves. Also in ***Fusobacterium necrophorum***, isolated from lame cattle and sheep, resistance was uncommon.

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

Streptococcus zooepidemicus from the respiratory tract of horses were uniformly susceptible to penicillin, but resistance to trimethoprim-sulphonamides was common.

Penicillinase production was the most common resistance trait in ***Staphylococcus aureus*** from skin samples of equine origin (36%). Only 5% were multiresistant.

Most ***Staphylococcus pseudintermedius*** from dogs with dermatological disorders were resistant to penicillin. Resistance to clindamycin, erythromycin, fusidic acid or tetracycline was also common (between 25 and 31%). One third of *S. pseudintermedius* were multiresistant and 9% were resistant to at least five antimicrobials.

The number of Methicillin-resistant ***Staphylococcus pseudintermedius (MRSP)*** confirmed has increased since first isolated in 2006. During 2009, 121 MRSP from dogs, 7 from cats and 1 from a horse were verified.

Pseudomonas aeruginosa isolated from the external ear canal of dogs were susceptible to polymyxin B, whereas 5% of the isolates were resistant to gentamicin and 25% to enrofloxacin.

Sammanfattning

SVARM 2009 visar att läget avseende antibiotikaresistens hos bakterier från djur är fortsatt gynnsamt ur ett internationellt perspektiv. Under de tio år som resistens övervakats i SVARM har läget varit i huvudsak stabilt. Men det finns exempel på oroande och oönskade trender. Meticillinresistent *Staphylococcus pseudintermedius* (MRSP) har påvisats hos sällskapsdjur och blivit ett kliniskt problem i djursjukvården. Samtidigt har meticillinresistent *Staphylococcus aureus* (MRSA) letat sig in i svenska djurpopulationer och en klon av vankomycinresistenta enterokocker (VRE) spridits i svensk slaktkycklingproduktion. Dessa tre exempel visar att situationen snabbt kan förändras och pekar samtidigt på vikten av kontinuerlig övervakning av resistens och antibiotikaförbrukning. Sådan övervakning är ett viktigt verktyg i arbetet mot antibiotikaresistens men av helt avgörande betydelse är insatser för ansvarsfull antibiotikaanvändning liksom åtgärder för att förbättra smittskydd och djurhälsa.

Försäljningen av antibiotika till djur var totalt 15 368 kg under 2009, vilket är den lägsta siffran på 30 år. Volymen antibiotika för inblandning i foder eller vatten har minskat med 8 % sedan 2006 och utgör idag endast 13 % av den totala försäljningen. Försäljningen av produkter för individuellt bruk har minskat med 10 % sedan 2006. Försäljningen av cefalosporiner, främst produkter för hund, har minskat med 39 % sedan 2006. Antalet recept som skrivs ut för hund har minskat med 14 % sedan 2006, vilket troligen förklaras av pågående nationella och lokala aktiviteter.

Meticillinresistent *Staphylococcus aureus* (MRSA) påvisades hos två hundar, två katter och två hästar under 2009. Sedan det första fallet hos svenska djur 2006 har MRSA konfirmerats hos 15 hundar, 2 katter och 12 hästar fram till och med april 2010. Hittills har MRSA inte påvisats från animalieproducerande djur i Sverige. Isolaten från hundar och katter var av spa-typerna t032, t127 och t002 som alla är vanliga bland

MRSA från människor i Sverige. Däremot är isolaten från hästarna av spa-typ t011 som är ovanlig i svensk sjukvård men som är vanlig bland MRSA (CC398) från livsmedelsproducerande djur i många länder. MRSA betraktas som ett zoonotiskt smittämne och läget i djurpopulationer bör därför övervakas. Dessutom bör det utarbetas rutiner och rekommendationer för hur spridning av MRSA kan motverkas liksom rekommendationer för hantering av djur med MRSA.

Salmonella är ovanligt hos svenska djur och de fall som inträffar orsakas oftast av antibiotikakänsliga stammar. Under 2009 var 91 % av isolaten känsliga för alla testade antibiotika. Bara 4 av 74 isolat från livsmedelsproducerande djur och 2 av 24 isolat från sällskapsdjur var multiresistenta. Inget isolat var resistent mot tredje generationens cefalosporiner. Det finns inga tecken på en ökad förekomst av resistens men med tanke på folkhälsoaspekterna är fortsatt vaksamhet mot resistent *Salmonella* hos livsmedelsproducerande djur berättigad. Detta illustreras av de tre fall av multiresistent monofasisk *Salmonella* subspecies I, O 4,5,12;i- som påvisades hos nötkreatur under 2009.

Resistens hos indikatorbakterier (*Escherichia coli* och *Enterococcus* spp.) från tarmfloran hos friska djur anses återspegla selektionstrycket från användning av antibiotika i en djurpopulation. Hos indikatorbakterier från mellankalvar, som undersöktes 2009, var resistens ovanlig. Inget isolat av *E. coli* var resistant mot fluorokinoloner och överförbar resistens mot tredje generationens cefalosporiner påvisades inte trots att samtliga prover undersöktes specifikt för *E. coli* med sådan resistens. Bland enterokocker påvisades inte resistens mot vankomycin, linezolid eller streptograminer. Resultaten överensstämmer med tidigare undersökningar och visar att *E. coli* och enterokocker hos svenska nötkreatur äldre än sex månader inte är en betydelsefull reservoar av resistensgener och att selektionstrycket för resistens är lågt i dessa djurpopulationer.

Vankomycinresistenta enterokocker (VRE) hos slaktkyckling har ökat i förekomst från mindre än en procent 2000 till 41 % av 99 prov av tarminnehåll undersökta 2005. Ökningen som berodde av spridning av en klon av *E. faecium* med *van*A-genen påvisades med odlingsmedier med tillsats av vankomycin. Under 2009 påvisades VRE i 23 % av 105 prov, samma andel positiva prov som 2006-2008, vilket visar att läget har stabiliserats.

Escherichia coli från kliniska prov från grisar, kalvar, hästar, hundar och katter var ofta resistenta mot ampicillin, tetracyklin eller trimetoprim-sulfa. Hos *E. coli* från grisar med diarré var också resistens mot enrofloxacin vanlig (12 %). Frekvensen multiresistens varierar mellan djurslag och var lägst (4 %) hos isolat från katter och högst (33 %) hos isolat från kalvar.

Sedan 2007 har produktion av **ESBL** (extended spectrum betalactamases) ur grupperna CTX-M-1 och/eller SHV konfirmerats hos 14 isolat av *Enterobacteriaceae* från hundar, katter och hästar. Alla isolaten var multiresistenta.

Hos ***Brachyspira pilosicoli*** från grisar förekom resistens mot tiamulin men däremot inte bland ***B. hyodysenteriae***. Majoriteten av såväl *B. pilosicoli* som *B. hyodysenteriae* är resistenta mot tylosin.

Actinobacillus pleuropneumoniae och ***Pasteurella*** spp. från luftvägarna hos grisar liksom *Pasteurella* spp. från kalvar med luftvägssjukdom var känsliga för de flesta antibiotika som används för behandling. Även *Fusobacterium necrophorum* från får och nötkreatur med klövproblem var känsliga för de antibiotika som används för behandling.

Bland ***Aeromonas salmonicida*** subsp. ***achromogenes***, ***Flavobacter columnare*** och ***Flavobacter psychrophilum*** från odlad fisk förekommer isolat med avvikande höga MIC-värden mot nalidixinsyra, tetracyklin eller florenikol. Detta tyder på att några isolat förvärvat resistens mot dessa antibiotika.

Streptococcus zooepidemicus från luftvägarna hos hästar var genomgående känsliga för penicillin men resistens mot trimetoprim-sulfa var vanlig.

En stor andel ***Staphylococcus aureus*** från huden på hästar var resistenta mot penicillin genom produktion av penicillinas (36 %) men bara 5 % var multiresistenta.

Staphylococcus pseudintermedius isolerade från hudprover från hundar var i stor utsträckning resistenta mot penicillin. Resistens mot klindamycin, erytromycin, fusidinsyra, eller tetracyklin var också vanlig (mellan 25 och 31 %). En knapp tredjedel av *S. pseudintermedius* var multiresistenta och 9 % var resistenta mot minst fem antibiotika.

Antalet **meticillinresistenta *S. pseudintermedius* (MRSP)** har ökat sedan 2006 då första fallet påvisades i Sverige. Under 2009 konfirmerades 121 isolat av MRSP från hundar, 7 från katter och ett isolat från häst.

Pseudomonas aeruginosa isolerade från yttre hörselgången hos hund var alla känsliga för polymyxin B, medan 5 % av isolaten var resistenta mot gentamicin och 25 % mot enrofloxacin.

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.

In Sweden, antimicrobials for use in animals are only available on veterinary prescription and all pharmaceuticals are dispensed by pharmacies. In 1986, the Feedstuffs Act restricted the use of antimicrobials for veterinary medicinal purposes, i.e. their use as growth promoters was no longer authorised.

Up to and including year 2002, the source for the statistics has been sales of drugs from wholesalers to Swedish pharmacies. From year 2003, the data collected are the amounts of drugs dispensed by pharmacies. Both systems have a high degree of completeness. Data represent an approximation of the real use of antimicrobials, assuming that the amount sold is also used during the observation period.

The data include the sales of antimicrobials in veterinary medicinal products for systemic, intramammary and obstetric use, and intestinal anti-infectives for all terrestrial animal species (i.e. excluding farmed fish). Drugs authorised for human use but prescribed for animals are not included. Such antimicrobials are almost exclusively prescribed in small animal medicine. Between 2005 and 2009, 6-8% of the total number of prescriptions for dogs was for products authorised for human use. Data for 2009 were provided by Apotekens Service AB.

Data on sales of antimicrobials and drugs is also reported by the Swedish Board of Agriculture (SBA). In those reports, also sales for use in animals of products authorised for use in humans are included. Further, data is presented by the animal species for which the prescription was written, if such information is available. Data compiled from the report on year 2008 has been included in the highlight 'Use of antimicrobials for different animal species'.

Ionophoric antimicrobials given to control coccidiosis are currently classified as feed additives, and are not included in the overall statistics based on sales from pharmacies. Zinc oxide is available on veterinary prescription and is mixed in feed (2000 ppm zinc) to control weaning diarrhoea in piglets. Figures on the sales of these products, based on statistics collected by the SBA from feed mills, are given under the section on group treatment (Table AC III).

Details on animal numbers are found in Appendix 1, on methodology in Appendix 2 and on antimicrobial agents with general marketing authorisation in Sweden in Appendix 4.

Overall use

The total yearly sales of antimicrobials over the last decade are presented in Table AC I. As noted in previous SVARM reports, the lower total sales of antimicrobials for animals shown for years 2003-2005 are uncertain, as there was a change in the system for data retrieval in year 2003. It is possible that initially, sales of some of the products sold with special licence prescription were not captured by searches in the new system. This problem has been addressed, and from year 2006 all products dispensed should be captured.

Changes in the numbers of animals may affect trends in statistics on use of antimicrobials. The decrease in number of dairy cows continues and the figure was 9% lower in 2009 than in 2005. The number of beef cows, however, has increased by 8% in the same period. The number of pigs slaughtered in 2009 was 9% lower than in year 2005 but in the last three years there has been little change. The number of slaughtered broilers was roughly unchanged.

The potency of different antimicrobials is not equal and therefore each class should be evaluated separately. Nevertheless, the overall figures may indicate general trends. The total sales expressed as kg active substance in 2009 were 10% lower than in 2007 and are the lowest figure reported since 1980 (for earlier data see SVARM 2000). The decrease is explained by a decrease in products for group medication of pigs (see 'Treatment of groups or flocks') but also products for

TABLE AC I. Yearly sales of antimicrobial drugs for veterinary use expressed as kg active substance. Based on sales statistics provided by Apoteket AB and from Apotekens Service AB.

ATCvet code	Antimicrobial class	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
QJ01AA, QG01A	Tetracyclines	1 754	1 453	1 415	1 307	1 329	1 562	1 516	1 853	1 649	1 174
QJ01CE, QJ01R, QJ51	Benzylpenicillin	8 254	8 414	8 179	7 579	7 814	7 571	7 860	7 582	7 758	7 721
QJ01CA, QJ01CR	Aminopenicillins	852	752	767	870	875	911	920	927	938	1 068
QJ01D, QJ51CA	Other betalactams	315	474	676	832	928	1 009	1 217	954	820	738
QA07AA, QJ01G, QJ01R, QJ51R	Aminoglycosides & polymixins	797	770	753	645	606	762	750	718	643	609
QA07AB, QJ01E	Sulphonamides	2 338	2 485	2 477	2 326	2 462	2 535	2 543	2 427	2 303	2 128
QJ01E	Trimethoprim & derivatives	390	414	414	381	406	437	450	438	416	379
QJ01F	Macrolides & lincosamides	1 352	1 510	1 412	1 124	1 095	1 080	1 254	1 520	1 096	988
QJ01MA	Fluoroquinolones	156	182	185	184	187	184	195	180	169	164
QJ01XX92, QJ01XX94	Pleuromutilins	871	841	988	744	387	338	459	506	572	398
Total		17 079	17 295	17 266	15 992	16 089	16 389	17 164	17 106	16 400	15 368

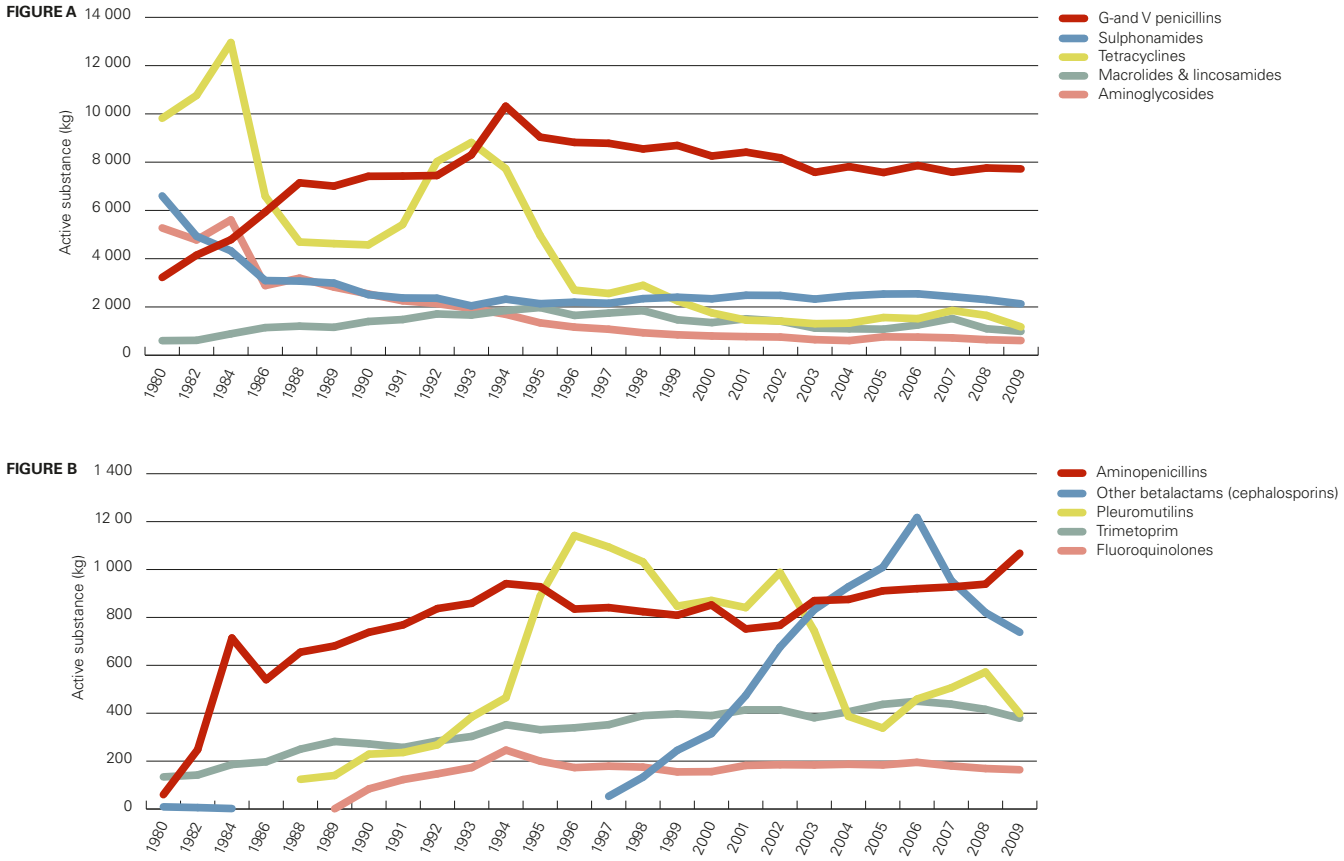

FIGURE AC I A & B. Sales of antimicrobials for animals from 1980-2009. Amphenicols, nitroimidazoles, streptogramins, quinoxalines and other feed additives were withdrawn from the market during the time period and are not shown. Note that the scales on the Y-axis are different in figure a and b. Based on sales statistics provided by Apoteket AB and Apotekens Service AB.

oral treatment of horses and dogs (see 'Treatment of individual animals').

Most of the total sales are products formulated for systemic treatment of individual animals. In 2009, 62% of the sales were products for injection, 24% for oral medication of individual animals (e.g. tablets) and only 13% for medication of groups or flocks via feed or water. The proportion of the total sales of the latter subset has been roughly unchanged over the last decade.

Long term trends in total sales of classes that are currently used are illustrated in Figure AC I a & b. Comments on recent trends are found in the following sections.

Administration to individual animals

In table AC II, the sales of products for use in individual animals, excluding topical, intrauterine and intramammary use are presented. The total sales in this subset have decreased by 10% since 2006.

The sales of intestinal anti-infectives for individual use

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 intenstinal anti-infective (QA07) are included. Based on sales statistics provided by Apoteket AB and from Apotekens Service AB.

ATCvet code	Antimicrobial class	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
QA07A	Intestinal anti-infectives	587	614	594	594	586	496	434	372	364	355
QJ01A	Tetracyclines	634	623	628	606	611	623	609	632	605	576
QJ01CE	Benzylpenicillin[a]	8 185	8 343	8 127	7 536	7 769	7 493	7 777	7 504	7 671	7 641
QJ01CA; CR	Aminopenicillins	852	752	767	870	875	911	909	899	828	802
QJ01D	Cephalosporins	315	474	676	832	928	1 009	1 212	950	817	735
QJ01E	Sulfonamides & trimethoprim	2 336	2 478	2 483	2 280	2 427	2 610	2 689	2 619	2 486	2 270
QJ01F	Macrolides & lincosamides	531	522	477	430	382	400	417	413	352	332
QJ01G	Aminoglycosides[a,b]	474	454	460	367	344	362	345	343	318	301
QJ01M	Fluoroquinolones	150	169	178	177	180	179	190	177	164	159
QJ01X	Pleuromutilins	56	48	49	77	32	29	39	36	36	28
	Total	14 120	14 477	14 439	13 769	14 134	14 112	14 622	13 944	13 640	13 198

[a] The amount includes QJ01R; [b] Does not include QA07A, intestinal anti-infectives.

Use of antimicrobials for different animal species

Statistics reported by the Swedish Board of Agriculture

The Swedish Board of Agriculture (SBA) annually reports statistics on sales of antimicrobials, antiparasitics, hormones, immunologicals, sedatives and anti-inflammatory drugs. The statistics include all sales for use in animals, i.e. both products authorised for use in animals and for use in humans. When possible, the sales data are split by animal species based on the records from pharmacies and other information. For drugs sold for use in veterinary practice, the animal species is not known to the pharmacies. Efforts are made to assign those sales to species or 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. A compilation of figures on sales of antimicrobials for animals as presented by SBA are given in Table AC I and II.

The sales of aminopenicillins and other beta-lactams (cephalosporins) are mostly for companion animals, while benzyl-penicillin, tetracyclines and trimethoprim-sulphonamides dominate the sales for food producing animals (Table AC I). Most of the trimethoprim-sulphonamides sold are intended for horses, and pleuromutilins, macrolides and tetracyclines mainly for pigs (Table AC II). With the current system, a large amount of the benzylpenicillins, other beta-lactams (mainly cephalosporins) and fluoroquinolones cannot be assigned to a specific food producing animal species (Table AC II).

Prescriptions for dogs

A marked decrease in total sales expressed as total number of prescriptions dispensed for dogs was noted from 2006 to

TABLE AC I. Sales of antimicrobial drugs for veterinary use (kg active substance) per category of animals in 2008. Data are from the Swedish Board of Agriculture's report on usage of veterinary medicines (www.sjv.se; in Swedish), and is based on sales statistics provided by Apoteket AB.

Antimicrobial class[a]	Companion animals	Food producing animals (incl horses)	Other or unknown
Tetracyclines	87	1 515	74
Benzylpenicillin[b]	118	7 649	50
Aminopenicillins	762	182	92
Other betalactams	847	28	0
Aminoglycosides & polymixins[a]	61	570	17
Sulphonamides	205	2 119	3
Trimethoprim & derivatives	15	405	1
Macrolides & lincosamides	238	801	69
Fluoroquinolones	48	122	0
Pleuromutilins	1	571	3

[a] For included ATC groups see table AC I; [b] Pro-drugs calculated to benzyl penicillin.

have declined by 28% over the last five years. Products for individual use classified in this ATCvet group contain either aminoglycosides or certain formulations of sulphonamides. The decrease is largely explained by changes in sales of products of the latter type, which currently are not generally available on the Swedish market but are sold with 'special licence prescription'.

The products for systemic use containing penicillins are exclusively products formulated for injection, mostly benzylpenicillin and procaine-benzylpenicillin. The main indication for these products is treatment of mastitis in dairy cows. Over the last five years, the sales of this class have been relatively unchanged but the number of dairy cows has decreased by 9%. Thus, the overall use per animal may have increased. Alternatively, it is possible that the use of penicillins for other animals than dairy cows (e.g. pigs or horses) has increased.

Until year 2006, the sales of aminopenicillins and cephalosporins increased steadily. Since, the sales have decreased by 12 and 39%, respectively. In 2009, 67 and 94% of the sales of these two classes was dispensed for use in dogs. Hence, changes within these groups are almost entirely explained by the amounts prescribed for dogs.

The sales of sulphonamides and trimethoprim for individual use have increased steadily over time, but have decreased somewhat from year 2005 (13%). Around two thirds of the sales in the last five years of the combination sulphonamides and trimethoprim were products for oral use in horses (paste or powder) and observed trends are derived from that type of products.

The sales of fluoroquinolones for therapy of individual animals have decreased by 11% since 2005. This is explained both by a marked decrease of products for oral use in dogs and cats (20% decrease of that subset) and of products for injection (10% decrease of that subset).

TABLE AC II. Sales of antimicrobial drugs for veterinary use (kg active substance) for food producing animals in 2008. Data are from the Swedish Board of Agriculture's report on usage of veterinary medicines (www.sjv.se; in Swedish), and is based on sales statistics provided by Apoteket AB.

Antimicrobial class[a]	Horses	Cattle	Pig	Poultry	Food producing animals, unspecified
Tetracyclines	4	238	840	5	428
Benzylpenicillin[b]	215	743	1 097	1	5 593
Aminopenicillins	-	3	121	56	1
Other betalactams	2	8	-	-	18
Aminoglycosides & polymixins[a]	43	168	200	-	159
Sulphonamides	1 446	-	365	-	308
Trimethoprim & derivatives	291	6	72	-	36
Macrolides & lincosamides	4	10	597	29	161
Fluoroquinolones	1	20	18	3	80
Pleuromutilins	1	-	568	-	2

[a] For included ATC groups see table AC I; [b] Pro-drugs calculated to benzylpenicillin.

2008 as repo rted in SVARM 2008. A follow up to those data is presented in Figure AC. The dataset includes prescriptions dispensed for dogs of drugs authorised for systemic oral use in animals (ATC vet code QJ01) as well as for humans (ATC code J01) and corresponds to out-patient care of dogs. Since 2008, the overall sales have decreased by 3% measured as number of prescriptions and the total decrease since 2006 is 14%. The most prominent changes relative 2006 are noted for cephalosporins (-37%), aminopenicillins with clavulanic acid (-23%), luorquinolones (-26%) and lincosamides (+19%). As discussed 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 that together probably led to changes in prescribers' behaviour, which in turn explains the downward trends in sales of antimicrobials for dogs.

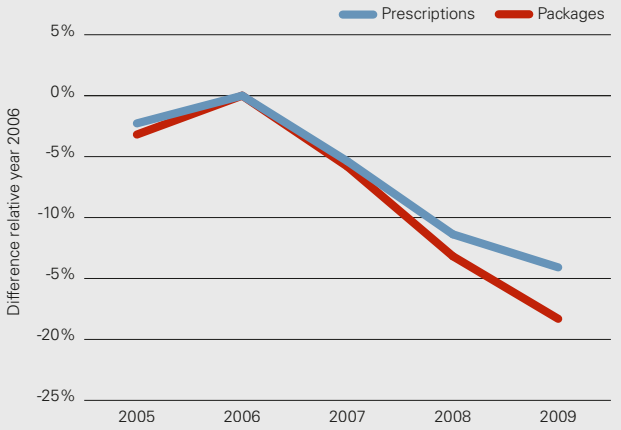

FIGURE AC. Trends in sales of antimicrobials for oral use in dogs as percent prescriptions and packages sold relative year 2006. Based on statistics provided by Apoteket AB and Apotekens Service AB.

Administration to groups or flocks

When considering the risk for development of resistance, the consumption of antimicrobials intended for group or flock medication, e.g. administration via feed or water, is of special interest.

Data on sales of antimicrobials formulated for medication of groups of animals over the last decade are given in Table AC III. Data for 1984 are given historical reference. In Figure AC II, the development of sales of veterinary medicines formulated for medication of groups of animals and of antimicrobial feed additives (before 1986) is shown. Substances grouped as 'others' are the feed additives and other substances that are no longer available on the market (e.g. nitroimidazoles). Overall, the sales of products intended for administration to groups of animals have decreased by 92% since 1984. This reduction is not only explained by the cessation of growth promoting use, as the decrease since 1988 is 87%.

When considering trends over the last ten years, two methodological factors must be taken into account. Firstly, intestinal anti-infectives prescribed with special license for medication of groups were not included in the statistics before year 2005. Secondly, as noted previously the retrieval system was changed in 2003 and it cannot be excluded that part of the sales of drugs with special licence prescription were initially not captured by the system. However, none of these factors would affect the figures on sales of macrolides or pleuromutilins.

Today antimicrobial products for medication of groups of animals represents but 13% of the overall sales (total sum of Table AC III divided by total sum of Table I). Antimicrobials for group treatment are mainly used in pigs except aminopenicillins of which about 70% were used for poultry in 2009 and the remainder for pigs, and for fluoroquinolones that are mainly used for poultry but also in minor quantities for other species.

TABLE AC III. Yearly sales of antimicrobial drugs authorised for group treatment and ionophoric anticoccidials sold expressed as kg active substance. Based on sales statistics provided by Apoteket AB, Apotekens Service AB and from the Board of Agriculture.

ATCvet code	Antimicrobial class	1984	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
QA07A	Intestinal anti-infectives[a]		-	-	-	-	-	163	170	158	106	107
QJ01A	Tetracyclines[b]	12 300	1 111	822	777	695	712	934	903	1217	1040	594
QJ01C	Beta-lactams	-	-	-	-	-	-	-	11	28	111	266
QJ01F	Macrolides & lincosamides	607	821	988	935	694	713	680	837	1 107	744	657
QJ01M	Fluoroquinolones	-	7	13	7	8	7	5	5	3	5	5
QJ01M	Quinoxalines[c]	9 900	-	-	-	-		-	-	-	-	-
QJ01XX91	Streptogramins[c]	8 800	-	-	-	-		-	-	-	-	-
QJ01XX92, QJ01XX94	Pleuromutilins	-	815	793	939	667	355	309	420	471	536	370
QP51AA	Nitroimidazoles	1 440	-	-	-	-	-	-	-	-	-	-
	Feed additives[d]	700	-	-	-	-	-	-	-	-	-	-
	Total	*33 747*	*2 754*	*2 616*	*2 658*	*2 064*	*1 787*	*1 928*	*2 175*	*2 984*	*2 524*	*1 999*
QP51AH	Ionophoric antibiotics (coccidiostats)[e]	7 900	9 368	10 019	8 439	10 920	10 486	11 095	12 335	12 527	13 376	NA[f]
QA07XA91	Zinc oxide	-	3 359	4 796	3 542	5 300	9 656	10 719	16 177	17 286	24 573	NA[f]

[a] Drugs with special licence prescription are included from year 2005; [b] Drugs marketed with special licence prescription are included from year 2000; [c] Years 1980-1984 sold as feed additives, thereafter on veterinary prescription at therapeutic dosages; [d] Feed additives other than quinoxalines and streptogramins: avoparcin, bacitracin, nitrovin, oleandomycin and spiramycin; [e] Data from the Feed Control of the SBA (www.sjv.se); [f] not available at the time of publication.

A prominent increase in use of zinc oxide mixed in feed has been noted in the reports from the SBA. As this may influence the sales of antimicrobials for group medication, figures on sales of zinc oxide for feed medication have been included in Table AC III. Zinc oxide is authorized to prevent post weaning diarrhoea on veterinary prescription at 2000 ppm zinc in feed for 14 days around weaning. According to the policy of the Swedish Veterinary Association on group medication of pigs (Odensvik et al 1999), antimicrobials or zinc oxide should only be prescribed for weaning diarrhoea following investigation and diagnosis of the problem, and only in conjunction with other measures aiming to prevent the problems by other means (e.g. changes in management and feed). Partly, the increase in use of zinc oxide could reflect increased problems with weaning diarrhoea but considering the magnitude of the change there must be other factors influencing the sales.

It is notable that the sales of zinc oxide start to increase when postweaning multisystemic wasting syndrome (PMWS) emerged in Sweden in 2003 (Wallgren et al, 2007). Increased sales of antimicrobials for group medication were also noted between 2005 and 2007, but that has been followed by a decrease. In 2009, the total sales of antimicrobials for group medication were 33% lower than in 2007. The PMWS is associated with porcine circovirus 2 in combination with other infections or stressors. In the first years following introduction of PMWS, antimicrobials and probably also zinc oxide were often applied in affected herds with the intent to treat concomitant infections. The recent drop in use of macrolides and tetracyclines is likely to reflect an improved knowledge on how to manage problems in herds affected with PMWS, including introduction of vaccination strategies and an awareness that in most cases, antimicrobials have no or limited effect. It is now ten years since the latest issue of the above mentioned policy on group medication of pigs was published and it is possible that its implementation has gradually become

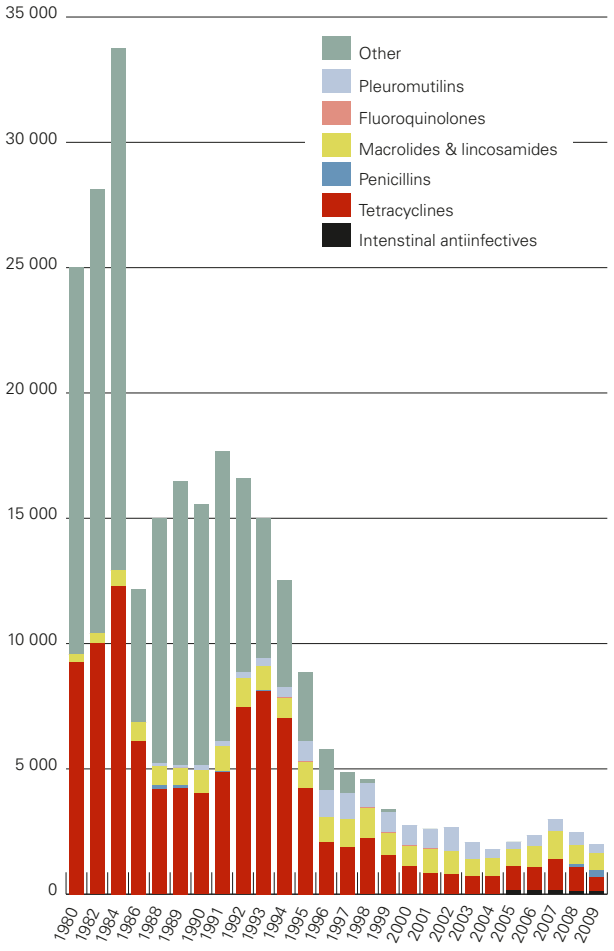

FIGURE AC II. Yearly sales of antimicrobial drugs authorised for group treatment measured as kg active substance (based on Table AC III and data from SVARM 2000). Use of antimicrobials for growth promotion ceased in 1986. Based on data provided by Apoteket AB and Apotekens Service AB and from the Board of Agriculture.

more lax and that today, herds that have experienced problems with PMWS use zinc oxide routinely around weaning.

Increased use of zinc oxide may partly explain the decreased sales of antimicrobials for group medication, but other factors are also likely to be of importance. Temporally coinciding with the spread of PMWS, increasing problems with acute respiratory infections caused by *Actinobacillus pleuropneumoniae* were noted. It is possible that the decreasing trend in antimicrobial sales since 2007 is also partly associated with a reduced incidence of such outbreaks, particularly in sow pool productions (cooperatives of farmers specializing in different stages of the production).

In the last decade, the sales of pleuromutilins decreased gradually until 2004-2005, then increased until 2008 and are in 2009 back to the figures that are comparable with 2004. Pleuromutilins (tiamulin, valnemulin) are authorised for use in pigs with swine dysentery as the main indication. It is probable that efforts to control the disease through e.g. a certification programme resulted in a decreased need to treat swine dysentery, leading to overall declining sales figures since the mid 90s (Figure AC I). The reasons for the recent increasing trend are unclear but it could be a reflection of strategic medication in one or several large herds such as sow pool productions as part of a control strategy. The lower figure for 2009 would then represent successful completion of such a strategy.

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

Antimicrobial use in human and veterinary medicine

Data included

Data collection and analysis was made in collaboration between Strama (the Swedish strategic programme against antimicrobial resistance in human medicine) and Strama VL (the corresponding programme for veterinary medicine and food). The figures on total amount of antimicrobials sold for systemic use of antimicrobials to humans (ATC group J01 and JA07AA oral glycopeptides; out-patient and hospital sales) were retrieved as defined daily doses and calculated to kg active substance. Figures on sales of antimicrobials for use in animals (QJ01 and and QJA07AA, total sales) are those presented in SVARM 2009. Sales for aquaculture were not included, nor were sales of drugs authorized for human use but sold for animals. The contribution of such sales to the total volumes is minor.

Calculation of biomass

The estimated biomass liable to be treated was calculated from the population census data and statistics on number of animals slaughtered, as presented by Statistics Sweden, and estimates of live weight. Briefly, for humans data on population numbers by age were multiplied with the corresponding average body weights from studies made by Statistics Sweden. For animal body mass, the method used by Moulin and co-workers (2008) was used with some modifications. Briefly, data on populations of all main species likely to be treated were used, i.e. species that are minor in Sweden such as fur animals, minor poultry species and goats were not included. For animals in place at the end of the year, such as dairy cows, sows, horses and pets the census figures were used and multiplied with assumed average body weights. For slaughter pigs and slaughter poultry, the number of animals slaughtered during the year was multiplied with an assumed average live weight during the life-span of this type of animals. The numbers of animals imported for slaughter are negligible. No attempts were made to validate the chosen average weights.

Comparison of sales

In 2009, 64 476 kg active substance of antimicrobials were sold for use in humans and 15 197 kg for animals. Further discussions on the relative contribution of human medicine and veterinary medicine to the total amount of antimicrobials expressed in kg active substance is presented and discussed in SWEDRES 2009.

In human medicine, the usage expressed as mg/kg weight was 105.5, to which beta-lactam antimicrobials contributed with 82%. In veterinary medicine, 15.4 mg/kg weight were sold with beta-lacams as the largest group (62%), but tetracyclines and trimethoprim & sulphonamides were also relatively significant (8 and 16%, respectively).

A comparison between human and veterinary usage of antimicrobials in year 1980 has been published by Wierup and co-workers (1987). The inclusion was broader than in the present material (all antimicrobial substances, including e.g. products for topical use and antibacterial antiparasitics (P51 and QP51). The amounts sold were calculated to mg active substance per kg metabolic weight. The ratio between total use of antibacterial drugs for humans and for animals (including antibacterial growth promoters) was 4.7 and for therapeutic use only 7.1. Interestingly, the corresponding ratio in the present study was 6.9.

Sales of classes where the total amount was at least 3 mg/kg are presented in Figures a and b. Human usage contributed with 85% or more to the total sum per antimicrobial class. The exceptions were the pleuromutilins (not shown), aminoglycosides (not shown) and trimethoprim-sulphonamides (Figure b).

As discussed by Moulin and co-workers (2008), data on the total usage does not take the heterogeneity of the likelihood of exposure within the population into account. This is especially true for data on sales for animals, as certain substances may only or mainly be sold for use in one particular animal species. This means that the selective pressure in a particular subset of the population can be far larger than in the total population. Overall figures can therefore be misleading. For example, the sales of trimethoprim & sulphonamides were 2.5 mg/kg weight of the total animal population. However, about 70% of volume of this class sold in 2009 was products formulated for use in horses. If only the weight of the equine population is used in the calculations for that subset, the result is 14 mg/kg weight of horses.

Ideally, for comparisons of the contribution of use of antimicrobials in different populations to the overall selective pressure on bacterial communities statistics by animal species, and preferably by production type and age category, should be used. Less refined data such as those presented here at most provide rough estimates of the situation in different compartments and should be interpreted with caution.

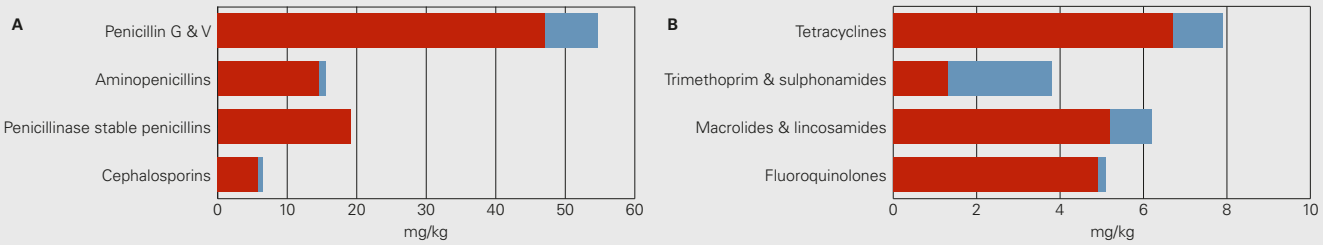

FIGURE A & B. Relative contribution of veterinary and human medicine to the total amount of antimicrobials sold 2009, mg active substance/kg estimated bodyweight.

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. Findings of *Salmonella* in animals are notifiable in Sweden and susceptibility of isolates from notified incidents is regularly monitored in SVARM. Also findings of MRSA in animals are notifiable and an update on the situation is presented in SVARM.

In addition, *Campylobacter* from the animal species sampled for indicator bacteria are usually tested (see Indicator bacteria). This year calves were sampled for indicator bacteria but culture for *Campylobacter* was not performed since these bacteria are rare in this category of cattle. Therefore no data on antimicrobial susceptibility of *Campylobacter* are presented this year.

More information on infections with zoonotic bacteria in Sweden is presented in the yearly Swedish zoonoses report, available at www.sva.se.

In SVARM, isolates are classified as susceptible or resistant by epidemiological cut-off values issued by EUCAST (see 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. To facilitate comparisons when retrospect data are presented, levels of resistance have been recalculated using current cut-off values if not otherwise stated.

TABLE SALM I. Number of *Salmonella enterica* tested for antimicrobial susceptibility year 2009.

Serotype	Cattle	Pig	Sheep	Poultry	Horse	Dog	Cat	Wild birds	Wild mammals	Total
S. Agona	1			1						2
S. Derby	1									1
S. Dublin	13								1	14
S. Duesseldorf	2									2
S. Enteritidis, not phage typed						1			1	2
S. Enteritidis, NST									2	2
S. Goldcoast				1						1
S. Livingstone				1						1
S. Montevideo						1				1
S. Reading	7	1								8
S. SanDiego				1						1
S. Typhimurium DT 1	1								3	4
S. Typhimurium DT 2								1		1
S. Typhimurium DT 7		1								1
S. Typhimurium DT 9									1	1
S. Typhimurium DT 40	1	2		1						4
S. Typhimurium DT 41		1			1			1		3
S. Typhimurium DT 104						1				1
S. Typhimurium DT 120	3	3								6
S. Typhimurium DT 146					3	1				4
S. Typhimurium NST	4	2		9		1				16
S. Typhimurium NST, U277					1	1				2
S. Typhimurium NT				1	1					2
S. Typhimurium, not phage typed	2		1	1		1	10	7		22
Subsp. diarizonae (IIIb)	4		3	1					1	9
Subsp. *enterica* (I)						1				1
Subsp. *enterica* (I), O 4,5,12;b;-	1									1
Subsp. *enterica* (I), O 4,5,12;i;-	3									3
Subsp. *enterica* (I), O 4,5:b:H5;-								1		1
Total	43	10	4	17	6	8	10[a]	10[b]	9	117
Percent of total	37	9	3	15	5	7	9	9	8	

[a] Selected from 37 isolates available; [b] selected from 16 isolates available.

Salmonella

Antimicrobial susceptibility was tested in one isolate from each involved warm-blooded animal species (wild and domesticated) of incidents notified 2009. In incidents involving more than one serotype or phage type, one isolate of each serotype and phage type was tested. In addition, isolates from incidents notified before 2009 but still under restrictions were included. Also, isolates obtained in the salmonella surveillance programme from samples collected at slaughter were tested. For details on methodology see Appendix 3.

Results and comments

Altogether 117 isolates were tested 2009. About two thirds (63%) of the isolates were from major food-producing animals (cattle, sheep, pigs and poultry), 21% were from dogs, cats or horses and 16% were from wildlife (Table Salm I). Fiftyseven percent of the isolates were *S.* Typhimurium. Notably three isolates from cattle were of the monophasic serotype O 4,5,12;b;-.

The majority of isolates (91%) were susceptible to all antimicrobials tested but 10 were resistant to at least one substance (Table Salm II). The resistant isolates were from nine separate incidents.

In two incidents in dogs *S.* Typhimurium DT 104 resistant to ampicillin, chloramphenicol, florfenicol, streptomycin, sulphonamide and tetracycline was isolated. One of the isolates was resistant also to quinolones (ciprofloxacin and nalidixic acid) which is a resistance trait rarely found in *S.* Typhimurium from Swedish animals (Table Salm V).

Two epidemiologically linked incidents in horses involved *S.* Typhimurium DT 146 resistant to sulphonamides and trimethoprim. In one of the incidents the same serotype was isolated also from dogs on the farm.

One incident in cattle involved *S.* Duesseldorf resistant to sulphonamides, streptomycin and tetracycline and another *S.* Dublin susceptible to nalidixic acid but with low level resistance to ciprofloxacin, MIC 0.12 mg/L. The latter phenotype indicates transferable resistance of e.g. *qnr*-type (Cavaco & Aarestrup, 2009). This is the first documented isolate with this resistance phenotype among *S.* Dublin from Swedish food-producing animals. Also, there is only one other documented isolate (*S.* Enteritidis) with the phenotype among other serotypes from food-producing animals since 2000. In light of possible transferability of this resistance the findings deserves further study and the isolates will be characterized by molecular methods to determine the genetic background of the resistance.

In three epidemiologically linked cattle herds, monophasic *Salmonella enterica*, (subspecies I, O 4,5,12;i;-) was isolated. Isolates from all three incidents were resistant to ampicillin, streptomycin, sulphonamide and tetracycline. This is a rare resistance phenotype in Swedish isolates but it has been previously observed in *S.* Typhimurium (Table Salm VI). Monophasic *Salmonella* with this resistance phenotype and of the same clonal lineage is increasingly isolated from humans in Italy (Dionisi et. al., 2009). Moreover, monophasic *Salmonella* is recognised as an increasing problem worldwide (Switt et al., 2009) and vigilance for further spread among Swedish livestock is warranted.

From a public health perspective resistance in *Salmonella* from food-producing animals is more important than resistance in isolates from wild animals or pets. In the period 2000-09, 459 isolates from notified incidents in food-producing animals have been tested in SVARM. This includes the vast majority of isolates from notified incidents in food-producing animals in the period. Of these isolates, 212 (46%) were *S.* Typhimurium. Almost half of these were from pigs (44%), one fourth from cattle (28%) and poultry (26%), respectively and five isolates (2%) were from sheep. Distributions of MICs and occurrence of resistance among these isolates are given in Table Salm VI. Among *S.* Typhimurium, 30 isolates (14%) were resistant to at least one antimicrobial and 18 isolates to three or more substances, i.e. multiresistant (Table Salm VII). Among other serovars than Typhimurium, 23 isolates (9%) were resistant to at least one antimicrobial and seven of these to two substances or more.

All 18 multiresistant isolates of *S.* Typhimurium are from incidents in 2004-2008. The isolates are from 16 separate incidents of which nine involved only cattle, three involved pigs only and one incident involved both pigs and cattle. Of the remaining incidents one was in sheep, one in ducks for

TABLE SALM II. MICs (mg/L) of *Salmonella* enterica resistant to at least one antimicrobial. 2009. Shaded fields indicate resistance.

Animal species	Sevovar	Am[a]	Ctx	Cm	Ff	Gm	Km	Sm	Ci	Nal	Su	Tc	Tm
Dog	*S.* Typhimurium DT 104	>64	0.12	256	32	1	8	128	0.06	4	>1024	16	0.5
Dog	*S.* Typhimurium, not phagetyped	>64	0.12	256	32	1	4	128	0.25	256	>1024	16	<0.25
Dog	*S.* Typhimurium DT 146	1	0.12	4	4	1	4	16	0.06	4	>1024	1	>32
Horse	*S.* Typhimurium DT 146	1	0.12	4	4	1	2	16	0.03	4	>1024	1	>32
Horse	*S.* Typhimurium DT 146	1	<0.06	4	4	1	4	16	0.03	4	>1024	1	>32
Cattle	*S.* Duesseldorf	1	0.12	4	4	1	4	>256	0.03	4	>1024	>64	<0.25
Cattle	*S.* Dublin	2	0.5	8	16	0.5	1	16	0.12	8	256	4	1
Cattle	Subsp. *enterica* (I) O 4,5,12;i;-	>64	0.12	8	8	1	2	256	0.06	8	>1024	>64	<0.25
Cattle	Subsp. *enterica* (I) O 4,5,12;i;-	>64	0.12	4	4	1	4	256	0.06	4	>1024	>64	<0.25
Cattle	Subsp. *enterica* (I) O 4,5,12;i;-	>64	0.12	4	4	1	4	256	0.06	4	>1024	>64	<0.25

[a] Am: ampicillin; Ctx: cefotaxime; Cm: chloramphenicol; Ff: florfenicol; Gm: gentamicin; Km: kanamycin; Sm: streptomycin; Ci: ciprofloxacin; Nal: nalidixic acid; Su: sulphonamide; Tc: tetracycline; Tm: trimethoprim

Salmonella in reptiles

ANTIMICROBIAL resistance in *Salmonella* from warm-blooded wild and domesticated animals is investigated yearly in SVARM. The situation in these animal populations is favourable since *Salmonella* is rare and most isolates are susceptible to antimicrobials. However *Salmonella* is not an uncommon finding in reptiles such as snakes, lizards and turtles kept as pets. Such pets sometimes live in close contact with household members and could be a reservoir of *Salmonella* causing human infections. This risk has been emphasized but the magnitude of the problem is unknown and little is known of antimicrobial susceptibility of *Salmonella* from reptiles (Bertrand et al., 2008).

To investigate the situation in Sweden, an inventory of SVA´s collection of *Salmonella* strains from 2006-2009 was made for isolates from reptiles. Seventeen strains found were tested for susceptibility using the same panel of antimicrobials as for *Salmonella* from warm-blooded animals (see Appendix 3 for details).

Nine strains were from snakes, five from lizards and three from turtles. The strains were of a large variety of serotypes (Table I) which agrees with data from Germany (Bertrand et. al., 2008). Also, the specific serotypes represented largely overlap with the German data.

Most of the 17 strains were susceptible to all twelve antimicrobials tested but three strains were resistant to streptomycin (Table II). The number of strains tested was small but the results do not indicate that reptiles kept as pets are an important reservoir of resistant *Salmonella*.

TABLE I. Serotypes of *Salmonella enterica* from reptiles tested for antimicrobial susceptibility, 2006-09.

Serovar	Number of strains
S. Braenderup	1
S. Cubana	1
S. Infantis	1
S. Livingstone	1
S. Louisiana	1
S. Muenchen	1
S. Oranienburg	1
S. Potsdam	1
S. Remete	1
S. Tennessee	2
S. Waycross	1
Subspecies arizonae (IIIa)	2
Subspecies diarizonae (IIIb)	1
Subspecies houtenae (IV)	2
Total	17

TABLE II. Distribution of MICs for *Salmonella enterica* (n=17) from reptiles, 2006-09.

	Resis-tance	Distribution *(%)* of MICs[a] (mg/L)																		
Antimicrobial	(%)	≤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	0							17.6	76.5	5.9										
Cefotaxime	0				41.2	47.6	11.8													
Chloramphenicol	0									11.8	64.8	23.5								
Ciprofloxacin	0			76.5	23.5															
Florfenicol	0									17.6	47.6	35.3								
Gentamicin	0							35.3	64.8											
Kanamycin	0									47.6	41.2	11.8								
Nalidixic acid	0									11.8	76.5	11,8								
Streptomycin	18										11.8	23.5	35.3	11.8	17.6					
Sulphonamide	0													23.5	64.8	5.9	5.9			
Tetracycline	0								41.2	58.8										
Trimethoprim	0						52.9	5.9	41.2											

[a] Grey fields denote range of dilutions tested. Values above the range denote MICs greater than the highest concentration tested. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Vertical lines indicate cut-off values for resistance.

food production 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. Resistance phenotypes of the isolates are given in Table Salm VI.

In contrast none of 52 isolates of *S.* Typhimurium from food-producing animals from 2000-03 were multiresistant. But multiresistant *Salmonella* occurred in Swedish food-producing animals also before 2004. In 1997 to 1999, five of 51 incidents in food-producing animals involved multiresistant *S.* Typhimurium, either DT 104 or DT 193. The cluster of incidents with multiresistant strains in 2004-2008 is therefore probably coincidental and not an indication of an overall increased occurrence. This is corroborated by the fact that none of 33 isolates of *S.* Typhimurium from food-producing animals in 2009 was resistant to any of the substances tested.

The overall situation of *Salmonella* among Swedish animals is favourable from an international perspective. Food-producing animals are virtually free from *Salmonella*, most likely a result of the strategies in the Swedish *Salmonella* control programme, and few incidents involve multiresistant strains. Nevertheless, in view of public health consequences vigilance towards resistant *Salmonella* in food-producing animals is warranted. This is emphasised by the three incidents this year of multiresistant monophasic *Salmonella* subspecies I, O 4,5,12;i- in cattle. Also occurrence of multiresistant *Salmonella* in pets is of concern for both veterinary and human healthcare as is a scenario with strains in livestock carrying transmissible fluoroquinolone resistance.

TABLE SALM III. Distribution of MICs for all serotypes of *Salmonella enterica* (n=117) from animals, 2009.

Antimicrobial	Resistance (%)	Distribution (%) of MICs[a] (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	4							8.5	85.5	1.7						4.3				
Cefotaxime	0				37.6	59.0	2.6	0.9												
Chloramphenicol	2									24.8	68.4	5.1					1.7			
Ciprofloxacin	2			65.0	33.3	0.9	0.9													
Florfenicol	2									37.6	55.6	4.3	0.9	1.7						
Gentamicin	0							35.0	60.7	4.3										
Kanamycin	0								5.1	52.1	41.0	1.7								
Nalidixic acid	<1									3.4	91.5	4.3					0.9			
Streptomycin	5									0.9	0.9	17.1	65.0	11.1		1.7	2.6	0.9		
Sulphonamide	8											0.9	0.9	10.3	38.5	34.2	7.7			7.7
Tetracycline	5								53.8	40.2	0.9		1.7			3.4				
Trimethoprim	3						41.0	55.6	0.9						2.6					

[a] White fields denote range of dilutions tested. Values above the range denote MICs greater than the highest concentration tested. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Vertical lines indicate cut-off values for resistance.

TABLE SALM IV. Distribution of MICs for *Salmonella* Typhimurium (n=67) from animals, 2009.

Antimicrobial	Resistance (%)	Distribution (%) of MICs[a] (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	3							3.0	92.5	1.5						3.0				
Cefotaxime	0				23.9	73.1	3.0													
Chloramphenicol	3									13.4	83.6						3.0			
Ciprofloxacin	1			61.2	37.3		1.5													
Florfenicol	3									38.8	58.2			3.0						
Gentamicin	0							23.9	76.1											
Kanamycin	0									50.7	47.8	1.5								
Nalidixic acid	1									1.5	95.5	1.5					1.5			
Streptomycin	3											22.4	70.1	4.5		3.0				
Sulphonamide	7											1.5		1.5	41.8	38.8	9.0			7.5
Tetracycline	3								38.8	58.2			3.0							
Trimethoprim	4						35.8	59.7							4.5					

[a] White fields denote range of dilutions tested. Values above the range denote MICs greater than the highest concentration tested. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Vertical lines indicate cut-off values for resistance.

TABLE SALM V. Resistance (%) and source of isolates in *Salmonella* Typhimurium from animals 1978-2009.

Antimicrobial	Cut-off value (mg/L)	Resistance (%) 1978-88[a] (n=125)	1989-99 (n=317)	2000–02 (n=108)	2003–05 (n=183)	2006 (n=53)	2007 (n=72)	2008 (n=64)	2009 (n=67)
Ampicillin	>4	2[b]	6[b]	3	2	17	8	13	3
Cefotaxime	>0.5	-	-	-	-	0	0	0	0
Ceftiofur	>2	-	-	0	0	0	-	-	-
Chloramphenicol	>16	4[b]	5[b]	3	6	2	1	8	3
Ciprofloxacin	>0.06	-	-	-	-	0	0	3	1
Enrofloxacin	>0.25	-	1	0	<1	-	-	-	-
Florfenicol	>16	-	-	3	4	2	1	8	3
Gentamicin	>2	-	0[b]	0[c]	<1	0	0	0	0
Kanamycin	>16	-	-	-	-	0	0	0	0
Nalidixic acid	>16	-	-	4	<1	0	0	2	1
Neomycin	>4	0[b]	1[b]	4	0	-	-	-	-
Streptomycin	>32	74	15	4	7	11	4	13	3
Sulphonamide	>256	-	-	3	7	15	7	13	7
Tetracycline	>8	13	6	3	7	11	4	11	3
Trimethoprim	>2	-	-	0	<1	0	0	0	4
Trim/sulph.	>0.5/9.5	0	3	-	-	-	-	-	-
Percent of isolates from:									
Cattle, sheep, pigs, poultry		100	46	45	21	40	53	70	49
Horses, cats, dogs			29	36	65	36	17	16	31
Wildlife			25	19	14	24	30	14	19

[a] 1988 includes isolates to September, isolates from October-December 1988 given under 1989; [b] Cut-off value for resistance >8 mg/L; [c] Cut-off value for resistance >4 mg/L.

TABLE SALM VI. Distribution of MICs for *Salmonella* Typhimurium (n=212) from food-producing animals 2000-2009.

Antimicrobial	Resistance (%)	Distribution (%) of MICs[a] (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	11							2.8	68.4	16.5	1.4				10.8					
Cefotaxime[b]	0				22.9	69.4	7.6													
Ceftiofur[c]	0							28.7	68.3	3.0										
Chloramphenicol	6									9.4	81.6	3.3				0.9	4.7			
Ciprofloxacin[d]	<1			54.2	45.0			0.8												
Enrofloxacin[e]	0				54.3	42.0	3.7													
Florfenicol	5										91.5	2.8	0.5	5.2						
Gentamicin	2							17.0	70.3	10.8	1.9									
Kanamycin[d]	0									28.2	67.2	3.8	0.8							
Nalidixic acid	1									1.4	77.4	14.6	5.7	0.5			0.5			
Neomycin[e]	0									84.0	16.0									
Streptomycin	9										0.5	19.3	57.5	13.2	2.8	2.4	2.8	1.4		
Sulphonamide	11														49.5	33.0	6.6			10.8
Tetracycline	8								30.7	54.7	6.1		1.9	0.9	2.4	3.3				
Trimethoprim	0						33.0	59.9	7.1											

[a] White fields denote range of dilutions tested. Values above the range denote MICs greater than the highest concentration tested. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Vertical lines indicate cut-off values for resistance; [b] 144 isolates tested; [c] 101 isolates tested; [d] 131 isolates tested; [e] 81 isolates tested

TABLE SALM VII. Resistance phenotypes and multiresistance (%) of *Salmonella* Typhimurium (n=213) from food-producing animals years 2000-2009. All isolates tested for susceptibility to ampicillin, ceftiofur/cefotaxime, enrofloxacin/ciprofloxacin, florfenicol, gentamicin, chloramphenicol, nalidixic acid, streptomycin, sulphametoxazole, tetracycline, and trimethoprim. Breakpoints for resistance are given in Table Salm V.

		Phage type																		
Resistance pattern[a]	**Animal species**	**104**	**120**	**195**	**193**	**151**	**126**	**99**	**41**	**40**	**15A**	**10**	**12**	**9**	**7**	**1**	**NST**	**U277**	**NT**	**Not typed**	**Total**
AmFfCmNalSmSuTcCi	Pig	1																			1
AmFfCmSmSuTc	Cattle	5	1																	1	7
AmFfCmSmSuTc	Pig	1																		1	2
AmFfCmSmSuTc	Sheep	1																			1
AmCmSmSuTc	Cattle	1																			1
AmSmSuTc	Cattle					1													2		3
AmSmSuTc	Pig		1																		1
AmSmSuTc	Poultry																		2		2
AmSu	Cattle	2																			2
AmSu	Pig	1																			1
SmSu	Poultry										2										2
Am	Poultry																2				2
Gm	Cattle								1												1
Gm	Pig									1											1
Gm	Poultry								1								1				2
Nal	Pig												1								1
Susceptible	Cattle	1	5				2		3	1	1	2				3	19		1	6	44
Susceptible	Pig	2	6					1	8	37			2		1	1	17	1	3	7	86
Susceptible	Sheep															1				3	4
Susceptible	Poultry		1	1	1				2	4			1	1		1	32	1	3		48
Number of isolates		15	14	1	1	1	2	1	15	43	3	2	4	1	1	6	71	2	11	18	213
percent of total		7	7	<1	<1	<1	<1	<1	7	20	1	<1	2	<1	<1	3	33	<1	5	9	100
Multiresistance (%)																					
Susceptible to all antimicrobials		20	86	100	100		100	100	87	98	33	100	75	100	100	100	96	100	64	89	85
Resistant to 1 antimicrobial									13	2			25				4				3
Resistant to 2 antimicrobials		20									67										3
Resistant to 3 antimicrobials																					
Resistant to >3 antimicrobials		60	14			100													36	11	8

[a] Am: ampicillin; Ff : florfenicol; Cm: chloramphenicol; Sm: streptomycin; Su: sulphonamide; Tc: tetracycline; Nal: nalidixic acid; Gm: gentamicin.; Ci: ciprofloxacin.

Methicillin-resistant *Staphylococcus aureus* (MRSA)

METHICILLIN-RESISTANT *Staphylococcus aureus* (MRSA) is a serious global problem in human healthcare and recently MRSA has emerged in several animal species worldwide. This is of concern mainly from a public health perspective, since MRSA can be transferred between animals and man. But MRSA cause infections in animals too and is in such cases of clinical importance also in animal healthcare.

The public health significance of MRSA in animals and food was recently assessed by the Panel on Biological Hazards of the European Food Safety Authority (EFSA) (EFSA, 2009). One conclusion of the panel is that livestock-associated lineages, i.e. CC398, can be a major contributor to the overall 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.

In Sweden, MRSA in animals was first verified in 2006 and was made notifiable to the Swedish Board of Agriculture in 2008. Up to and including the first quarter of 2010 a total of 29 cases have been confirmed by the National Veterinary Institute (SVA). The current situation is summarized below.

Dogs and cats

MRSA has been confirmed in 15 dogs and 2 cats including the first Swedish animal isolate from a dog in 2006 (Table). Altogether six different animal healthcare settings in different counties have been involved. Most isolates are from wound infections, mainly post operative wounds, but one is from urine of a cat and another isolate from a skin wound due to mange in a dog.

Fifteen of the isolates are of spa-type t032, one is of t217 and one of t002 (Table). All isolates are negative for genes coding for Panton Valentine Leukocidin toxin (PVL). These *spa*-types are all common among MRSA from humans in Sweden (SWEDRES 2009). *Spa*-types t032 and t002 were the most common types among human isolates of MRSA in 2007 and 2008, respectively. This supports the view that humans often are a source of MRSA in small companion animals (EFSA 2009, CVMP 2009).

Horses

The first isolation of MRSA from horses in Sweden was in a screening study 2007 using selective culture of nasal swabs. MRSA was isolated from only one of 300 horses screened. The isolate, of spa-type t011 and clonal complex CC398, was resistant to beta-lactams, gentamicin, kanamycin, tetracycline and trimethoprim (Table).

The first documented outbreak of MRSA infections in Swedish horses occurred in 2008. At an equine hospital, six horses with postoperative wound infections were confirmed with MRSA. On screening of contact horses outside the hospital, one horse, without any signs of infection, was revealed as carrier of MRSA in the nostrils. The index case of the outbreak was not established. Five of the seven isolates obtained were subtyped and were of spa-type t011 and negative for genes coding PVL. Both antibiogram and spa-type are the same as of the CC398 isolate from the screening study in 2007.

Since then, MRSA have been confirmed in two additional horses sampled at the equine hospital where the outbreak occurred and in two horses sampled elsewhere. These four isolates have the same antibiogram as the previous MRSA isolated from Swedish horses. Three isolates are of spa-type t011 and one of t064 (Table).

Clonal complex CC398 is the livestock associated MRSA mostly found in pigs and other food-producing animals but which also occur in other animals including horses and is reported from humans too (EFSA 2009, CVMP 2009). In Sweden, MRSA of *spa*-types correlating to CC398 (i.e. t011, t108, t034 and t571) and negative for *pvl*-gene was documented in 12 humans in 2006-09 (SWEDRES 2009). Of these, five isolates are of spa-type t011 which is the dominating type among MRSA from pigs in Europe and also the spa-type of the isolates from Swedish horses.

Food-producing animals

MRSA in food-producing animals is reported globally, mostly in pigs but the prevalence is high also among veal calves and broilers and MRSA occur among dairy cows too (for a review see EFSA, 2009). In production animals, the livestock associated MRSA CC398 dominates.

In Sweden MRSA has not been isolated from food-producing animals even though several surveys were carried out in recent years. In 2007, slaughter pigs on 100 pig production holdings were screened for MRSA by culture of nasal swabs. Also, samples of milk from dairy cows were screened on several occasions, and in 2003 *S. aureus* isolated from chicken carcasses were tested for methicillin resistance by the Food Production Agency.

In 2008 a decision was taken that all Member States of the European Union should screen holdings with breeding pigs for MRSA by culture of dust using harmonized methodology (Decision 208/55/EC). Overall, MRSA was confirmed on 27% of the holdings in the EU but from none of the 208 Swedish holdings sampled.

Future strategies

Reported incidents of MRSA in animals is still scarce in Sweden but the situation can rapidly change if livestock associated lineages are introduced to populations of intensively reared food-producing animals. Likewise inadequate infection control in animal healthcare can lead to a rapid spread of MRSA among companion animals and horses. Sweden is still a country with a comparatively low prevalence of human MRSA infection (SWEDRES 2009) and therefore measures should be taken to avert a situation where animals constitute a reservoir for MRSA spreading into human healthcare.

As discussed in two recent reports from EU authorities, a measure to mitigate MRSA could be improved biosecurity to hinder spread to, between and within farms with food-producing animals (EFSA 2009, CVMP 2009). Other options discussed are improved infection control in animal healthcare,

to prevent spread and nosocomial infections in companion animals, and a reduction of antimicrobial selection pressure in animal populations by prudent use of antimicrobials. Other strategies could be to decolonize carriers and clear environments from MRSA but here knowledge is lacking and studies are needed. The reports acknowledge that basic hygiene measures such as hand washing and disinfection is of key importance to control transfer of MRSA between humans and animals. Also, it is recognised that periodical monitoring of MRSA in food producing animals is essential for decisions on control strategies and evaluation of their effect.

In 2010, active monitoring of MRSA in Swedish animals will include screening studies among pigs, horses and dairy cows. In addition, since MRSA is notifiable there is a passive surveillance by culture of routine samples from animal healthcare. But to mitigate spread among animals, awareness of the problem among stakeholders such as farmers, animal owners, veterinarians and laboratory personnel is crucial. Awareness is likely to increase vigilance for MRSA-infections as well as compliance to recommendations on infection control and prudent use of antimicrobials. Relevant information and recommendations on practical measures are therefore important components of strategies against MRSA.

TABLE. Cases of Methicillin-resistant *Staphylococcus aureus* (MRSA) in Swedish animals up to and including March 2010. All isolates were positive for the *mec*A and nuc genes by molecular methods. All isolates tested for spa-type were negative for *pvl*-gene. White areas indicate MIC above EUCAST cut-off values for the wild-type population.

Animal species	Year	Background	Antimicrobial[a]													Spa-type
			Ox[b]	Fox	Pc	Ct	Cl	Em	Tc	Fu	Gm	Km	Ci	Tm	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
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
Horse	2007	screening	>16	-	>4	1	≤0.25	0.5	64	0.5	>64	>32	1	>32	8	t011
Horse	2008	post-op wound (synovia)	>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	nt[c]
Horse	2008	post-op wound	2	>16	4	4	≤0.25	≤0.25	32	0.12	4	32	0.25	>32	4	nt[c]
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

[a] Pc: penicillin; Ct: cephalothin; Ox: oxacillin; Em: erythromycin; Cm: chloramphenicol; Cl: clindamycin; Tc: tetracycline; Fu: fusidic acid; Gm: gentamicin; Km: kanamycin; Ci: ciprofloxacin; Tm: trimethoprim; Fox: cefoxitin, [b] tested with 2% NaCl, [c] Not tested.

Indicator bacteria

THE PREVALENCE of acquired antimicrobial resistance in commensal bacteria of the enteric microflora of healthy animals indicates the magnitude of the selective pressure from use of antimicrobials in an animal population. By regular monitoring of resistance, effects of changes in use of antimicrobials in the population can be evaluated. In SVARM, *Escherichia coli* and *Enterococcus* spp. from healthy animals serve as indicator bacteria for the normal enteric microflora.

Most bacteria of the enteric microflora 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. The exposure of humans to such reservoir is indicated by occurrence of resistant bacteria in food of animal origin. It is the intention in SVARM to regularly monitor resistance among indicator bacteria from meat at retail but this year no such data are available.

Resistance to more than one antimicrobial in a bacterium (co-resistance) can indicate that resistance genes are located on the same genetic element. Evaluation of resistance patterns, i.e. phenotypes, can give insight in resistance selection since use of one antimicrobial can select for resistance to other, unrelated antimicrobials (co-selection) and a single transfer event can convey resistance to several antimicrobials to a recipient bacterium (co-transfer).

In SVARM, isolates of indicator bacteria are classified as susceptible or resistant by epidemiological cut-off values issued by EUCAST (see 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 does not always implies clinical resistance. To facilitate comparisons when retrospect data are presented, levels of resistance have been recalculated using current cut-off values if not otherwise stated.

This year resistance in indicator bacteria from fattened calves was studied. Caecal content from healthy calves, about half a year old, were collected at slaughter and cultured for *Escherichia coli* and *Enterococcus* spp. All samples were in addition screened for *E. coli* resistant to third generation cephalosporins by culture on media supplemented with cefotaxime (1mg/L). Also occurrence of vancomycin-resistant enterococci (VRE) in broilers was studied. Caecal content from healthy broilers were sampled at slaughter and cultured for VRE using media supplemented with vancomycin (16 mg/L). For details on sampling strategy and methodology see Appendix 3.

Escherichia coli

Calves

Escherichia coli were isolated from 87% of 256 samples. The majority (95%) of the 223 isolates was susceptible to all 12 antimicrobials tested but 11 isolates (15%) were resistant to at least one substance (Table EC I & EC IV). Ten isolates (4%)

TABLE EC I. Resistance (%) and multiresistance (%) of *Escherichia coli* from calves, 2009. Previous data from SVARM given for comparison.

		Resistance (%) (95% confidence interval in brackets)													
		Calves		**Dairy cows**		**Calves/Yearlings**		**Sheep**		**Broilers**		**Pigs**		**Dogs**	
Antimicrobial	**Cut-off value** (mg/L)	**2009** n=223		**2006** n=314		**2000** n=293		**2006-09** n=115		**2007** n=296		**2008** n=349		**2006** n=257	
Ampicillin	>8	<1	(0.0-2.5)	0	(0.0-1.2)	0	(0.0-1.3)	2	(0.2-6.1)	5	(2.6-7.8)	6	(3.5-8.7)	5	(3.0-9.0)
Cefotaxime	>0.25	0	(0.0-1.6)	0	(0.0-1.2)	-		0	(0.0-3.2)	1	(0.2-2.9)	0	(0.0-1.0)	<1	(0.0-2.1)
Ceftiofur	>1	-		0	(0.0-1.2)	0	(0.0-1.3)	-		1	(0.2-2.9)	-		<1	(0.0-2.1)
Chloramph.	>16	0	(0.0-1.6)	0	(0.0-1.2)	0	(0.0-1.3)	0	(0.0-3.2)	<1	(0.0-1.9)	3	(1.4-5.2)	<1	(0.1-2.9)
Ciprofloxacin	>0.06	0	(0.0-1.6)	<1	(0.1-2.3)	<1[b]	(0.0-1.9)	<1	(0.0-4.8)	7	(4.5-10.7)	1	(0.3-2.9)	2	(0.6-4.5)
Florfenicol	>16	0	(0.0-1.6)	0	(0.0-1.2)	0	(0.0-1.3)	0	(0.0-3.2)	0	(0.0-1.2)	<1	0.0-1.6)	0	(0.0-1.4)
Gentamicin	>2	0	(0.0-1.6)	<1	(0.2-2.8)	<1[c]	(0.1-2.4)	3	(0.5-7.4)	<1	(0.0-1.9)	<1	0.0-1.6)	<1	(0.0-2.1)
Kanamycin	>8	<1	(0.0-2.5)	<1	(0.2-2.8)	-		2	(0.2-6.1)	2	(0.6-3.9)	1	(0.3-2.9)	2	(0.9-5.0)
Nalidixic acid	>16	0	(0.0-1.6)	<1	(0.1-2.3)	<1	(0.1-2.4)	0	(0.0-3.2)	7	(4.2-10.3)	1	(0.3-2.9)	2	(0.6-4.5)
Streptomycin	>16	4	(2.2-8.1)	2	(0.3-3.3)	5	(2.9-8.3)	3	(0.5-7.4)	4	(1.9-6.6)	14	(10.3-17.8)	7	(4.2-10.8)
Sulphonamide	>256	2	(0.5-4.5)	2	(0.5-3.7)	0	(0.0-1.3)	5	(1.9-11.0)	6	(3.7-9.5)	9	(5.9-12.0)	7	(3.9-10.4)
Tetracycline	>8	2	(0.5-4.5)	2	(0.5-3.7)	1	(0.4-3.5)	<1	(0.0-4.8)	3	(1.6-6.1)	9	(6.1-12.4)	2	(0.9-5.0)
Trimethoprim	>2	<1	(0.0-2.5)	<1	(0.0-1.8)	1	(0.4-3.5)	2	(0.2-6.1)	<1	(0.1-2.4)	5	(3.3-8.4)	4	(1.9-7.0)
Multiresistance[a]															
Susceptible to all		95		97		92		88		85		79		86	
Resistant to 1		3		<1		6		9		10		10		6	
Resistant to 2		<1		<1		<1		2		1		3		4	
Resistant to 3		<1		<1		<1		1		1		2		2	
Resistant to >3		<1		<1		<1		1		3		6		3	

[a] Enrofloxacin/ciprofloxacin/nalidixic acid as well as cefotaxime/ceftiofur considered as one substance; [b] Enrofloxacin tested, cut-off value >0.12mg/L; [c] Cut-off value >4 mg/L.

TABLE EC II. Resistance phenotypes of *Escherichia coli from* intestinal content of calves 2009. "R" in shaded fields indicates resistance. Previuos data from SVARM given for comparison; 2006 Dairy cows and 2000 Calves/Yearlings.

Year			**Resistance pattern**[a]								
2009 n=223	**2006** n=314	**2000** n=293	**Sm**	**Su**	**Tm**	**Tc**	**Am**	**Gm**	**Km**	**Ef/Ci**	**Nal**
	1		R	R	R	R					
1			R	R	R		R		R		
2	3	2	R	R		R					
		1	R	R						R	R
1	1	1	R	R							
1		1	R			R					
5	1	10	R								
		5			R						
1	1	1				R					
		2						R			
	1								R		
		1									R
	2									R	R
11 (4.8%)	**10** (3.2%)	**24** (8.2%)	Number of isolates (percent of all isolates)								

[a] Sm: streptomycin; Su: sulphonamide; Tc: tetracycline; Am. Ampicillin; Gm: gentamicin; Cm: chloramphenicol; Tm: trimethoprim; Km: kanamycin; Ef: enrofloxacin; Ci: ciprofloxacin; Nal: nalidixic acid.

TABLE EC III. Association between resistance traits in *Escherichia coli* from cattle 2000, 2006 and 2009. 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 therefor not be calculated.

Single substance susceptibility		n	Resistance (%)[a]								
			Am	Cm	Ff	Gm	Nal	Sm	Su	Tc	Tm
Ampicillin	S	829	0.0	0.0	0.0	0.2	0.5	3.6	1.4	1.6	0.7
	R	1	100.0	0.0	0.0	0.0	0.0	100.0	100.0	0.0	100.0
Cefotaxime	S	537	0.2	0.0	0.0	0.0	0.4	3.0	1.7	1.7	0.4
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Ceftiofur	S	607	0.0	0.0	0.0	0.3	0.7	3.5	1.5	1.5	1.0
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Chloramph.	S	830	0.1	0.0	0.0	0.2	0.5	3.7	1.6	1.6	0.8
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Ciprofloxacin	S	535	0.2	0.0	0.0	0.0	0.0	3.0	1.7	1.7	0.4
	R	2	0.0	0.0	0.0	0.0	100.0	0.0	0.0	0.0	0.0
Enrofloxacin	S	482	0.0	0.0	0.0	0.4	0.2	3.9	1.5	1.7	1.2
	R	1	0.0	0.0	0.0	0.0	100.0	100.0	100.0	0.0	0.0
Florfenicol	S	830	0.1	0.0	0.0	0.2	0.5	3.7	1.6	1.6	0.8
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Gentamicin	S	828	0.1	0.0	0.0	0.0	0.5	3.7	1.6	1.6	0.8
	R	2	0.0	0.0	0.0	100.0	0.0	0.0	0.0	0.0	0.0
Kanamycin	S	535	0.0	0.0	0.0	0.0	0.4	2.8	1.5	1.7	0.2
	R	2	50.0	0.0	0.0	0.0	0.0	50.0	50.0	0.0	50.0
Nalidixic acid	S	826	0.1	0.0	0.0	0.2	0.0	3.6	1.5	1.6	0.8
	R	4	0.0	0.0	0.0	0.0	100.0	25.0	25.0	0.0	0.0
Neomycin	S	483	0.0	0.0	0.0	0.4	0.4	4.1	1.7	1.7	1.2
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Streptomycin	S	799	0.0	0.0	0.0	0.3	0.4	0.0	0.0	0.4	0.6
	R	31	3.2	0.0	0.0	0.0	3.2	100.0	41.9	32.3	6.5
Sulphonamide	S	817	0.0	0.0	0.0	0.2	0.4	2.2	0.0	0.6	0.6
	R	13	7.7	0.0	0.0	0.0	7.7	100.0	100.0	61.5	15.4
Tetracycline	S	817	0.1	0.0	0.0	0.2	0.5	2.6	0.6	0.0	0.7
	R	13	0.0	0.0	0.0	0.0	0.0	76.9	61.5	100.0	7.7
Trimethoprim	S	823	0.0	0.0	0.0	0.2	0.5	3.5	1.3	1.5	0.0
	R	7	14.3	0.0	0.0	0.0	0.0	28.6	28.6	14.3	100.0

[a] Am: ampicillin; Cm: chloramphenicol; Ff: florfenicol; Gm: gentamicin; Nal: nalidixic acid; Sm: streptomycin; Su: sulphonamide; Tc: tetracycline; Tm: trimethoprim.

were resistant to streptomycin, which was the most common resistance trait. Occasional isolates (<2%) were resistant to sulphonamides, tetracycline, ampicillin, kanamycin or trimethoprim. No isolate was resistant to quinolones (nalidixic acid and ciprofloxacin), amphenicols (chloramphenicol and florfenicol), cefotaxime or gentamicin.

Five isolates (2%) were resistant to more than one antimicrobial. Two of these isolates were resistant to two antimicrobials and three isolates to three or more antimicrobials (Table EC I). The phenotypes of the resistant isolates are presented in Table EC II. Notably resistance to streptomycin, sulphonamide, trimethoprim and tetracycline are often associated (Table EC III).

E coli resistant to cefotaxime (MIC 0.5-2 mg/L) were obtained from 11 of 256 samples when cultured on media supplemented with cefotaxime. All 11 isolates were negative for production of extended spectrum beta-lactamases (ESBLs) but positive for production of AmpC when tested by phenotypic tests. On additional testing by molecular methods, i.e. microarray, transferable genes coding for ESBL or plasmidic AmpC were not confirmed (see Appendix 3 for details). This indicates that resistance to third generation cephalosporins was by mutational hyperproduction of AmpC type beta-lactamases.

Enterococcus

Calves

Enterococci were isolated from 90% of 271 samples cultured. *Enterococcus hirae* was isolated from 60%, *E. faecium* from 9% and *E. faecalis* from 4% of the samples (Table ENT I). From each sample one isolate of each of these three species were tested for antimicrobial susceptibility if available.

Of ten isolates of *E. faecalis*, three were resistant to tetracycline which was the only resistance trait observed (Table ENT II & V). Of 24 isolates of *E. faecium*, one isolate was resistant to bacitracin and another to streptomycin (Table ENT III & VIII). Of 163 isolates of *E. hirae* only two were resistant to any antimicrobial. One isolate was resistant to streptomycin and another to tetracycline (Table ENT III & VIII).

Broilers

Vancomycin-resistant enterococci (VRE) were isolated from 24 (23%) of 105 samples cultured on vancomycin supplemented media (16 mg/L) (Fig ENT I). All 24 isolates were *E. faecium* with MIC for vancomycin >128 mg/L. All isolates were susceptible to ampicillin, tetracycline, virginiamycin and linezolid but MICs for narasin were elevated (4-8 mg/L) as were MICs for erythromycin (8-16 mg/L) in all but one isolate. This isolate also deviated with respect to MIC for bacitracin which was >128 mg/L in comparison to the other isolates which all had MICs <1 mg/L. Eight isolates examined by molecular methods all carried the *van*A-gene.

Comments

Calves

The studies of fattened calves, about half a year old, as well as previous studies in SVARM of dairy cows and calves/yearlings, show that resistance in *E. coli* and enterococci from older cattle is rare and that that there are no trends in occurrence. Conclusions regarding *E. faecalis* and *E. faecium* should however be made cautiously since only a small number of isolates have been available for testing.

These findings indicate a low selection pressure for resistance in Swedish cattle older than six months and show that *E. coli* and *Enterococcus* in these categories of cattle is no significant reservoir of resistance genes. Notably, this year no isolate of *E. coli* was resistant to fluoroquinolones and transferable resistance to third generation cephalosporins was not observed although all samples were screened for this type of resistance. Likewise, resistance to vancomycin, linezolid or the streptogramin virginiamycin was not observed in enterococci.

However, in *E. coli* from younger calves, resistance and multiresistance is quite common in Swedish cattle (SVARM 2006). Such age related occurrence of resistance in *E. coli* from cattle has been observed also elsewhere and is thought to be due not only to a selection pressure by use of antimicrobials but also to other factors favouring colonization of the intestine of young calves by resistant strains of *E. coli* (Call et al., 2008).

Broilers

The prevalence of VRE among broilers, screened by culture on vancomycin supplemented media, gradually increased from less than one percent in 2000 to a peak of 41% of 99 samples cultured in 2005 (Figure ENT I). It has been shown that the increase was caused by spread of a single clone of *E. faecium* carrying the *van*A gene (Nilsson et al., 2009). This year, VRE were isolated from 23% of the samples which is similar to the prevalence in 2006-2008 indicating that the spread has abated.

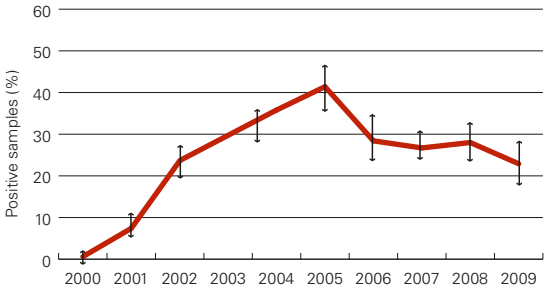

FIGURE ENT I. Proportion (%) samples of intestinal content from healthy broilers positive for VRE when cultured on vancomycin supplemented media (16 mg/L), 95% confidence intervals indicated. Number of samples cultured each year between 99 and 351.

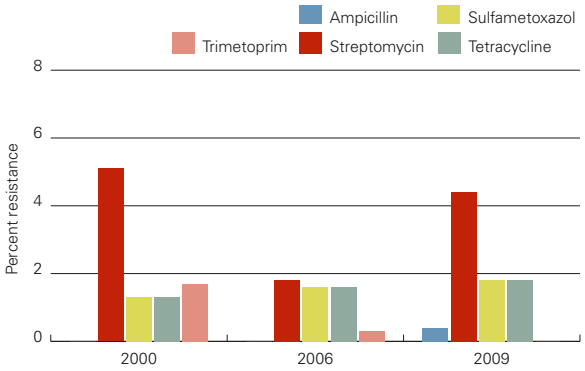

FIGURE EC I. Resistance (%) in *Escherichia coli* from cattle 2000 (calves/yearlings n=293); 2006 (dairy cows n= 314); 2009 (fattened calves n=223).

TABLE ENT I. Isolation frequency of enterococci from caecal content, calves 2009. Previous data from SVARM given for comparison.

Year	Animal category	No. of samples cultured	Cultures positive for enterococci	*Enterococcus* species isolated No. of isolates (% of samples cultured)			
				E. faecalis	*E. faecium*	*E. hirae*	Other spp.
2009	Calves	271	90%	10 (4%)	24 (9%)	163 (60%)	136 (50%)
2006	Dairy cows	461	83%	13 (3%)	98 (21%)	147 (32%)	125 (27%)
2000	Calves/Yearlings	415	67%	22 (5%)	71 (17%)	127 (31%)	57 (14%)

TABLE ENT II. Resistance (%) and multiresistance (%) of *Enterococcus faecalis* from calves, 2009. Previous data from SVARM given for comparison.

		Resistance (%) (95% confidence interval in brackets)													
		Calves		**Dairy cows**		**Calves/ Yearlings**		**Sheep**		**Broilers**		**Pigs**		**Dogs**	
Antimicrobial	**Cut-off value** (mg/L)	**2009** n=10		**2006** n=13		**2000** n=22		**2006-09** n=24		**2007** n=28		**2008** n=68		**2006** n=135	
Ampicillin	>4	0	(0.0-30.9)	0	(0.0-24.7)	0	(0.0-15.4)	0	(0.0-14.2)	0	(0.0-12.3)	0	(0.0-5.3)	<1	(0.0-4.1)
Bacitracin	>32	0	(0.0-30.9)	0	(0.0-24.7)	0	(0.0-15.4)	0	(0.0-14.2)	11	(2.3-28.2)	0	(0.0-6.5)	1	(0.2-5.2)
Chloramph.	>32	0	(0.0-30.9)	0	(0.0-24.7)	-		0	(0.0-14.2)	0	(0.0-12.3)	1	(0.0-9.7)	7	(3.1-12.3)
Erythromycin	>4	0	(0.0-30.9)	0	(0.0-24.7)	5	(0.1-22.8)	0	(0.0-14.2)	29	(13.2-48.7)	24	(17.6-42.9)	14	(8.7-21.1)
Gentamicin	>32	0	(0.0-30.9)	0	(0.0-24.7)	0	(0.0-15.4)	0	(0.0-14.2)	0	(0.0-12.3)	3	(0.4-12.5)	<1	(0.0-4.1)
Kanamycin	>1024	0	(0.0-30.9)	0	(0.0-24.7)	-		0	(0.0-14.2)	4	(0.1-18.3)	3	(0.4-12.5)	4	(1.6-9.4)
Linezolid	>4	0	(0.0-30.9)	0	(0.0-24.7)	-		0	(0.0-14.2)	0	(0.0-12.3)	0		0	(0.0-2.7)
Narasin	>2	0	(0.0-30.9)	8	(0.2-36.0)	0	(0.0-15.4)	0	(0.0-14.2)	36	(18.6-55.9)	0	(0.0-6.5)	1	(0.2-5.2)
Streptomycin	>512	0	(0.0-30.9)	0	(0.0-24.7)	14[a]	(2.9-34.9)	4	(0.1-21.1)	0	(0.0-12.3)	13	(7.8-28.8)	9	(4.7-15.0)
Tetracycline	>4	30	(6.7-65.2)	15	(1.9-45.4)	14	(2.9-34.9)	8	(1.0-27.0)	57	(37.2-75.5)	62	(63.0-86.8)	32	(24.1-40.4)
Vancomycin	>4	0	(0.0-30.9)	0	(0.0-24.7)	0	(0.0-15.4)	0	(0.0-14.2)	0	(0.0-12.3)	0	(0.0-6.5)	0	(0.0-2.7)
Virginiamycin	>32	0	(0.0-30.9)	0	(0.0-24.7)	0	(0.0-15.4)	0	(0.0-14.2)	0	(0.0-12.3)	0	(0.0-6.5)	0	(0.0-2.7)
Multiresistance															
Susceptible to all above		70		77		73		92		25		29		25	
Resistant to 1		30		23		23		4		36		46		38	
Resistant to 2						4		4		21		22		27	
Resistant to 3										14				2	
Resistant to >3										4		3		7	

[a] Cut-off value >128 mg/L;

TABLE ENT III. Resistance (%) and multiresistance (%) of *Enterococcus faecium* from calves, 2009. Previous data from SVARM given for comparison.

		Resistance (%) (95% confidence interval in brackets)													
		Calves		**Dairy cows**		**Calves/ Yearlings**		**Sheep**		**Broilers**		**Pigs**		**Dogs**	
Antimicrobial	**Cut-off value** (mg/L)	**2009** n=24		**2006** n=98		**2000** n=71		**2006-09** n=15		**2007** n=197		**2008** n=39		**2006** n=29	
Ampicillin	>4	0	(0.0-14.2)	0	(0.0-3.7)	1	(0.0-7.6)	0	(0.0-21.8)	1	(0.1-3.6)	0	(0.0-9.0)	0	(0.0-11.9)
Bacitracin	>32	4	(0.1-21.1)	1	(0.1-5.6)	1	(0.0-7.6)	0	(0.0-21.8)	23	(17.2-29.3	10	(2.9-24.2)	3	(0.1.17.8)
Chloramph.	>32	0	(0.0-14.2)	0	(0.0-3.7)	-		0	(0.0-21.8)	0	(0.0-1.9)	0	(0.0-9.0)	0	(0.0-11.9)
Erythromycin	>4	4	(0.1-21.1)	7	(2.9-14.2)	6	(1.6-13.8)	0	(0.0-21.8)	11	(7.1-16.4)	13	(4.3-27.4)	28	(12.7-47.2)
Gentamicin	>32	0	(0.0-14.2)	0	(0.0-3.7)	0	(0.0-5.1)	0	(0.0-21.8)	0	(0.0-1.9)	0	(0.0-9.0)	0	(0.0-11.9)
Kanamycin	>1024	0	(0.0-14.2)	0	(0.0-3.7)	-		0	(0.0-21.8)	0	(0.0-1.9)	0	(0.0-9.0)	0	(0.0-11.9)
Linezolid	>4	0	(0.0-14.2)	0	(0.0-3.7)	-		0	(0.0-21.8)	0	(0.0-1.9)	0	(0.0-9.0)	0	(0.0-11.9)
Narasin	>4	0	(0.0-14.2)	0	(0.0-3.7)	0	(0.0-5.1)	0	(0.0-21.8)	35	(28.4-42.1)	0	(0.0-9.0)	7	(0.8-22.8)
Streptomycin	>128	0	(0.0-14.2)	0	(0.0-3.7)	0	(0.0-5.1)	7	(0.2-32.0)	1	(0.1-3.6)	3	(0.1-13.5)	0	(0.0-11.9)
Tetracycline	>4	0	(0.0-14.2)	3	(0.6-8.7)	6	(1.6-13.8)	7	(0.2-32.0)	14	(9.7-19.9)	15	(5.9-30.5)	17	(5.8-35.8)
Vancomycin	>4	0	(0.0-14.2)	0	(0.0-3.7)	1	(0.0-7.6)	0	(0.0-21.8)	0	(0.0-1.9)	0	(0.0-9.0)	0	(0.0-11.9)
Virginiamycin	>4	0	(0.0-14.2)	1	(0.1-5.6)	7	(2.3-15.7)	0	(0.0-21.8)	4	(1.8-7.8)	0	(0.0-9.0)	0	(0.0-11.9)
Multiresistance															
Susceptible to all above		92		89		85		87		39		64		62	
Resistant to 1		8		10		10		13		36		33		30	
Resistant to 2				1		4				23				6	
Resistant to 3						1				2		3			
Resistant to >3														2	

TABLE ENT IV. Resistance (%) and multiresistance (%) of *Enterococcus hirae* from calves, 2009. Previous data from SVARM given for comparison.

		Resistance (%) (95% confidence interval in brackets)											
		Calves		**Dairy cows**		**Calves/Yearlings**		**Sheep**		**Broilers**		**Pigs**	
Antimicrobial	**Cut-off value** (mg/L)	**2009** n=163		**2006** n=147		**2000** n=127		**2006-09** n=33		**2007** n=36		**2008** n=111	
Ampicillin	>4	0	(0.0-2.2)	0	(0.0-2.5)	2	(0.2-5.6)	0	(0.0-10.6)	0	(0.0-9.7)	0	(0.0-3.3)
Bacitracin	>32	0	(0.0-2.2)	0	(0.0-2.5)	0	(0.0-2.9)	0	(0.0-10.6)	8	(1.7-22.5)	0	(0.0-3.3)
Chloramph.	>8	0	(0.0-2.2)	0	(0.0-2.5)	-		0	(0.0-10.6)	0	(0.0-9.7)	0	(0.0-3.3)
Erythromycin	>2	0	(0.0-2.2)	1	(0.0-3.7)	0	(0.0-2.9)	0	(0.0-10.6)	19	(8.2-36.0)	9	(4.4-15.9)
Gentamicin	>32	0	(0.0-2.2)	0	(0.0-2.5)	0	(0.0-2.9)	0	(0.0-10.6)	0	(0.0-9.7)	0	(0.0-3.3)
Kanamycin	>1024	0	(0.0-2.2)	0	(0.0-2.5)	-		0	(0.0-10.6)	0	(0.0-9.7)	4	(1.0-9.0)
Linezolid	>4	0	(0.0-2.2)	0	(0.0-2.5)	-		0	(0.0-10.6)	0	(0.0-9.7)	0	(0.0-3.3)
Narasin	>4	0	(0.0-2.2)	1	(0.0-3.7)	0	(0.0-2.9)	0	(0.0-10.6)	33	(18.6-51.0)	0	(0.0-3.3)
Streptomycin	>128	<1	(0.0-3.4)	0	(0.0-2.5)	0	(0.0-2.9)	3	(0.1-15.8)	0	(0.0-9.7)	5	(1.5-10.2)
Tetracycline	>4	<1	(0.0-3.4)	0	(0.0-2.5)	<1	(0.0-4.3)	0	(0.0-10.6)	11	(3.1-26.1)	14	(7.8-21.3)
Vancomycin	>4	0	(0.0-2.2)	0	(0.0-2.5)	0	(0.0-2.9)	0	(0.0-10.6)	0	(0.0-9.7)	0	(0.0-3.3)
Virginiamycin	>4	0	(0.0-2.2)	0	(0.0-2.5)	15	(9.3-22.4)	0	(0.0-10.6)	3	(0.0-9.7)	<1	(0.0-4.9)
Multiresistance													
Susceptible to all		99		97		82		97		42		80	
Resistant to 1		1		3		16		3		44		14	
Resistant to 2						2				11		2	
Resistant to 3										3		4	
Resistant to >3												1	

TABLE ENT V. Resistance phenotypes of *Enterococcus faecalis* and *Enterococcus faecium* from calves, 2009. "R" in shaded fields indicates resistance. Previous data from SVARM given for comparison.

E. faecalis							
Year			**Resistance pattern**[a]				
2009 n=10	**2006** n=13	**2000** n=22	**Tc**	**Sm**	**Em**	**Na**	
		1	R	R			
3	2	2	R				
		2		R			
		1			R		
	1					R	
3 (30%)	**3** (23%)	**6** (27%)	Number of isolates (percent of all isolates)				

E. faecium									
Year			**Resistance pattern**[a]						
2009 n=24	**2006** n=98	**2000** n=71	**Tc**	**Em**	**Am**	**Ba**	**Vi**	**Va**	
		1	R	R	R				
	1	1	R	R					
		1	R				R		
	2	1	R						
		1		R			R		
1	6	1		R					
	1	3					R		
1	1	1				R			
		1						R	
2 (8%)	**11** (11%)	**11** (15%)	Number of isolates (percent of all isolates)						

[a] Tc: tetracycline; Sm: streptomycin; Em: erythromycin; Na: narasin; Am: ampicillin; Ba: bacitracin; Vi: virginiamycin; Va: vancomycin.

TABLE ENTVI. Association between resistance traits in *Enterococcus faecalis* and in *Enterococcus faecium*, respectively. Isolates from cattle years 2000, 2006 and 2009. 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 therefor not be calculated.

Single substance susceptibility	*E. faecalis*											*E. faecium*									
			Cross resistance (%)[a]											Cross resistance (%)[a]							
		n	Am	Ba	Em	Gm	Na	Sm	Tc	Va	Vi		n	Am	Ba	Em	Gm	Na	Sm	Tc	Va	Vi
Ampicillin	S	45	-	0.0	2.2	0.0	2.2	6.7	17.8	0.0	0.0	S	192	-	1.6	5.7	0.0	0.0	0.0	3.1	0.5	3.1
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	R	1	100.0	0.0	100.0	0.0	0.0	0.0	100.0	0.0	0.0
Avilamycin	S	32	0.0	0.0	3.1	0.0	3.1	9.4	12.5	0.0	0.0	S	128	0.8	0.8	8.6	0.0	0.0	0.0	5.5	0.8	3.9
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	R	1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Bacitracin	S	45	0.0	-	2.2	0.0	2.2	6.7	17.8	0.0	0.0	S	190	0.5	-	6.3	0.0	0.0	0.0	3.7	0.5	3.2
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	R	3	0.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Chloramph.	S	23	0.0	0.0	0.0	0.0	4.3	0.0	21.7	0.0	0.0	S	122	0.0	1.6	6.6	0.0	0.0	0.0	2.5	0.0	0.8
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Erythromycin	S	44	0.0	0.0	-	0.0	2.3	6.8	18.2	0.0	0.0	S	181	0.0	1.7	-	0.0	0.0	0.0	2.2	0.6	2.8
	R	1	0.0	0.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	R	12	8.3	0.0	100.0	0.0	0.0	0.0	25.0	0.0	8.3
Flavomycin	S	26	0.0	0.0	3.8	0.0	0.0	11.5	15.4	0.0	0.0	S	129	0.8	0.8	8.5	0.0	0.0	0.0	5.4	0.8	3.9
	R	6	0.0	0.0	0.0	0.0	16.7	0.0	0.0	0.0	0.0	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Gentamicin	S	45	0.0	0.0	2.2	-	2.2	6.7	17.8	0.0	0.0	S	193	0.5	1.6	6.2	-	0.0	0.0	3.6	0.5	3.1
	R	0	0.0	0.0	0.0	-	0.0	0.0	0.0	0.0	0.0	R	0	0.0	0.0	0.0	-	0.0	0.0	0.0	0.0	0.0
Kanamycin	S	23	0.0	0.0	0.0	0.0	4.3	0.0	21.7	0.0	0.0	S	122	0.0	1.6	6.6	0.0	0.0	0.0	2.5	0.0	0.8
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Linezolid	S	23	0.0	0.0	0.0	0.0	4.3	0.0	21.7	0.0	0.0	S	122	0.0	1.6	6.6	0.0	0.0	0.0	2.5	0.0	0.8
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	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	44	0.0	0.0	2.3	0.0	-	6.8	18.2	0.0	0.0	S	193	0.5	1.6	6.2	0.0	-	0.0	3.6	0.5	3.1
	R	1	0.0	0.0	0.0	0.0	100.0	0.0	0.0	0.0	0.0	R	0	0.0	0.0	0.0	0.0	-	0.0	0.0	0.0	0.0
Streptomycin	S	42	0.0	0.0	2.4	0.0	2.4	-	16.7	0.0	0.0	S	193	0.5	1.6	6.2	0.0	0.0	-	3.6	0.5	3.1
	R	3	0.0	0.0	0.0	0.0	0.0	100.0	33.3	0.0	0.0	R	0	0.0	0.0	0.0	0.0	0.0	-	0.0	0.0	0.0
Tetracycline	S	37	0.0	0.0	2.7	0.0	2.7	5.4	-	0.0	0.0	S	186	0.0	1.6	4.8	0.0	0.0	0.0	-	0.5	2.7
	R	8	0.0	0.0	0.0	0.0	0.0	12.5	100.0	0.0	0.0	R	7	14.3	0.0	42.9	0.0	0.0	0.0	100.0	0.0	14.3
Vancomycin	S	45	0.0	0.0	2.2	0.0	2.2	6.7	17.8	-	0.0	S	192	0.5	1.6	6.3	0.0	0.0	0.0	3.6	-	3.1
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	-	0.0	R	1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	100.0	0.0
Virginiamycin	S	45	0.0	0.0	2.2	0.0	2.2	6.7	17.8	0.0	-	S	187	0.5	1.6	5.9	0.0	0.0	0.0	3.2	0.5	-
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	-	R	6	0.0	0.0	16.7	0.0	0.0	0.0	16.7	0.0	100.0

[a] Am: ampicillin; Ba: bacitracin; Em: erythromycin; Gm: gentamicin; Na: narasin; Sm: streptomycin; Tc: tetracycline; Va: vancomycin; Vi: virginiamycin.

TABLE EC IV. Distribution of MICs for *Escherichia coli from* calves, 2009 (n=223). Previuos data for cattle from SVARM given for comparison; 2006 Dairy cows (n=314) and 2000 Calves/Yearlings (n=293).

		Resis-	Distribution (%) of MICs[a] (mg/L)																		
Antimicrobial	**Year**	tance (%)	**≤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**
	2009	<1							0.4	12.1	63.7	22.9	0.4				0.4				
Ampicillin	2006	0						0.3	3.8	17.2	51.3	20.7	6.7								
	2000	0								1.4	18.8	78.8	1.0								
	2009	0				69.5	30.0	0.4													
Cefotaxime	2006	0				66.9	31.8	1.3													
Ceftiofur	2000	0						24.9	72.0	3.1											
	2009	0									10.8	68.2	21.1								
Chloramph.	2006	0									12.4	75.2	12.4								
	2000	0									1.0	37.9	60.8	0.3							
	2009	0		4.9	87.4	7.6															
Ciprofloxacin	2006	<1			73.6	25.8			0.3		0.3										
Enrofloxacin	2000	<1			29.4	69.3	1.0		0.3												
	2009	0									1.8	47.1	50.7	0.4							
Florfenicol	2006	0										51.6	48.4								
	2000	0									0.7	23.5	70.6	5.1							
	2009	0							30.9	64.1	4.9										
Gentamicin	2006	1							21.3	69.1	8.6	1.0									
	2000	<1							2.4	37.2	49.8	9.9	0.7								
	2009	<1									28.3	64.1	7.2		0.4						
Kanamycin	2006	<1									9.7	80.6	8.9	0.8							
	2000																				
	2009	0									32.3	63.7	4.0								
Nalidixic acid	2006	<1								3.8	19.4	71.3	4.8			0.3		0.3			
	2000	<1									0.7	22.5	70.3	5.8		0.3		0.3			
	2009	4										32.7	57.4	5.4		1.3	2.2	0.9			
Streptomycin	2006	2										15.0	76.8	6.4	0.3	0.6	0.6		0.3		
	2000	5									0.7	13.0	67.2	14.0		1.4	1.0	1.7	1.0		
	2009	2											14.3	50.2	31.4	2.2					1.8
Sulphon-amide	2006	2												79.3	18.5	0.6					1.6
	2000	1														42.3	54.6	1.7	0.3	1.0	
	2009	2							0.4	59.6	38.1					0.9	0.9				
Tetracycline	2006	2							0.3	65.6	31.8	0.6			0.3	0.3	1.0				
	2000	1								8.9	57.7	30.7	1.4			0.3	1.0				
	2009	<1						30.0	56.5	12.6	0.4					0.4					
Trimethoprim	2006	<1						46.2	51.0	2.2	0.3					0.3					
	2000	2					3.1	9.2	34.8	42.3	8.9	1.7									
			≤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**

[a]White fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate epidemiological cut-off values for resistance.

TABLE ENT VII. Distribution of MICs for *Enterococcus faecalis* from calves, 2009 (n=10). Previuos data for cattle from SVARM given for comparison; 2006 Dairy cows (n=13) and 2000 Calves/Yearlings (n=22).

			Distribution (%) **of MICs**[a] (mg/L)															
Antimicrobial	**Year**	**Resis-tance** (%)	**≤0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**256**	**512**	**1024**	**2048**	**>2048**
	2009	0				100.0												
Ampicillin	2006	0			23.1	61.5	15.4											
	2000	0		13.6	18.2	59.1		9.1										
	2009	0						20.0	60.0	10.0	10.0							
Bacitracin[b]	2006	0					7.7		38.5	46.2	7.7							
	2000	0			9.1	9.1	9.1	27.3	27.3	4.5	13.6							
	2009	0						50.0	50.0									
Chloramphenicol	2006	0						30.8	69.2									
	2000	Not tested																
	2009	0				20.0	60.0	20.0										
Erythromycin	2006	0			30.8	23.1	23.1	23.1										
	2000	5		13.6	18.2	9.1	31.8	22.7				4.5						
	2009	0							60.0	40.0								
Gentamicin	2006	0						15.4	23.1	61.5								
	2000	0				4.5	4.5	9.1	40.9	40.9								
	2009	0									20.0	70.0	10.0					
Kanamycin	2006	0									7.7	84.6		7.7				
	2000	Not tested																
	2009	0				10.0	80.0	10.0										
Linezolid	2006	0					84.6	15.4										
	2000	Not tested																
	2009	0		60.0	30.0	10.0												
Narasin	2006	8		7.7	38.5	30.8	15.4		7.7									
	2000	0	9.1	31.8	40.9	13.6	4.5											
	2009	0										50.0	50.0					
Streptomycin	2006	0									15.4	76.9	7.7					
	2000	14								4.5	13.6	40.9	27.3			9.1	4.5	
	2009	30			20.0	50.0					30.0							
Tetracycline	2006	15			76.9	7.7					7.7	7.7						
	2000	14			13.6	27.3	45.5			4.5	9.1							
	2009	0				10.0	30.0	60.0										
Vancomycin	2006	0				38.5	30.8	30.8										
	2000	0				27.3	63.6	9.1										
	2009	0			10.0					70.0	20.0							
Virginiamycin	2006	0					15.4	23.1		53.8	7.7							
	2000	0			9.1	9.1	18.2	13.6	22.7	22.7	4.5							
			≤0.12	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**256**	**512**	**1024**	**2048**	**>2048**

[a] White fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate cut-off values for resistance; [b] MIC in U/mL, see Appendix 3 for details.

TABLE ENT VIII. Distribution of MICs for *Enterococcus faecium* from calves, 2009 (n=24). Previuos data for cattle from SVARM given for comparison; 2006 Dairy cows (n=98) and 2000 Calves/Yearlings (n=71).

			Distribution (%) **of MICs**[a] (mg/L)															
Antimicrobial	**Year**	**Resistance** (%)	**≤0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**256**	**512**	**1024**	**2048**	**>2048**
	2009	0		12.5	16.7	58.3	8.3	4.2										
Ampicillin	2006	0		10.2	30.6	45.9	13.3											
	2000	1		4.2	1.4	12.7	63.4	16.9	1.4									
	2009	4						29.2	12.5	41.7	12.5			4.2				
Bacitracin[b]	2006	1				1.0	1.0	3.1	16.3	66.3	11.2	1.0						
	2000	1			2.8	25.4	21.1	5.6	12.7	12.7	18.3	1.4						
	2009	0					4.2	41.7	54.2									
Chloramphenicol	2006	0					1.0	24.5	72.4	2.0								
	2000	Not tested																
	2009	4			33.3	4.2	20.8	37.5	4.2									
Erythromycin	2006	7			29.6	24.5	13.3	25.5	7.1									
	2000	6		5.6	53.5	14.1	9.9	11.3		2.8		2.8						
	2009	0					4.2	25.0	58.3	12.5								
Gentamicin	2006	0					3.1	33.7	57.1	6.1								
	2000	0					4.2	5.6	56.3	31.0	2.8							
	2009	0									8.3	25.0	50.0	12.5	4.2			
Kanamycin	2006	0								4.1	36.7	28.6	20.4	7.1	3.1			
	2000	Not tested																
	2009	0					83.3	16.7										
Linezolid	2006	0				2.0	78.6	19.4										
	2000	Not tested																
	2009	0		4.2	62.5	33.3												
Narasin	2006	0		1.0	36.7	55.1	7.1											
	2000	0	5.6	26.8	23.9	39.4	2.8	1.4										
	2009	0								4.2	8.3	79.2	8.3					
Streptomycin	2006	0								3.1	34.7	62.2						
	2000	0							1.4	2.8	52.1	38.0	5.6					
	2009	0			62.5	37.5												
Tetracycline	2006	3			62.2	34.7					3.1							
	2000	6		1.4	5.6	62.0	23.9	1.4			2.8	2.8						
	2009	0				58.3	25.0	16.7										
Vancomycin	2006	0				75.5	10.2	14.3										
	2000	1				77.5	16.9	4.2	1.4									
	2009	0			4.2	37.5	16.7	41.7										
Virginiamycin	2006	1			25.5	16.3	18.4	38.8	1.0									
	2000	7			21.1	21.1	33.8	16.9	5.6			1.4						
			≤0.12	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**256**	**512**	**1024**	**2048**	**>2048**

[a] White fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate cut-off values for resistance; [b] MIC in U/mL, see Appendix 3 for details.

TABLE ENT IX. Distribution of MICs for *Enterococcus hirae* from calves, 2009 (n=163). Previuos data for cattle from SVARM given for comparison; 20ß06 Dairy cows (n=147) and 2000 Calves/Yearlings (n=127).

			Distribution (%) **of MICs**[a] (mg/L)															
Antimicrobial	**Year**	**Resis-tance** (%)	**≤0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**256**	**512**	**1024**	**2048**	**>2048**
	2009	0		11.7	14.7	50.3	23.3											
Ampicillin	2006	0		10.9	11.6	30.6	46.3	0.7										
	2000	2		11.8	3.9	15.0	46.5	21.3	1.6									
	2009	0				82.8	16.6			0.6								
Bacitracin[b]	2006	0				30.6	57.1	4.1	3.4	2.7	2.0							
	2000	0				27.6	41.7	24.4	2.4	2.4	1.6							
	2009	0					8.6	87.7	3.7									
Chloramphenicol	2006	0				0.7	3.4	78.2	17.7									
	2000	Not tested																
	2009	0			99.4	0.6												
Erythromycin	2006	1			93.2	3.4	2.0	0.7	0.7									
	2000	0		36.2	60.6	0.8	2.4											
	2009	0						3.1	64.4	27.0	5.5							
Gentamicin	2006	0					3.4	6.8	50.3	35.4	4.1							
	2000	0					4.7	8.7	52.8	27.6	6.3							
	2009	0								1.2	31.9	62.0	4.9					
Kanamycin	2006	0								4.1	32.7	55.8	6.1	1.4				
	2000	Not tested																
	2009	0				15.3	83.4	1.2										
Linezolid	2006	0			0.7	5.4	90.5	3.4										
	2000	Not tested																
	2009	0	0.6	41.7	50.3	7.4												
Narasin	2006	1		8.2	59.2	27.2	3.4	0.7	1.4									
	2000	0		15.0	36.2	44.1	3.1	1.6										
	2009	<1									13.5	66.3	19.6	0.6				
Streptomycin	2006	0							0.7		13.6	76.9	8.8					
	2000	0								6.3	22.8	60.6	10.2					
	2009	<1			68.1	31.3						0.6						
Tetracycline	2006	0			85.7	14.3												
	2000	<1			8.7	43.3	44.9	2.4				0.8						
	2009	0				79.1	20.9											
Vancomycin	2006	0				86.4	13.6											
	2000	0				88.2	11.8											
	2009	0			15.3	3.7	38.7	42.3										
Virginiamycin	2006	0			10.2	7.5	35.4	46.9										
	2000	15			20.5	9.4	47.2	7.9	15.0									
			≤0.12	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**256**	**512**	**1024**	**2048**	**>2048**

[a] White fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate cut-off values for resistance; [b] MIC in U/mL, see Appendix 3 for details.

Strama VL – strategies against antimicrobial resistance

IN 2006, THE SWEDISH PARLIAMENT decided on a Swedish strategic programme against antimicrobial resistance. The strategy involves both human and veterinary medicine (Government bill 2005/06:50). The mission of this programme is to preserve the efficacy of antibiotics for treatment of humans and animals.

A coordinated strategy

The core elements of the Swedish strategy are illustrated in the figure below. Experience from Sweden and other countries shows that effective strategies against antimicrobial resistance should be multifaceted. Core elements are: monitoring of use and resistance; prevention and control of infections; prudent use of antimicrobials. Continuous information, education and research are key to increase awareness and bridge knowledge gaps. Resistance is a global problem impacting on both public and animal health, and it is therefore essential that countries work together and share experiences. Lastly, for these activities to be fully effective, a platform for exchange of experiences, collaboration and coordination is needed.

In human medicine in Sweden, a coordinating function is filled by Strama (www.strama.se), an organization that is active both locally and nationally. Since 2008, a secretariat to support a similar organization, Strama VL (VL stands for veterinary and food), has been operative at the National Veterinary Institute (SVA). Its tasks are to coordinate activities aiming to contain antibiotic resistance within the veterinary and food sector and to take initiatives in prioritized areas. Strama VL was mandated by the Swedish Government, and is to work in close collaboration with Strama.

Examples of activities during 2009 are:

- A workshop on antimicrobial treatment for pig practitioners, in collaboration with SVARMpat, SVA and the Swedish Animal Health Services,
- An international seminar on antimicrobial resistance arranged by the Royal Swedish Academy of Agriculture and Forestry,
- An upgrade of information on antimicrobial resistance on SVA's website,
- Studies on use of antimicrobials for dogs, including a pilot study on indication based statistics on prescription of antimicrobials for dogs,
- Participation in a number of multidisciplinary national working groups,
- Participation in seminars and workshops at international, national and regional level,
- Coordination of the revision of guidelines for use of antimicrobials in dogs and cats of the Swedish Veterinary Society,
- Participation in working groups in the European Union, in Task Force on Antimicrobial Resistance of the Codex Alimentarius and in WHO advisory group on integrated surveillance of antimicrobial resistance.

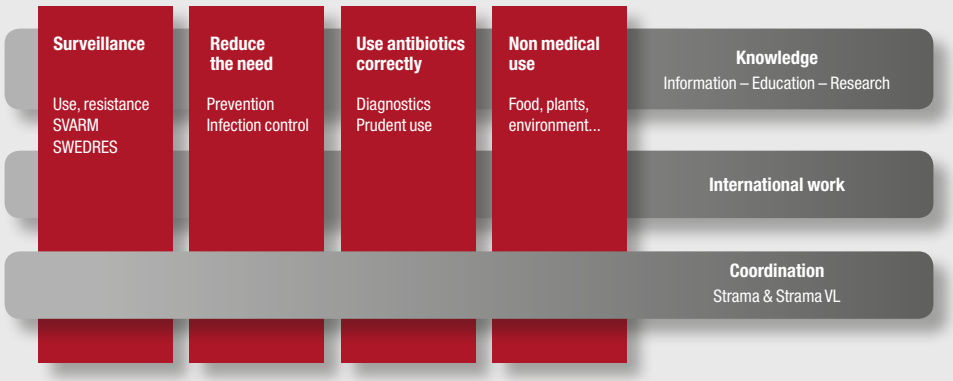

FIGURE. Core elements of the Swedish strategy on antimicrobial resistance.

Animal pathogens

ISOLATES TESTED are from clinical submission of samples to SVA if not otherwise stated. For these 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 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. Some cut-off values defining resistance (breakpoints) previously used in SVARM have been changed. To facilitate comparisons, resistance data from earlier reports have been recalculated using current cut-off values when possible.

Pig

Escherichia coli

Isolates of *Escherichia coli* from years 1992-2009 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* isolated from the gastro-intestinal tract were susceptibility tested. After that date, the criteria for susceptibility testing were changed and only *E. coli* that harbour genes coding for virulence factors are tested for susceptibility. The following genes are analysed 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 2009 (Table Pig I). In the 70s and 80s, prevalence of *E. coli* resistant to ampicillin was only around seven percent (Franklin, 1976; Franklin, 1984). From the early 90s to year 2004, prevalence of ampicillin resistance rose gradually to 22%. In 2007, the figure increased further but in 2008 and 2009 it has decreased to the same level as before 2007. In 2009, all of the ampicillin resistant isolates were resistant to at least one other antimicrobial. Before 2009, resistance to enrofloxacin has never been above 9%, but this year the figure has increased to 12%. Although it is too early for conclusions on trends, enrofloxacin resistance must be monitored closely in coming years.

Multiresistance (i.e. resistance to three or more antimicrobials) occurred in 19% of the isolates. This figure was 14% in 2008 and 25% in 2007. The resistance combination tetracycline, ampicillin and trimethoprim-sulphonamides and the combination ampicillin, trimethoprim-sulphonamides and streptomycin were found in 32% of the multiresistant strains. The resistance combination streptomycin, tetracycline and ampicillin and the combination streptomycin, tetracycline and trimethoprim-sulphonamides were found in 26%. Six percent of the strains were resistant to four or more antimicrobials and one percent was resistant to five or more.

Brachyspira hyodysenteriae

Isolates of *Brachyspira 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.*

TABLE PIG I. Resistance (%) in *Escherichia coli* from pigs 1989-2009 and distribution of MICs for isolates from 2009. Isolates are from clinical submissions of faecal samples or samples taken post mortem from the gastro-intestinal tract.

	Resistance (%)									**Distribution** (%) **of MICs**[a] (mg/L)									
Antimicrobial	**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** n=93	**2008** n=83	**2009** n=102	**≤0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**>32**
Ampicillin	6	10	9	11	17	22	30	18	19				19.6	55.9	4.9	1.0	18.6		
Ceftiofur	-	-	-	-	<1[h]	<1	0	0	0		70.6	29.4							
Enrofloxacin[b]	1[g]	7	5	6	8	9	4	6	12	88.2	3.9	1.0	3.9	2.9					
Florfenicol	-	-	-	-	<1[h]	<1	0	0	0					4.9	56.9	34.3	3.9		
Gentamicin[c]	1	1	<1	1	4	1	2	0	0					94.1	5.9				
Neomycin	17	14	9	6	5[i]	4	3	6	9						89.2	2.0		1.0	7.8
Streptomycin[d]	44	44	32	30	36	36	40	40	33						22.5	32.4	11.8	6.9	26.5
Tetracycline	28	35	31	33	30	26	27	25	31				35.3	26.5	5.9	1.0	31.4		
Trim/Sulph.[e,f]	17	15	13	14	19	25	27	22	16[j]			84.0				16.0			

[a] White fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate cut-off values defining resistance; [b] Cut-off value >0.25 mg/L until 2001; [c] Cut-off value >8 mg/L until 2002; [d] Cut-off value >32 mg/L until 2001; [e] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphametoxazole); [f] Cut-off value >4 mg/L until year 2001; [g] 227 isolates tested; [h] 688 isolates tested; [i] 926 isolates tested; [j] 100 isolates tested.

TABLE PIG II. Resistance (%) in *Brachyspira hyodysenteriae* from pigs 2001-2009 and distribution of MICs for isolates from 2009. Isolates are from clinical submissions of faecal samples.

	Resistance (%)								**Distribution** (%) **of MICs**[a] (mg/L)											
Antimicrobial	**2001** n=75	**2002** n=109	**2003** n=100	**2005** n=31	**2006** n=26	**2007** n=23	**2008** n=15	**2009** n=24	**≤0.06**	**0.125**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**>128**
Tiamulin	0	0	0	0	0	0	0	0	29.2	45.8	16.7	4.2	4.2								
Tylosin	83	73	89	81	85	65	93	71							8.3	20.8					70.8
Tylvalosin	-	-	-	-	-	-	ND[b]	ND					29.2	4.2	16.7	29.2	20.8				

[a] White fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration; [b] ND=not determined because no cut-off value is available.

TABLE PIG III. Resistance (%) in *Brachyspira pilosicoli* from pigs 2002-2009 and distribution of MICs for isolates from 2009. Isolates are from clinical submissions of faecal samples.

	Resistance (%)						**Distribution** (%) **of MICs**[a] (mg/L)											
Antimicrobial	**2002-03** n=93	**2005** n=57	**2006** n=72	**2007** n=44	**2008** n=31	**2009** n=24	**≤0.06**	**0.125**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**>128**
Tiamulin	14	16	12	9	16	8	33.8	37.5	12.5	4.2		4.2			8.3				
Tylosin	50[b]	63	67	61	55	63							29.2	8.3			8.3	4.2	50.0
Tylvalosin	-	-	-	-	39	38				8.3	8.3	41.7	4.2			25.0	12.5		

[a] White fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration; [b] 86 isolates tested.

hyodysenteriae was tested with an agar dilution technique, and 20% of the isolates were resistant to tylosin (Gunnarsson et al., 1991). In year 2001, the figure had increased dramatically to around 80% (Table Pig II). This year´s figure is lower but the small number of isolates precludes valid conclusions on trends.

The last two 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 and due to the small number of *B. hyodysenteriae* tested a value cannot be determined from the distribution of MICs. However, 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.

Sweden has a programme for controlling swine dysentery by 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. Nevertheless, it is imperative that all herds where treatment failure is suspected are thoroughly investigated. Since only macrolides and tiamulin are authorised for treatment of swine dysentery in pigs it is important to monitor resistance development in *B. hyodysenteriae*.

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 Swedish 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 frequency of resistance to tylosin has been around 60% during the last years (Table Pig III).

Tylvalosin is a macrolide authorised for treatment of swine dysentery in the European Union, however, not for treatment of spirochaetal diarrhoea. Nine of the twelve strains with MICs >128 mg/L for tylosin have MICs for tylvalosin that are 32 or more. A correlation between MICs for tylosin and tylvalosin was shown by Karlsson et al. (2004) for *B. hyodysenteriae*. This indicates that macrolide resistance caused by structural changes of ribosomal RNA also affects the binding of tylvalosin. With this background, together with the distribution of the MICs in this material a cut-off value for tylvalosin of >4 mg/L is suggested.

In 2009, one isolate was resistant to all three substances tested. 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. Susceptibility testing of *B. pilosicoli* from herds where tiamulin is to be used is of importance.

Actinobacillus pleuropneumoniae

Actinobacillus pleuropneumoniae from years 1992-2000 were isolated from the respiratory tract (nasal swabs and lung, including regional lymph nodes) but from years 2005-2009 all isolates are from lungs sampled post mortem.

Since 2005, *A. pleuropneumoniae* has been susceptible to almost all antimicrobials tested (Table Pig IV). Before 2005 only sporadic isolates of *A. pleuropneumoniae* were susceptibility tested. In 2005, the surveillance programme SVARMpat for antimicrobial resistance started and although the number of strains tested yearly has increased it is still low. Pneumonia caused by *A. pleuropneumoniae* is an important problem in Swedish pig production and a higher frequency of sampling and susceptibility testing is desirable if emerging resistance is to be detected early.

TABLE PIG IV. Resistance (%) in *Actinobacillus pleuropneumoniae* from pigs the years 1992-2000 and 2005-2009. Distribution of MICs for isolates from 2009. Isolates are from clinical submissions of samples from the respiratory tract or from post mortem investigations of lungs.

	Resistance (%)				**Distribution** (%) **of MICs**[a] (mg/L)														
Antimicrobial	**1992-00** n=18	**2005-07** n=84	**2008** n=39	**2009** n=24	**≤0.03**	**0.06**	**0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**256**	**512**	**>512**
Ampicillin	6	0	0	0			20.8	79.2												
Cefotaxime	-	0	0	0		100.0														
Ceftiofur	-	0	0	0			100													
Chloramph.	11	0	0	0						100.0										
Ciprofloxacin	6[b]	0	0	0	8.3	91.7														
Florfenicol	-	0	0	0								100.0								
Gentamicin	-	0	0	0								87.5	12.5							
Nalidixic acid	-	0	0	0						4.2	95.8									
Penicillin	6	0	0	0				79.2	20.8											
Streptomycin	-	0	0	4											95.8	4.2				
Sulphonamide	-	0	0	0											8.3	16.7	70.8	4.2		
Tetracycline	11[c]	1	0	0					45.8	54.2										
Trimethoprim	-	0	0	0				95.8	4.2											

[a] White fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate cut-off values defining resistance; [b] enrofloxacin tested, cut-off value 2 mg/L.; [c] cut-off value >8 mg/L.

TABLE PIG V. Resistance (%) in *Pasteurella* spp. from pigs 2000-2001 and 2005-2009. Distribution of MICs for isolates from 2009. Isolates are from the respiratory tract, isolated from nasal swabs or from post mortem investigations of lungs.

	Resistance (%)				**Distribution** (%) **of MICs**[a] (mg/L)															
Antimicrobial	**2000-01** n=75	**2005-07** n=38	**2008** n=25	**2009** n=24	**≤0.008**	**0.016**	**0.03**	**0.06**	**0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**256**	**>256**
Ampicillin	0	0	0	0							100.0										
Cefotaxime	-	0	0	0		95.8	4.2														
Chloramph.	1	0	0	0									100.0								
Ciprofloxacin	1b	0	0	0	8.3	79.2	8.3	4.2													
Florfenicol	-	0	0	0										100.0							
Gentamicin	4	0	0	0									70.8	29.2							
Nalidixic acid	-	0	0	0								58.3	29.2	8.3		4.2					
Penicillin	0	0	0	0					8.3	66.7	25.0										
Streptomycin	4	0	0	4											37.5	33.3	25.0	4.2			
Tetracycline	1	0	0	0								100.0									
Trimethoprim	-	0	0	0					33.3	41.7	25.0										

[a] White fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate cut-off values defining resistance; [b] enrofloxacin tested, cut-off value 2 mg/L.

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 collected in the control programme are not from clinical submissions and they are likely from healthy pigs. 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). Due to methodological problems with reproducibility, the results for sulphonamide have been excluded.

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

THIS HIGHLIGHT summarises information on bacterial isolates producing extended spectrum beta-lactamases (ESBL). All isolates are from diagnostic samples and were referred to the National Veterinary Institute (SVA) for confirmation. Diagnostic laboratories are advised to submit isolates of *Enterobacteriacae* phenotypically resistant to third generation cephalosporins to SVA where confirmatory phenotypic and genotypic tests for ESBL and AmpC are performed (See Appendix 3).

Details on each isolate are shown in the table below. In total, ESBL-production has been confirmed in 14 isolates since 2007; 8 *Escherichia coli*, 4 *Klebsiella* spp. and 2 *Enterobacter* spp. Ten of these isolates are from horses, three from dogs and one from a cat. The beta-lactamases found belonged to groups CTX-M-1 and SHV. CTX-M-1 is the most common ESBL-group found in ESBL producing isolates from humans in Sweden (SWEDRES 2009).

In addition, during 2009 diagnostic submissions from dogs and pigs were screened for ESBL by culture on selective media, i.e. MacConkey agar with cefotaxime added (1mg/L). Almost 1000 urine samples from dogs and more than 300 rectal samples from pigs were analysed in this way and no ESBL producing *Enterobacteriacae* were found. During 2010 samples from the genital tract of mares will be screened in a similar manner.

In conclusion, ESBL producing Gram-negative bacteria are still uncommon in routine clinical diagnostic samples but the situation in horses warrants closer monitoring. In a clinical condition where the patient needs to be treated with antimicrobials, multiresistant *Enterobacteriacae*, as those in the table, 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. *Enterobacteriacae* producing extended spectrum beta-lactamases (ESBL). Isolates from diagnostic submissions from animals up to and including March 2010. White fields indicate an MIC above the epidemiological cut-off value (ECOFF) set by EUCAST for the specific bacterial species. Red fields indicate that an ECOFF for *Klebsiella* spp. or *Enterobacter* spp. is not available but that the MIC is above the ECOFF for *Escherichia coli*.

Animal species	Year	Sampled site	Bacterial species	ESBL group	MIC[a] (mg/L)									
					Ct	Ci[b]	Nal	Ff	Cm	Gm	Km	Sm	Tc	Tp
Cat	-10	Urine	*E. coli*	CTX-M-1	>2	>1	>128	16	4	0.25	≤8	4	64	<0.12
Dog	-08	Wound	*E. coli*	CTX-M-1	>2	>1	>128	8	8	1	8	8	>64	0.5
Dog	-09	Post-op wound	*Kleb. pneumoniae*	CTX-M-1, SHV	>8	0.06	4	4	4	>32	8	256	>64	>32
Dog	-09	Post-op wound	*Enterob. cloacae*	CTX-M-1	>2	>1	>128	8	>64	>16	>16	128	32	>16
Horse	-07	Uterus	*Kleb. pneumoniae*	SHV	1	0.06	4	≤4	128	64	>16	64	>64	>32
Horse	-08	Uterus	*E. coli*	SHV	>2	0.5	64	8	8	>64	>16	>256	2	>32
Horse	-08	Synovia	*E. coli*	SHV	>2	0.06	4	8	8	64	>16	256	2	>32
Horse	-09	Persisting urachus	*Kleb. pneumoniae*	SHV	1	0.06	4	8	>256	>32	>16	64	>64	>32
Horse	-09	Cervix	*E. coli*	CTX-M-1	>8	0.06	4	8	256	>32	>16	>256	>64	>32
Horse	-09	Osteomyelitis	*E. coli*	CTX-M-1	8	0.5	256	8	256	16	4	128	>64	>32
Horse	-09	Wound	*Kleb. pneumoniae*	CTX-M-1, SHV	>8	0.06	4	4	4	>32	4	256	64	>32
Horse	-09	Eye	*Enterob. hormaechei*	SHV	4	0.03	4	8	4	>32	>16	256	2	>32
Horse	-09	Cervix	*E. coli*	CTX-M-1	>2	>1	>128	8	>64	16	16	4	>128	>16
Horse	-10	Wound	*E. coli*	CTX-M-1	>2	0.03	4	8	>64	>16	≤8	256	64	>16

[a] All isolates had ampicillin MICs>32 mg/L and 13 isolates had sulphonamide MICs >2048 mg/L, one had sulphonamide MIC 32 mg/L; Ctx: cefotaxime; Ci: ciprofloxacin; Nal: nalidixic acid; Ff: florfenicol; Cm: chloramphenicol; Gm: gentamicin; Km: kanamycin; Sm: streptomycin; Tc: tetracycline; Sul: sulphonamide; Tp: trimethoprim; [b] Cut-off value >0.06 mg/L, see Appendix 3 for details.

Cattle and sheep

Escherichia coli

Isolates of *Escherichia coli* are from the gastro-intestinal tract of cattle. The frequency of resistance to ampicillin, neomycin, streptomycin or tetracycline was above 20%. Tetracycline was the most common trait occurring in more than half of the isolates in 2007-2009 (Table Cattle I). Multiresistance (i.e. resistance to three or more antimicrobials) occurred in 13 isolates (33%). This is higher than previous years but the small number of isolates tested precludes conclusions on trends. The resistance combination streptomycin, tetracycline and neomycin was the most common combination, occurring in six isolates.

Pasteurella spp.

The *Pasteurella* spp. from 2005 to 2009 were isolated from clinical submissions of samples from calves with respiratory disease or from post-mortem investigations of lungs. The isolates from years 1997-2000 are from a field study on respiratory pathogens in calves presented in SVARM 2000.

Antimicrobial resistance among isolates of *Pasteurella* spp. is rare (Table Cattle II). One isolate in 2009 had MIC above the cut-off value for ceftiofur. This is most likely not a true value, since the MIC for penicillin was 0.12 mg/L. Isolates of beta-lactamase producing *Pasteurella* spp. has been confirmed in Sweden from one herd in 2003. Since 2005, resistance to penicillin and tetracycline, the substances commonly used for therapy of respiratory disease in calves, has not been detected. Penicillin is considered as the substance of choice for treatment of pneumonia in calves. The number of isolates is low and more frequent sampling of calves with respiratory disorders and subsequent susceptibility testing is desirable if emerging resistance is to be detected early.

Fusobacterium necrophorum

Interdigital necrobacillosis and foot-root are common diseases in cattle and sheep, respectively. These diseases are often treated with antimicrobials. *Fusobacterium necrophorum* is the major pathogen in interdigital necrobacillosis in cattle while *Dichelobacter nodosus* is the major causative agent for foot-root in sheep and *F. necrophorum* plays a minor role. In

TABLE CATTLE I. Resistance (%) in *Escherichia coli* from cattle 1992-2002, 2004 and 2005-2009. Distribution of MICs for isolates from 2007-2009. 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**[a] (mg/L)									
Antimicrobial	**1992-02** n=220	**2004** n=87[h]	**2005-06** n=63	**2007-09** n=40	**≤0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**>32**
Ampicillin	24	29	32	20				2.5	52.5	25.0		20.0		
Ceftiofurb	0[i]	0	0[j]	0		27.5	70.0	2.5						
Enrofloxacin[c]	10	14	13	5	95.0	2.5	2.5							
Florfenicol	0[i]	0	0	3					2.5	25.0	67.5	2.5	2.5	
Gentamicind	5	0	0	3					80.0	17.5			2.5	
Neomycin	8	7	13	23						67.5	10.0			22.5
Streptomycine	42	48	54	43						2.5	30.0	25.0		42.5
Tetracycline	31	37	49	55				17.5	22.5	2.5	2.5	55.0		
Trim/Sulph.[f,g]	11	10	21	13			87.5				12.5			

[a] White fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate cut-off values defining resistance; [b] Cut-off value >2 mg/L until 2006; [c] Cut-off value >0.25 mg/L until 2004; [d] Cut-off value >8 mg/L until 2001; [e] Cut-off value >32 mg/L until 2006; [f] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphametoxazole); [g] Cut-off value >4 mg/L until 2006; [h] 1/3 of the isolates were from calves with diarrhoea; [i] 16 isolates tested; [j] 62 isolates tested.

TABLE CATTLE II. Resistance (%) in *Pasteurella* spp. from calves 1997-2000 and 2005-2009. Distribution of MICs for isolates from 2009. Isolates are from the respiratory tract of calves.

	Resistance (%)				**Distribution** (%) **of MICs**[a] (mg/L)									
Antimicrobial	**1997-00** n=254	**2005-07** n=27	**2008** n=32	**2009** n=14	**≤0.06**	**0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**>16**
Ampicillin	1	0	0	0					100.0					
Ceftiofur	-	0	0	7			92.9	7.1						
Enrofloxacin	2	0	0	0[c]		100.0								
Florfenicol	-	0	0	0						100.0				
Penicillin	0	0	0	0		50.0	42.9	7.1						
Tetracycline	3	0	0	0					100.0					
Trim/Sulph.[b]	2	0	0	0				100.0						

[a] White fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate cut-off values defining resistance; [b] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphametoxazole); [c] 11 isolates tested.

TABLE CATTLE AND SHEEP I. Distribution of MICs among *Fusobacterium necrophorum* ssp. *necrophorum* from cows (n=41) and sheep (n=24), 2008-2009. Isolates are from samples from interdigital necrobacillosis.

		Distribution (%) of MICs[a] (mg/L)												
Antimicrobial	**Animal species**	**≤0.03**	**0.06**	**0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**>64**
Cephalothin	Cows		2.4	14.6	82.9									
	Sheep		4.2	8.3	83.3	4.2								
Ciprofloxacin	Cows			4.9	14.6	34.1	46.3							
	Sheep				16.7	33.3	50.0							
Erythromycin	Cows							14.6	58.5	26.8				
	Sheep							20.8	79.2					
Penicillin	Cows	87.8	12.2											
	Sheep	75.0	25.0											
Tetracycline	Cows					100								
	Sheep					100								
Trimethoprim	Cows									7.3	26.8	46.3	19.5	
	Sheep										20.8	58.3	20.8	

[a] White fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration.

Sweden, these diseases are usually treated with penicillin or tetracycline.

Fusobacterium necrophorum comprises two subspecies where ssp. *necrophorum* is virulent and ssp. *funduliforme* is less pathogenic. It is difficult to distinguish between these two subspecies phenotypically. Moreover, there are few publications on antimicrobial susceptibility of *Fusobacterium necrophorum*. To improve knowledge in this field a PCR-method to facilitate subtyping of *F. necrophorum* (Narongwanichgarn et al., 2003) was started, and a broth dilution method for susceptibility testing was developed within SVARMpat during 2007.

During 2008-2009, 106 samples from interdigital necrobacillosis in cattle were cultured at SVA, and from these, 48 *F. necrophorum* were isolated. Forty-one of these were identified as *F. necrophorum* ssp. *necrophorum* by PCR. The same period, 151 samples from foot-root in sheep were cultured. In 33 of them *F. necrophorum* were isolated, of which 24 were confirmed to be *F. necrophorum* ssp *necrophorum*. The results of susceptibility testing of these isolates are shown in Table Cattle and Sheep I. To our knowledge there are no accepted cut-off values for resistance for *F. necrophorum* and from this small data set it is not possible to propose a cut-off value. Anyhow, *F. necrophorum* ssp. *necrophorum* had low MICs for both penicillin and tetracycline and the MICs for these antimicrobials are concordant with those presented by Lechtenberg et al. (1998). The MICs for penicillin and tetracycline are on a level with those of β-hemolytic streptococci. Isolates of β-hemolytic streptococci with MIC of ≤0.03 for penicillin and of ≤0.5 for tetracycline are regarded as susceptible according to CLSI (2008). Therefore *F. necrophorum* ssp. *necrophorum* with these MICs should be considered susceptible for treatment with penicillin or tetracyclines. On the other hand, fluoroquinolones and trimethoprim seem not to be suitable for treatment of interdigital necrobacillosis due to comparatively high MICs.

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. In 2009, the majority of *A. salmonicida* subsp. *achromogenes* and *F. columnare* are from brown trout, 61 and 70%, respectively, whereas the majority of *F. psychrophilum* are from rainbow trout, 83%. A similar distribution among fish species applies for isolates from 2005-2008.

Until recently there have been no accepted standard reference methods for testing antimicrobial susceptibility of bacteria from fish. In 2005, the VetMIC™ microdilution system for testing bacteria from warm-blooded animals used at SVA was adapted to bacteria from fish according to recommendations by Alderman & Smith (2001). The methodology has since been used for routine testing of isolates from clinical submissions of fish.

At present there are no accepted interpretative criteria for MIC data of bacteria from aquaculture. Evaluation of the distributions of MICs however 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 for tetracycline in Flavobacter, and for florfenicol among *A. salmonicida* and *F. columnare*, indicate acquired resistance to these antimicrobials.

Occurrence of quinolone resistance is conceivable since the quinolone oxolinic acid is used therapeutically in aquaculture in Sweden. Also resistance to tetracycline or florfenicol is in agreement with the use of these antimicrobials in farmed fish. The amounts of antimicrobial prescribed for use in farmed fish was presented in SVARM 2007. The small number of isolates tested and the limited time period covered however preclude conclusions on trends in susceptibility.

TABLE FISH I. Distribution of MICs for *Aeromonas salmonicida* subsp. *achromogenes, Flavobacter columnare* and *Flavobacter psychrophilum*. Isolates from 2005-2008 and 2009.

Bacterial species	Antimicrobial	Year	Number of isolates	Distribution (%) of MICs[a] (mg/L)									
				≤0.25	0.5	1	2	4	8	16	32	64	>64
Aeromonas salmonicida subsp. *achromogenes*	Florfenicol	2009	23				95.7			4.3			
		2005-08	87				96.6	2.3	1.1				
	Nalidixic acid	2009	23		78.3	4.3						8.7	8.7
		2005-08	87		80.5	4.6				1.1	3.4	5.7	4.6
	Tetracycline	2009	23	78.3	13.0	4.3				4.3			
		2005-08	87	90.8	8.0			1.1					
Flavobacter columnare	Florfenicol	2009	10				100.0						
		2005-08	46				95.7	2.2			2.2		
	Nalidixic acid	2009	10		80.0	10.0	10.0						
		2005-08	46		73.9	13.0	4.3				2.2	2.2	4.3
	Tetracycline	2009	10	90.0	10.0								
		2005-08	46	84.8	6.5	4.3		2.2			2.2		
Flavobacter psychrophilum	Florfenicol	2009	24				95.8		4.2				
		2005-08	69				98.6	1.4					
	Nalidixic acid	2009	24				25.0	37.5			4.2	4.2	29.2
		2005-08	69		7.2		37.7	39.1		1.4	1.4		13.0
	Tetracycline	2009	24	41.7	8.3	20.8	8.3	16.7	4.2				
		2005-08	69	72.5	5.8	5.8	7.2	5.8	1.4	1.4			

[a] White fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration.

Horse

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. Moreover, this usage probably co-selects for streptomycin resistance, since 82% of isolates resistant to trimethoprim-sulphonamides were also resistant to streptomycin. 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* increased from only 2% in years 1992-1994 to about 20% in the beginning of year 2000 and has remained at that level.

In this year´s material, resistance to ampicillin, ceftiofur or gentamicin was more common compared to last year´s (Table Horse I). Resistance to ceftiofur or gentamicin only occurred in multiresistant *E. coli* and this increase could be due to a high number of multiresistant *E. coli* isolated originating from one stud farm, see text below. Only one of the six isolates resistant to ceftiofur was tested for production of extended-spectrum beta-lactamases (ESBL) according to CLSI (see Appendix 3) and it was positive. For more information on ESBLs in Sweden see highlight on "*Enterobacteriacae* producing extended spectrum beta-lactamases (ESBL) – isolates from diagnostic submissions".

TABLE HORSE I. Resistance (%) in *Escherichia coli* from horses 1992-2009 and distribution of MICs for isolates from 2009. Isolates are from clinical submissions of samples from the female genital tract.

	Resistance (%)								Distribution (%) of MICs[a] (mg/L)									
Antimicrobial	1992-94 n=48	1995-97 n=216	1998-00 n=222	2001-03 n=457	2004-06 n=473	2007 n=273	2008 n=174	2009 n=210	≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	15	17	10	9	7	8	6	16				5.7	56.2	22.3		15.7		
Ceftiofur	-	-	-	<1[g]	<1	<1	1	3		32.9	61.9	2.4		2.9				
Enrofloxacin[b]	8	3	3	2	4	1	3	2	97.6	1.0	0.5	0.5	0.5					
Florfenicol	-	-	-	0	0	<1	<1	1					1.9	31.0	63.3	2.8	1.0	
Gentamicin[c]	0	3	6	6	2	3	2	7					91.5	2.4	0.5	0.5	6.2	
Neomycin	4	5	5	3	4	1	2	3						93.8	2.8		0.5	2.8
Streptomycin[d]	31	24	21	23	21	19	22	24						8.1	46.7	21.0	3.3	21.0
Tetracycline	6	5	9	6	8	7	5	10				33.3	49.5	5.7	1.0	10.5		
Trim/Sulph.[e, f]	2	15	17	18	17	16	20	24			75.7				24.3			

[a] White fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate cut-off values defining resistance; [b] Cut-off value >0.25 mg/L until 2002; [c] Cut-off value >8 mg/L until 2002; d Cut-off value >16 mg/L until 2001¸ [e] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphametoxazole); [f] Cut-off value >4 mg/L until 2001; [g] 353 isolates tested.

Methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) – an update

SINCE 1ST OF JANUARY 2008, Methicillin-resistant coagulase positive staphylococci are notifiable in Sweden. On suspicion on Methicillin-resistant *Staphylococcus pseudintermedius* (MRSP), diagnostic laboratories are advised to send the isolates to the National Veterinary Institute (SVA) for confirmation by PCR for the presence of *mec*A gene.

The first Methicillin-resistant *S. pseudintermedius* isolated in Sweden was from a healthy dog in a screening for Methicillin-resistant *S. aureus* in 2006. Later the same year 13 clinical isolates from postoperative wounds were confirmed, mainly from dogs sampled at two referral animal hospitals. In 2007, the number of confirmed cases was 77. The majority of the 50 first confirmed MRSP displayed a similar profile on pulse field gel electrophoresis indicating that they were related. Most of them had a characteristic antibiogram, being susceptible only to two substances of those licensed for therapy in veterinary medicine in Sweden; fusidic acid and tetracycline (SVARM 2007). In 2008, 78 MRSP from dogs and 4 from cats were confirmed. During that year, the first isolates with resistance to tetracycline were found. During 2009, 121 MRSP from dogs, seven MRSP from cats and one MRSP from a horse were confirmed. The numbers are in accordance with the number of MRSP notified to the Swedish Board of Agriculture in 2009 with exception of on canine MRSP. Thirty-one of these were susceptibility tested and 26 had the characteristic antibiogram. Four of which were resistant to tetracycline and another one was resistant to fusidic acid.

In a study by Perreten and co-workers (2010), over 100 MRSP from eight different countries, both in Europe and North America, were analysed. Representative MRSP from Sweden were included. Most isolates in the study were resistant to most substances licensed for therapy in veterinary medicine. However, some isolates were susceptible to tetracycline, chloramphenicol and/or fusidic acid. This study also showed that a majority of the European isolates were clonally related. Most had similar PFGE-profile, the same spa-type (t02) and multilocus sequence type (ST71).

Nearly 60% of the first diagnosed 50 MRSP in Sweden (from 2006 to 2007) were from surgical site infections, indicating that transfer of MRSP occurred in animal health care facilities. In contrast, during 2008 and 2009, the majority of canine MRSP was isolated from skin samples or from wounds together with abscesses (see Table).

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, at many animal clinics and hospitals, infection control programs 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. One outcome of these actions is a decrease in the number of antimicrobial prescriptions to dogs (See Highlight on "Use of antimicrobials for different animal species"), but unfortunately, the number of MRSP has continued to increase.

TABLE. Sampling sites from dogs yielding Methicillin-resistant *Staphylococcus pseudintermedius* during 2008 and 2009.

	No. (%)	
Sampling site	**2008**	**2009**
Wound & abscesses	40 (51)	36 (30)
Skin	12 (15)	26 (21)
Ear	9 (12)	9 (7)
Urine	1 (1)	4 (3)
Miscellaneous	4 (5)	7 (6)
Carrier[a]	-	12 (10)
Unkown[b]	12 (15)	27 (22)
Total	78	121

[a]Pooled samples taken from multiple sites like pharynx, gingival, perineum etc; [b] Bacterial strains sent to SVA for confirmation of methicillin resistance.

Multiresistance (i.e. resistance to three or more antimicrobials) occurred in 14% of the isolates. This figure is higher than in the last five years. This year 17% of the *E. coli* was isolated from mares held at one specific stud farm and they contributed to 37% of the multiresistant *E. coli*. In 2008, 10% of the isolates were from this stud farm but none was multiresistant. In 80% of the multiresistant *E. coli*, resistance to ampicillin, streptomycin and trimethoprim-sulphonamides occurred. Half of the multiresistant *E. coli* were resistant to five or more antimicrobials, where resistance to ampicillin, gentamicin, streptomycin, tetracycline and trimethoprim-sulphonamides were the most common traits.

The observed increases in resistance seen in this material should be interpreted with caution since underlying factors, such as the indications for sampling, may vary over time. However, an increase in *E. coli* resistant to third generation cephalosporins is undesired and the situation needs to be closely monitored. Ceftiofur is not authorised for treatment of horses in Sweden, but ceftiofur, gentamicin and several other antimicrobials are used to treat mares with gynaecological disorders at stud farms which could select for multiresistant and ESBL-producing *E. coli*. These results could indicate that there is an urgent need for programs in antimicrobial stewardship and infection controls at stud farms.

TABLE HORSE II. Resistance (%) in *Streptococcus zooepidemicus* from horses 1992-2009 and distribution of MICs for isolates from 2009. Isolates are from clinical submissions of samples from the respiratory tract.

Antimicrobial	Resistance (%)								Distribution (%) of MICs[a] (mg/L)									
	1992-94 n=218	1995-97 n=402	1998-00 n=409	2001-03 n=505	2004-06 n=534	2007 n=180	2008 n=159	2009 n=152	≤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[c]	NR	NR	NR	NR	NR	NR	NR				59.2	40.8					
Florfenicol	-	-	-	1[d]	<1	0	0	0					98.0	1.3	0.7			
Gentamicin	NR	NR	NR	NR	NR	NR	NR	NR					1.3	2.0	33.6	54.6	8.6	
Neomycin	NR	NR	NR	NR	NR	NR	NR	NR						0.7		2.6	26.3	70.4
Penicillin	0	<1	0	0	0	0	0	0	100									
Spiramycin	<1	1	0	1	<1	0	0	<1						99.3			0.7	
Streptomycin	NR	NR	NR	NR	NR	NR	NR	NR							1.3	2.0	71.1	25.7
Tetracycline	4	3	4	5	3	3	2	4				59.2	33.6	3.3		3.9		
Trim/Sulph.[b]	1	11	57	36	42	17	21	18			69.1	8.6	4.6		17.8			

[a] White fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate cut-off values defining resistance; [b] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphametoxazole); [c] NR= Not relevant as the inherent susceptibility is above concentrations that can be obtained during therapy; [d] 370 isolates tested.

TABLE HORSE III. Resistance (%) in *Staphylococcus aureus* from horses 2007-2009 and distribution of MICs for isolates from 2009. Isolates are from clinical submissions of samples from skin.

Antimicrobial	Resistance (%)			Distribution (%) of MICs[a] (mg/L)									
	2007 n=113	2008 n=99	2009 n=96	≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Ceftiofur	0	2	2		7.3	25.0	61.5	4.2	2.1				
Enrofloxacin	3	2	2	66.7	29.2	2.1	1.0	1.0					
Florfenicol	2	3	1					28.1	57.3	13.5	1.0		
Gentamicin	9	7	6					93.8	2.1	1.0		3.1	
Oxacillin	-	-	2			91.7	6.3	2.1					
Penicillin[b]	26	36	36										
Spiramycin	1	0	0						47.9	41.7	10.4		
Streptomycin	12	14	9						62.5	21.9	6.3		9.4
Tetracycline	2	6	4				95.8	3.1			1.0		
Trim/Sulph.[c]	4	5	3			96.9	2.1	1.0					

[a] White fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. [b] Denotes β-lactamase production; [c] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphametoxazole).

Streptococcus zooepidemicus

The isolates included are from the respiratory tract of horses. As in previous years, *Streptococcus zooepidemicus* are uniformly susceptible to penicillin (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-sulphonamides in horses, but resistance to other antimicrobials is rare. *Streptococcus zooepidemicus* has a low inherent susceptibility to fluoroquinolones and aminoglycosides (i.e. gentamicin, neomycin and streptomycin) and it can be observed that MICs are above concentrations that can be obtained during systemic therapy with these antimicrobials.

Staphylococcus aureus

Isolates of *Staphylococcus aureus* are from skin samples, excluding wounds and abscesses. The number of resistant *S. aureus* has been stable during the last three years and resistance to penicillin is dominating (Table Horse III). In 2009, 36% of the isolates were resistant to penicillin due to penicillinase production. Still, penicillin should be considered the drug of choice if antimicrobial treatment is necessary in horses with skin disorders. Investigations on the underlying causes are of course crucial.

Two isolates had MICs >1 mg/L for oxacillin and were tested by PCR for the presence of *mec*A-gene but both were negative. However, Methicillin-resistant *S. aureus* (MRSA) have been isolated from horses in Sweden (See highlight on "Methicillin-resistant *Staphylococcus aureus* (MRSA)").

Occurrence of multiresistance (i.e. resistance to three or more antimicrobials) was rare; only 5% of the isolates. The most common multiresistant phenotype was resistant to penicillin, gentamicin and streptomycin. However, 5% of the isolates were resistant to both penicillin and gentamicin. No isolate was resistant to more than three substances.

Dog

Escherichia coli

Isolates of *Escherichia coli* are from samples of urine, submitted either as urine or as dip-slide cultures. The level of resistance in *E. coli* has remained stable during the years studied with exception of ampicillin, tetracycline and trimethoprim-sulphonamides (Table Dog I). Resistance to the two latter have been numerically lower during the last three years compared to the beginning of this decade. In addition, resistance to ampicillin have dropped in 2009 compared to last years´ levels. This could be explained by a change in the origin of the samples (clinic versus hospital) as discussed by Hagman & Greko (2005). In brief, patients with recurrent problems of urinary tract infections are often referred to animal hospitals and they have often been treated with antimicrobials prior to sampling. Therefore occurrence of resistance in *E. coli* was more common from urine samples from referral hospitals compared to clinics. However, in 2009, the proportion of samples from referral hospitals was the same as in 2008. An explanation for the drop in ampicillin resistance could be that urine from cases of uncomplicated urinary tract infections, i.e. from patients that probably was not treated with antimicrobials, was cultured more frequently than previously. The number of isolates has increased from 503 in 2008 to 599 in 2009 which is the highest number of *E. coli* in the years studied.

This year's isolates were tested for susceptibility to cefotaxime as an indicator of extended-spectrum beta-lactamase (ESBL) production and not as a treatment option. In four *E. coli*, ESBL production was suspected, MIC >0.5 mg/L, unfortunately, these isolates were not tested further. ESBL-production has been confirmed in *Enterobacteriacae* from dogs (see highlight "*Enterobacteriacae* producing extended spectrum beta-lactamases (ESBL) – isolates from diagnostic submissions").

In 2009, only in 5% of the isolates were multiresistant (i.e. resistant to three or more antimicrobials). Of the multiresistant isolates, 69% were resistant to at least ampicillin, trimethoprim-sulphonamides and tetracycline. Only six *E. coli* were resistant to five or more antimicrobials i.e. 1% of all isolates. The figures for this year cannot be compared with those in previous reports because a new panel without streptomycin was used for susceptibility testing during 2009. Streptomycin was commonly a part of multiresistant phenotypes in *E. coli*. If last year´s figures are calculated without streptomycin, the proportion of isolates with multiresistance is about the same as this year.

Uncomplicated cystitis in dogs is frequently treated with aminopenicillins, which are by far the most commonly prescribed antimicrobials for dogs (SVARM 2008). This could explain the high proportion of *E. coli* resistant to ampicillin. However, tetracycline and trimethoprim-sulphonamides are seldom prescribed for systemic treatment of dogs (SVARM 2008). Yet, resistance to these substances is around 10% most years. This is probably explained by co-resistance between ampicillin, tetracycline and trimethoprim-sulphonamides. Of isolates resistant to trimethoprim-sulphonamides, 87% are resistant also to ampicillin, and of isolates resistant to tetracycline, 72% are resistant to ampicillin. The excessive use of aminopenicillins therefore probably selects for resistance to the other two substances.

Besides aminopenicillins, urinary tract infections are often treated with fluoroquinolones, and occasionally with trimethoprim-sulphonamides. Two percent of all isolates were resistant to all these three antimicrobial groups.

Staphylococcus pseudintermedius

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

TABLE DOG I. Resistance (%) in *Escherichia coli* from dogs 1992-2009 and distribution of MICs for isolates from 2009. Isolates are from clinical submissions of urinary tract samples.

	Resistance (%)								**Distribution** (%) **of MICs**[a] (mg/L)									
Antimicrobial	**1992-94** n=245	**1995-97** n=296	**1998-00** n=418	**2001-03** n=621	**2004-06** n=917	**2007** n=425	**2008** n=503	**2009** n=599	**≤0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**>32**
Ampicillin	18	18	18	18	19	18	17	13				4.3	64.6	17.8	0.5	12.7		
Cefotaxime	-	-	-	-	-	-	-	NA[e]			97.8	1.8	0.4					
Enrofloxacin[b]	9	9	10	9	10	7	10	8	92.6	1.0	3.0	1.0		0.2	3.2			
Gentamicin[c]	2	1	2	2	1	<1	1	2					92.9	5.0	0.7	0.2	1.2	
Nitrofurantoin	3	3	1	2	2	<1	3	1								98.3	0.3	1.3
Polymyxin B	-	-	-	-	-	-	-	4					95.5	3.3	1.2			
Tetracycline	16	14	12	11	10	9	7	8				16.5	69.3	5.8	0.5	7.8		
Trim/Sulph.[d]	9	8	11	13	15	12	8	8			91.5	0.8	0.3		7.3			

[a] White fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate cut-off values defining resistance; [b] Cut-off value >0.25 mg/L until 2002; [c] Cut-off value >8 mg/L until 2001; [d] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphametoxazole) and cut-off value >4 mg/L until 2001; [e] NA=not applicable, cefotaxime used as indicator for extended spectrum beta-lactamases, 225 isolates tested.

the strain belongs to another related species (Devriese et al., 2008). 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 β-lactamases (penicillinase) in *S. pseudintermedius* is high, 90% (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 2009, as in previous years. Maybe a slight increase in the proportion of isolates resistant to clindamycin can be seen and that would be concordant with the rise in the number of prescriptions of clindamycin for dogs (see highlight on "Use of antimicrobials for different animal species").

Noteworthy in this year's material resistance to cephalothin and oxacillin is higher compared to previous years, which mostly is due to cases of pyoderma caused be Methicillin-resistant *S. pseudintermedius* (MRSP). At SVA, all isolates of *S. pseudintermedius* with MIC of >0.5 mg/L for oxacillin are examined for *mec*A gene with PCR (see Appendix 3 for details). In this material 5% (17 isolates) were analysed with PCR and 13 were confirmed as Methicillin-resistant. The new breakpoint for *S. pseudintermedius* (>0.25 mg/L) from CLSI in 2010 (http://jvdi.org/cgi/data/21/1/53/DC1/1) 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* – an update".

Resistance to trimethoprim-sulphonamides was low, possibly because this combination is seldom prescribed to dogs (SVARM 2008) and consequently the selective pressure is low. The prescription of tetracycline to dogs is also low (SVARM 2008) but resistance to tetracycline is common (30%) probably due to co-selection through clindamycin use see below.

Multiresistance (i.e. resistance to three or more antimicrobials) occurred in 33% of the isolates. Resistance to penicillin, clindamycin and erythromycin was the most common phenotype, occurring in 75% of multiresistant isolates. Almost half of these were also resistant to tetracycline. Resistance to enrofloxacin occurred only in multiresistant phenotypes with the exception of one isolate. Almost 9% of all isolates were resistant to five or more antimicrobials. Out of these 34 isolates, 13 (38%) were MRSP. 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, 84% of isolates resistant to erythromycin were also resistant to clindamycin.

Pyoderma is a common cause for dog owners to seek veterinary consultation and this condition is often treated with clindamycin or cephalosporins. In this data, there is a high probability of bias towards dogs with recurrent skin infections, previously treated with antimicrobials that 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. Fortunately, the total number of prescriptions for dogs continues to decline (see highlight on "Use of antimicrobials for different animal species"). To be able 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 species is considered clinically resistant to e.g. trimethoprim-sulphonamides, tetracyclines and aminopenicillins (including combinations with clavulanic acid). Enrofloxacin, gentamicin and polymyxin B, are the only substances licensed for treatment of pseudomonal infections in

TABLE DOG II. Resistance (%) in *Staphylococcus pseudintermedius* from dogs 1992-2009 and distribution of MICs for isolates from 2009. Isolates are from clinical submissions of samples from skin.

	Resistance (%)								**Distribution** (%) **of MICs**[a] (mg/L									
Antimicrobial	**1992-94** n=304	**1995-97** n=322	**1998-00** n=433	**2001-03** n=382	**2004-06** n=374	**2007** n=220	**2008** n=258	**2009** n=381	**≤0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**>32**
Cephalothin	<1	<1	0	1	1	<1	3	5					95.0	1.0	3.9			
Clindamycin	12	20	21	18	19	18	22	27				72.2		1.0	26.8			
Enrofloxacin	-	-	-	2[e]	2	4[h]	4	6	81.6	9.4	2.6	1.3	0.3		4.7			
Erythromycin[b]	21	28	27	24	26	25	25	31			67.5	1.0	0.3		31.2			
Fusidic acid	9	14	20[d]	20[f]	25	24	24	25					71.4	3.9	24.7			
Gentamicin	<1	<1	<1	0	1	2	2	3					96.1	0.5	1.8	1.0	0.5	
Nitrofurantoin	1	1	<1	1	<1	<1	<1	<1								99.2	0.3	0.5
Oxacillin	1	2	1	2	2	1	4	5			94.8	0.8	4.5					
Penicillin[c]	79	80	80	80	84	84	86	90										
Tetracycline	24	12	28	25[g]	32	32	28	30				69.3	0.3		0.3	30.2		
Trim/Sulph[d]	1	2	1	3	6	5	5	6			75.6	18.4	0.5	0.5	5.0			

[a] White fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate cut-off values defining resistance; b Cut-off value >4 mg/L until 2001; [c] Denotes β-lactamase production; [d] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphamethoxazole); [d] 421 isolates tested; [e] 273 isolates tested; [f] 346 isolates tested; [g] 381 isolates tested; [h] 212 isolates tested;.

SVARMpat – studies in progress

THE PURPOSE of SVARMpat is to increase the knowledge on resistance in animal pathogens from farm animals and the program has been running since 2005 (for more information See SVARM 2005). SVARMpat is a co-operation between the National Veterinary Institute (SVA) and the Swedish Animal Health Service and is financed by the Swedish Board of Agriculture. Results are reported yearly in the SVARM report, and in addition three times yearly in newsletters directly to veterinary practitioners. The purpose of the newsletters is to continuously inform practitioners on activities and results but also to deepen their knowledge on antimicrobials, antimicrobial treatment and resistance.

An important activity in SVARMpat is to encourage practitioners and pathologists to submit samples for microbiological culture and susceptibility testing. In this year's SVARM report some results from this work are presented, e.g. susceptibility data on *Actinobacillus pleuropneumoniae* and *Brachyspira* spp.from pigs, *Pasteuerella* spp. from both cattle and pigs, *Escherichia coli* from calves and *Fusobacterium necrophorum* from cattle and sheep. In addition, during 2009, a screening for production of extended spectrum beta-lactamase (ESBL) in *E. coli* from pigs with diarrhoea was done. Rectal swabs arriving at SVA was cultured on selected media (MacConkey agar with 1 mg/L of cefotaxime) and no ESBL-producing *E. coli* were found, see highlight "*Enterobacteriacae* producing extended spectrum beta-lactamases (ESBL) – isolates from diagnostic submissions".

Other activities in SVARMpat 2009:

- A workshop on antimicrobial treatment of swine was held for swine practitioners in December 2009 in collaboration with Strama VL and Swedish Animal Health Services.
- The PhD project – Vancomycin-resistant enterococci in Swedish broilers – is partly financed by SVARMpat. In the project, started in 2007, the spread of vancomycin-resistant enterococci (VRE) in Swedish broilers since 2000 is investigated. The aim is 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.
- *E. coli* from pigs with diarrhoea have been extensively analysed for genes coding for virulence factors, different serotypes and enlarged susceptibility testing in order to investigate correlations between these factors.
- Screening for causative agents of arthritis in piglets and the antimicrobial susceptibility of these bacteria has been initiated. One lame piglet per herd with more than 100 sows will be euthanized and an autopsy will be done together with bacteriological sampling of two joints. In total about 400 piglets will be analysed.

Activities planned for 2010:

- Slaughter pigs will be screened for MRSA. Nasal swabs will be taken at slaughter.
- The occurrence of *Mycoplasma bovis* in nasal samples from calves with respiratory symptoms will be investigated. Sampling from post mortem investigations of lungs will also be initiated.
- Sampling from cattle with interdigital necrobacillosis will continue, but focus will be on improving sampling technique and why some herds experience treatment failure.
- A screening for MRSA in milk samples from cows has started and will continue during 2010. Isolates of penicillinase producing *Staphylococcus aureus* will be further investigated.

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

	2002-03	2009	Distribution (%) of MICs[a] (mg/L)									
Antimicrobial	n=234	n=261	**≤0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**>32**
Enrofloxacin	NA	25	0.4	0.8	9.6	40.2	22.6	6.5	19.9			
Gentamicin	9	5					66.7	20.3	8.4	2.3	2.3	
Polymyxin B	-	0					89.3	10.7				

[a] White fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate cut-off values defining resistance; NA= not applicable because of the range of enrofloxacin concentrations tested.

dogs and therefore, the susceptibility data of these substances are presented in Table Dog III. All isolates were susceptible to polymyxin B. However, resistance to gentamicin (5%) and enrofloxacin (25%) occurred.

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). It is clear that the ratio would not be reached in most infection sites after systemic administration even for the more susceptible isolates. Local antimicrobial treatment in dogs with ear infections is of course recommended.

Cat

Escherichia coli

Isolates of *Escherichia coli* are from samples of urine, submitted either as urine or as dip-slide cultures. Resistance to ampicillin was most common and resistance to fluoroquinolones has numerically increased whereas resistance to trimethoprim-sulphonamides or tetracycline have declined during the last years (Table Cat I). If these are true trends or just reflections of changes in the material due to e.g. different indications for sampling over the years will be shown in the coming years.

In 2008, 4% of the isolates were multiresistant (i.e. resistant to three or more substances). The figures for this year cannot be compared with those in previous reports because a new panel without streptomycin was used for susceptibility testing during 2009. Streptomycin is commonly a part of the multiresistant phenotypes in *E. coli* from all animal species. If last year´s figures are calculated without streptomycin, the number of multiresistant is about the same as this year.

Of the ten multiresistant isolates, four were resistant to ampicillin, tetracycline and trimethoprim-sulphonamides. None of the isolates were resistant to five or more antimicrobials. 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 2% 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.

TABLE CAT I. Resistance (%) in *Escherichia coli* from cats 1992-2009 and distribution of MICs for isolates from 2009. Isolates are from clinical submissions of urine samples.

	Resistance (%)							**Distribution** (%) **of MICs**[a] (mg/L)									
Antimicrobial	**1992-97** n=61	**1998-00** n=74	**2001-03** n=135	**2004-06** n=224	**2007** n=131	**2008** n=170	**2009** n=245	**≤0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**>32**
Ampicillin	26	34	27	22	16	19	19				4.9	68.0	7.4	0.8	18.9		
Cefotaxime	-	-	-	-	-	-	NA[e]			97.8	1.8	0.4					
Enrofloxacin[b]	5	8	13	7	4	7	8	91.4	2.5	3.7	0.8		0.8	0.8			
Gentamicin[c]	0	3					1					96.3	2.5	0.4	0.8		
Nitrofurantoin	2	2	1	3	<1	1	2								96.7	1.6	1.6
Polymyxin B	-	-	-	-	-	-	6					94.3	2.9	2.9			
Tetracycline	28	16	16	14	8	9	7				27.0	59.4	5.3	1.2	7.0		
Trim-Sulph.[d]	7	10	15	7	5	6	4			94.7	1.2	0.8		3.3			

[a] White fields denote the range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate microbiological cut-off values defining resistance; [b] Cut-off value >0.25 (mg/L) until 2002; [c] Cut-off value >8 mg/L until 2001; [d] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphamethoxazole), cut-off value >4 mg/L until 2001; [e] NA=not applicable, cefotaxime used as indicator for extended spectrum beta-lactamases, 185 isolates tested.

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. For details on methodology, see the respective sources of the statistics.

Over the last two decades, the total number of dairy cows, pigs, and laying hens has decreased notably concomitantly with an increase in herd size. In the same period, the number of beef cows and sheep as well as the number of broilers slaughtered has increased.

TABLE AP1 I. Number of livestock and horses (in thousands) 1980-2009 (Yearbook of Agricultural Statistics, Sweden 2001 & 2009 and Statistical Message JO 20 SM 0901).

Animal Species	1980[a]	1985[a]	1990	1995	2000	2005	2007	2008	2009
Cattle									
Dairy cows	656	646	576	482	428	393	370	357	357
Beef cows	71	59	75	157	167	177	186	196	192
Other cattle >1 year	614	570	544	596	589	527	516	513	502
Calves <1 year	595	563	524	542	500	508	489	492	488
Total, cattle	1 935	1 837	1 718	1 777	1 684	1 605	1560	1 558	1 538
Pigs									
Boars & sows	290	260	230	245	206	188	181	170	160
Fattening pigs >20 kg [b]	1 254	1 127	1 025	1 300	1 146	1 085	1015	974	943
Piglets <20kg [c]	1 170	1 113	1 009	769	566	539	480	465	426
Total, swine	2 714	2 500	2 264	2 313	1 918	1 811	1 676	1 609	1 529
Sheep									
Ewes and rams	161	173	162	195	198	222	242	251	254
Lambs	231	252	244	266	234	249	267	273	287
Total, sheep	392	425	406	462	432	471	509	525	540
Laying hens									
Hens	5 937	6 548	6 392	6 100	5 670	5 065	5 328	5 546	5 261
Chickens reared for laying	2 636	2 159	2 176	1 812	1 654	1 697	1 753	1 649	1 898
Total, hens	8 573	8 708	8 568	7 912	7 324	6 762	7 080	7 195	7 159
Turkeys									
Total, turkeys	-	-	-	-	-	122	101	-	-
Horses									
Total, horses	-	-	-	-	-	283[d]	-	-	-

[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 & 2009 and Statistical Message JO 20 SM 0901).

Animal Species	1980	1985	1990	1995	2000	2005	2007	2008	2009
Cattle									
Dairy cows	44 143	35 063	25 921	17 743	12 676	8 548	7 096	6 474	6 020
Beef cows	12 436	10 310	10 883	17 069	13 861	12 821	12 494	12 345	11 922
Other cattle >1 year	63 179	52 652	42 696	39 160	30 457	24 808	22 501	21 536	20 330
Calves <1 year	62 314	52 001	41 986	36 542	27 733	22 888	20 780	19 911	18 965
Total holdings with cattle	70 503	58 872	47 292	41 990	32 063	26 179	23 878	22 844	21 733
Sheep	10 238	10 595	9 749	10 037	8 089	7 653	8 014	8 186	8 245
Pigs	26 122	19 937	14 301	10 753	4 809	2 794	2 277	2 380	2027
Laying hens	23 603	17 531	12 900	9 593	5 678	4 916	4 245	4 643	3 306
Chickens reared for laying	5 093	2 714	1 875	1 405	715	634	496	854	573
Broilers	-	-	-	-	-	234	212	198	183
Turkeys	-	-	-	-	-	383	130	-	-
Horses	-	-	-	-	-	56 000[a]	-	-	-

[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 1003).

Animal Species	1980	1985	1990	1995	2000	2005	2007	2008	2009
Cattle									
Cattle >1 year	574	584	523	502	490	433	420	401	431
Calves < 1 year	130	152	70	30	39	33	30	29	29
Total, cattle	704	736	593	532	529	466	450	430	460
Pigs	4 153	4 283	3 653	3 743	3 251	3 160	3 004	3 072	2 970
Sheep	302	328	280	189	202	206	231	235	255
Broilers	40 466[a]	36 410[a]	38 577[a]	61 313	68 617	73 458	73 663	75 087	73 504

[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 1003).

Animal Species	1990	1995	2000	2004	2005	2007	2008	2009
Cattle								
Cattle >1 year	139.5	140.1	145.4	137.8	131.4	129.2	124.5	135.4
Calves < 1 year	6.8	3.2	4.4	4.6	4.5	4.3	4.3	4.6
Total, cattle	146.3	143.3	149.8	142.4	135.9	133.9	128.8	140.0
Pigs	293.1	308.8	277.0	294.5	275.1	264.9	270.7	261.7
Sheep	5.0	3.5	3.9	3.8	4.1	4.6	4.6	5.1
Broilers	44.0[a]	73.6[a]	89.9	91.2	96.2	105.4	107.2	105.2

[a] Data supplied by the National Food Administration.

Appendix 2: Materials and methods, use of antimicrobials

Source for the statistics

The antimicrobial drugs used in veterinary medicine in Sweden are only available on veterinary prescription. Furthermore, antimicrobial drugs are dispensed through pharmacies only. Until July 2009, Apoteket AB had a monopoly on pharmacies and data on sales were kept in one central database. Today, there are several chains of pharmacies on the Swedish market. Infrastructure, including national statistics on sales is provided by Apotekens Service AB. All pharmacies are required to report sales of drugs to that company. Data for 2009 were provided by Apotekens Service AB.

From year 2003, statistics on drug sales is based on electronic records of amount of drugs dispensed at or from pharmacies, i.e. sales statistics. Data for years before 2003 are the amount of antimicrobial products sold from the wholesalers to the pharmacies.

Sweden has a long tradition in drug consumption statistics. Data on the total use of antimicrobials for animals in Sweden has been analysed and reported by SVA since 1980. From 2005, statistics is also reported by the Swedish Board of Agriculture.

Classification of drugs

Veterinary medicinal drugs are classified according to the Anatomical Therapeutic Chemical veterinary classification system (ATCvet) (WHO, Guidelines for ATCvet classification). The system is based on the same main principles as the ATC classification system for substances used in human medicine. In both the ATC and ATCvet systems, drugs are divided into groups according to their therapeutic use. First, they are divided into 15 anatomical groups, classified as QA-QV in the ATCvet system (without Q in the system for human drugs), on basis of their main therapeutic use. Thereafter subdivision is made according to therapeutic main groups, which is followed by a further division in chemical/therapeutic subgroups.

Most antimicrobials are classified in the QJ group: general anti-infectives for systemic use. Antimicrobials can also be found in other groups such as QA (alimentary tract and metabolism), QD (dermatologicals), QG (genito-urinary system) and QS (sensory organs) depending on the therapeutic use.

Inclusion criteria

All veterinary antibacterial drugs authorised for use in animals except dermatologicals, ophtalmologicals and otologicals (i.e., ATCvet codes QA, QG and QJ) were included. Drugs authorised for human use but prescribed for use in animals were not included.

Drugs with antibacterial activity can also be found in other groups, notably among the antiprotozoals (QP51). Of these, the nitroimidazoles were included earlier but no such substances are presently authorised for use in animals. Sulfaclozine is licensed for treatment of coccidiosis only and has therefore not been included. The ionophoric antibiotics are presently regulated as feed additives and not sold through pharmacies and are therefore not included in the wholesalers' statistics. 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.

Prescriptions for dogs

From the spring of 2004, animal species is recorded for all prescriptions dispensed to animal care-takers. Data on all prescriptions for dogs, i.e. drugs authorised for use in animals (ATC vet code QJ01) as well as for humans (ATC code J01) were retrieved and are presented in a highlight in this year's report. The data-set corresponds to out-patient use in human medicine.

Distribution of veterinary medicines in Sweden

Marketing of drugs in Sweden is regulated by the Medicinal Products Act, which applies both to human and veterinary drugs. According to the Act, a medicinal product may not be sold until it has been granted marketing authorisation by the Medical Products Agency (MPA). The MPA has issued provisions concerning authorisation, distribution and prescription of veterinary medicinal products. In case there are no authorised veterinary medicinal products for a certain condition, the MPA can also permit special license prescription for a drug.

All pharmacies are authorised by the Medical Products Agency and operate according to specified guidelines. Only pharmacies are permitted to sell drugs. This implies that veterinarians in Sweden are not permitted to sell drugs, although they may for practical reasons hand over medicines for emergency use. Veterinarians are, however, under no conditions permitted to make a profit from dispensing medicines.

Appendix 3: Materials and methods, resistance monitoring

Sampling strategy

Zoonotic bacteria

Salmonella

Salmonellosis in animals is a notifiable disease in Sweden and one isolate from notified incident must be confirmed at SVA. Data presented in SVARM include one isolate of each serovar, and when appropriate phage-type, from each warm-blooded animal species in each incident notified 2009. In addition, isolates from incidents previously notified and still under restrictions 2009 are included. Also included are isolates obtained 2009 in the salmonella surveillance programme from samples collected at slaughter (carcass swabs, neck skins and lymph nodes). In 2009 *Salmonella* isolates from 37 cats and 16 wild birds were available but from each of these animal species 10 isolates were randomly selected for testing.

To investigate resistance in *Salmonella* from cold-blooded animals in Sweden, an inventory of SVA´s collection of *Salmonella* strains sent for confirmation 2006-2009 was made for isolates from snakes, lizards and turtles.

Indicator bacteria

Calves

Indicator bacteria, *Escherichia coli* and *Enterococcus* spp., from calves were isolated from colon content of healthy calves sampled at slaughter. Only calves reared for slaughter and about 6-8 months old (fattened calves) were sampled. Nine geographically separated abattoirs participated in collection of samples. The abattoirs accounted for 92% of the total volume of calves slaughtered in Sweden 2008.

Samples were collected for two weeks in each of five separate periods; March, April, August, September-October and November. In each period an abattoir collected samples from one eligible calf from each herd. By these measures, bacterial isolates included are from randomly selected healthy fattened calves of Swedish herds. Each isolate of *Escherichia coli*, *Enterococcus faecalis*, *E faecium* or *E. hirae* is from a unique herd within a sampling period.

Broilers

The frequency of colonisation by VRE among broilers in 2009 was investigated in a separate study on samples of caeca obtained through the Swedish Campylobacter programme. From these samples, 50 and 55 caeca collected at slaughter were selected in order of arrival at SVA in May and September, respectively. Samples selected for culture were from unique flocks but not necessarily from unique production sites.

Animal pathogens

Isolates of animal pathogens included are from routine bacteriological examinations of clinical submissions or post-mortem examinations at SVA. *Actinobacillus pleuropneumoniae* from pigs and *Fusobacterium necrophorum* from cattle and sheep were however isolated from samples collected in surveys initiated within SVARMpat.

In pigs, *Escherichia coli* are isolated from the gastro-intestinal tract (gut content, faecal samples or mesenteric lymph nodes), *Brachyspira* spp. from faecal samples and *Pasteurella* spp. from nasal swabs collected within a control programme for atrophic rhinitis in nucleus and multiplying herds. *Actinobacillus pleuropneumoniae* are from tissue samples from lungs sampled post mortem.

Pasteurella spp. from cattle are from the respiratory tract and *Fusobacterium necrophorum* in cattle and sheep from swabs of the interdigital cleft. In horses, *Escherichia coli* are from the genital tract of mares, *Streptococcus zooepidemicus* from the respiratory tract and *Staphylococcus aureus* from skin samples.

In dogs, *E. coli* are from samples of urine, *Staphylococcus pseudintermedius* from skin samples and *Pseudomonas aeruginosa* from samples from the external ear. *E. coli* from cats are from samples of urine. 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 Nordic Committee on Food Analysis (NMKL Nr 71 5th ed., 1999). 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.

Indicator bacteria

Escherichia coli

Approximately 0.5 g of colon content from calves was diluted in 4.5 mL 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.

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) and β-glucuronidase (p-nitrophenyl-β-D- glucopyranosiduronic acid, PGUA). Only lactose-positive isolates with typical morphology and positive reactions in both tests 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 detection.

Enterococci

Colon content from calves was diluted as described for *E. coli* and cultured on solid media without antibiotics. Caecal content from broilers was diluted in the same way as the colon content from pigs but cultured only on selective plates with vancomycin (16 mg/L).

Culture without selective antibiotics: Diluted colon content (0.1 mL) was spread onto Slanetz-Bartley (SlaBa) agar. The plates were incubated for 48 h at 37°C. From the Enterococcosel broth 0.1 mL was cultured on SlaBa agar and incubated at 44°C for 48 h. One colony, randomly chosen, was 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 tested for antimicrobial susceptibility and 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-α-D-glucopyranoside.

Selective culture for vancomycin-resistant enterococci: Diluted colon content (0.1 mL) was cultured on SlaBa with vancomycin (16 mg/L). From plates showing growth of colonies typical for enterococci, at least one colony of each morphological type was sub-cultivated on bile-esculin agar and blood agar (37°C, for 24 h). Identification of presumptive enterococci was performed as above.

Animal pathogens

Animal pathogens were isolated and identified with accredited methodology, following standard procedures at SVA. Bacteria from terrestrial animals were isolated at the Dept. of Bacteriology, and bacteria from fish at the Dept. of Animal Health and Antibiotic Strategies.

Susceptibility testing

Microdilution

The Dept. of Animal Health and Antimicrobial Strategies or the Dept. of Bacteriology performed antimicrobial susceptibility tests on bacteria from terrestrial animal, with accredited methodology, using dilution methods in cation adjusted Mueller-Hinton broth (CAMBH). Tests were performed following the standards for microdilution of the Clinical and Laboratory Standards Institute (CLSI, 2007). The microdilution panels used, VetMICä, are produced at the Dept. of Vaccines and Bloodproducts, SVA. Different panels were used depending on the bacterial species tested and the original purpose of the investigation (monitoring or clinical diagnostics). Minimum inhibitory concentration (MIC) was recorded as the lowest concentration of the antimicrobial that inhibits bacterial growth.

The Dept. of Animal Health and Antibiotic Strategies performed 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*, a broth dilution method was used (Karlsson et al., 2003). The antimicrobials were 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 with 10% foetal calf serum (1x106-5x106 CFU/ml). The trays were incubated in an anaerobic atmosphere at 37°C for four days on a shaker.

Phenotypic confirmatory test for production of extended spectrum beta-lactamases (ESBLs) in *Escherichia coli* was performed by the double disc diffusion test recommended by CLSI (2007).

Genotyping

Presence of the *mec*A gene in *Staphylococcus aureus* and *S. pseudintermedius* was tested by polymerase chain reaction (PCR) according to Smyth et al. (2001) in isolates with a phenotype indicating methicillin resistance.

Genotypic screening of ESBL positive *Escherichia coli* was performed by using Identibact Array Tube test according to the manufacturer (www.identibact.com). The test allows detection of the most common resistance genes of gram-negative isolates (Anjum et al., 2007).

In ten randomly selected enterococcal isolate with MICs of vancomycin above >128 mg/L, the resistance genotype was confirmed with PCR for the *van*A gene according to Dutka-Malen et al. (1995).

PCR was used to subtype *Fusobacterium necrophorum* into subsp. *necrophorum* and subsp. *funduliforme* (Narongwanichgarn et al., 2003).

Cut-off values

Epidemiological cut-off values issued by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) (http://www.escmid.org) were used for interpretation of results of susceptibility testing of zoonotic bacteria (*Salmonella*) and indicator bacteria (*E. coli* and enterococci). When no cut-off value was available a value was defined on basis of the actual MIC distributions obtained in the SVARM programme. This approach was also used for ciprofloxacin in *E. coli* because the recommended cut-off value (>0.03 mg/L) cuts through distributions of MICs in SVARM in a manner not in agreement with the concept of wild-type distributions, causing an erroneously high frequency of resistance.

Also for animal pathogens epidemiological cut-off values issued by EUCAST were used when available. When no cut-off value was available, or the range of concentrations tested was inappropriate for the recommended value, a cut-off value was defined on basis of the actual MIC distributions obtained in SVARM. The clinical breakpoints recommended for animal pathogens by CLSI (2008) were also taken into consideration.

It should be understood that epidemiological cut-off values classifies isolates with acquired reduced susceptibility as resistant, which is relevant for monitoring purposes, but 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 mg of the US standard. However, according to the International Standard Preparations, one international unit is equivalent to 13.51 mg. 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 mg. Feedingstuff grade of bacitracin correspond to 42-50 units/mg (one unit=20-24 mg) (Otten et al., 1975).

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 and indicator bacteria, *Escherichia coli* ATCC 25922, *Enterococcus faecalis* ATCC 29212 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 B78T ATCC 27164T was used for quality control.

In the *Fusobacterium* subtyping PCR *Fusobacterium necrophorum* subsp. *necrophorum* CCUG 9994 and *Fusobacterium necrophorum* subsp. *funduliforme* CCUG 42162 were used as positive controls.

The Dept. of Animal Health and Antimicrobial Strategies participates in several proficiency tests for antimicrobial susceptibility testing. These are arranged either by the Community Reference Laboratory (CRL) 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. are routinely registered in an Oracle database at SVA. From this, relevant data were extracted to a Microsoft Access database for evaluation and compilation.

For indicator bacteria, data on animal species, date of sampling, abattoir and herd of origin were together with results of culture identification and susceptibility tests 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, Microsoft Excel, or EpiInfo.

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.

TABLE AP3 I. Cut-off values (mg/L) defining resistance. Values in red are current (April 2010) EUCAST epidemiological cut-off values (ECOFFs), values in italic lettering deviate from ECOFFs and for values in normal lettering no ECOFFs are defined (see "Susceptibility testing" above for details).

Antimicrobial	*Actinobacillus pleuropneumonia*	*Brachyspira hyodysenteriae*	*Brachyspira pilosicoli*	*Campylobacter jejuni*	*Campylobacter coli*	*Enterococcus faecalis*	*Enterococcus faecium*	*Enterococcus hirae*	*Escherichia coli* (indicator)	*Escherichia coli* (pathogen)	*Pasteurella* spp.	*Pseudomonas aeruginosa*	*Salmonella enterica*	*Staphylococcus pseudintermedius*	*Staphylococcus aureus*	*Streptococcus zooepidemicus*
Ampicillin	>1			**>8**	**>16**	**>4**	**>4**	**>4**	**>8**	**>8**	>1		**>4**			>8
Bacitracin[a]						**>32**	**>32**	>32								
Cefotaxime	>0.06								**>0.25**		>0.06		**>0.5**			
Cefoxitin															**>4**	
Ceftiofur	>0.25								**>1**	**>1**	>0.25		**>2**		>2	
Cephalothin														>2	**>1**	
Chloramphenicol	>2					**>32**	**>32**	**>8**	**>16**		>2		**>16**		**>16**	
Ciprofloxacin	>0.06			**>1**	**>1**				***>0.06***		>0.06		**>0.06**		**>1**	
Clindamycin														>4	**>0.25**	
Enrofloxacin				>0.5	>0.5				**>0.12**	**>0.12**	>0.25	>2	>0.25	>0.5	>0.5	
Erythromycin				**>4**	**>16**	**>4**	**>4**	**>2**						**>1**	**>1**	
Florfenicol	>16								**>16**	**>16**	>16		**>16**		**>8**	>8
Fusidic acid														>4	**>0.5**	
Gentamicin	>8			**>1**	**>2**	**>32**	**>32**	>32	**>2**	***>4***	>8	**>8**	**>2**	>4	**>2**	
Kanamycin						>1024	>1024	>1024	**>8**				>16		**>8**	
Linezolid						**>4**	**>4**	>4								
Nalidixic acid	>16			**>16**	**>32**				**>16**		>16		**>16**			
Narasin						**>2**	**>4**	>2								
Neomycin										**>8**			**>4**			
Nitrofurantoin										***>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**	**>128**	**>16**	**>16**	>32		>32		**>16**	
Sulphametoxazole	>256								>256				>256			
Tetracycline	>2			**>2**	**>2**	**>4**	**>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													
Tylvalosin			>4													
Vancomycin						**>4**	**>4**	>4								
Virginiamycin						**>32**	**>4**	>4								

[a] MIC in U/mL; [b] Concentration of trimethoprim given, tested with sulphamethoxazole in concentration ration 1/20; [c] β-lactamase production.

Appendix 4: Antimicrobial agents licensed

ANTIMICROBIALS licensed for use in veterinary medicine in Sweden year 2009 are listed in Table AP4 I. 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. 2009. For explanation of ATCvet code, see Appendix 2.

TABLE AP4 I. Antimicrobials licensed for use in cattle, sheep, pigs, poultry, horses, dogs and cats in Sweden, 2009. Routes of administration are indicated [a].

		Animal species						
Antimicrobial agent	**ATCvet code**	**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
Penicillin G, penetamathydroiodide	QJ01C E90	I						
Beta-lactams, cephalosporins								
Cephalexin	QJ01D B01						O	
Ceftiofur	QJ01D D90	I						
Cefovecin	QJ01D D91						I	I
Sulphonamides/Trimethoprim								
Sulphadiazine/Trimethoprim	QJ01E W10	I	I	I		I O	O	
Sulphadoxine/Trimethoprim	QJ01E W13	I		I		I		
Sulphonamides								
Sulphaclozin	QP51A G04				O			
Macrolides								
Spiramycin	QJ01F A02	I						
Tulathromycin	QJ01FA94	I		I				
Tylosin	QJ01F A90	I		I O	O		I	I
Lincosamides								
Clindamycin	QJ01F F01						O	O
Aminoglycosides								
Gentamicin	QJ01G B03					I U	I	I
Dihydrostreptomycin (DHS)	QA07A A90	O U	O U	O U		O U	O	O
Fluoroquinolones								
Danofloxacin	QJ01M A92	I						
Difloxacin	QJ01M A94						O	
Enrofloxacin	QJ01M A90	I		I	O		I O	I O
Marbofloxacin	QJ01M A93						O	O
Ibafloxacin	QJ01M A96						O	O
Pleuromutilins								
Tiamulin	QJ01X X92			I 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						
Penicillin G, ester/DHS	QJ51R C25	M						

[a] O = oral; I = injection; U = intrauterine; M = intramammary.

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Appendix 6: SVARM 2000-2009 – an overview

SINCE 2000, data on antimicrobial susceptibility of over 20 000 isolates of bacteria of the categories; zoonotic, indicator or animal pathogens have been presented in SVARM. Below the number of isolates categories is presented by bacterial species, animal species and year of presentation.

TABLE AP6 I. Number of isolates of zoonotic bacteria presented in SVARM 2000-2009.

	Source	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Salmonella	Warm-blooded animals	67	52	49	101	68	105	101	112	122	117
	Reptiles										17
Campylobacter	Cattle		67					68			
	Pig		98		105		100	46		97	
	Broiler		50	100		100				38	
	Raw meat		74								
	Water		19								

TABLE AP6 II. Number of isolates of indicator bacteria presented in SVARM 2000-2009.

Bacterial species	Source	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Escherichia coli	Cattle	293						314			223
	Pig	260	308		303		390		342	349	
	Pork									19	
	Broiler	274	296	306		300			296		
	Dog							257			
	Willow grouse						19				
	Wild boar			87							
	Sheep									115	
***Entreococcus* spp.** *(faecium/faecalis/ hirae)*	Cattle	220						258			197
	Pig	210	235		282		226			218	
	Pork									20	
	Broiler	226	280	291		245			284		
	Dog							186			
	Wild boar			56							
	Sheep									77	

TABLE AP6 III. Number of isolates of animal pathogens presented in SVARM 2000-2009.

Animal species & bacterial species	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Cattle										
Escherichia coli (enteric)			220		87	39	24			40
Escherichia coli (udder)				169						
Klebsiella spp. (udder)				44			24			
Pasteurella spp.	254			100				27	32	14
Staphylococcus aureus (udder)		100	100			96			87	
Streptococcus dysgalactiae (udder)			100							
Streptococcus uberis (udder)			100							
Fusobacterium necrophorum										41
Pig										
Actinobacillus pleuropneumoniae	18							84	39	24
Brachyspira hyodysenteriae	50	75	109	100		31	26	23	15	24
Brachyspira pilosicoli				93		57	72	44	31	24
Escherichia coli (enteric)	399	82	340	340	386	325	298	93	83	102
Pasteurella spp.		75						38	25	24
Staphylococcus hyicus					20					
Poultry (laying hens)										
Escherichia coli (infection)								70		
Sheep										
Staphylococcus aureus (udder)								25		
Fusobacterium necrophorum										24
Fish										
Aeromonas salmonicida subsp.*achrom.*								67	20	23
Flavobacter columnare								30	16	10
Flavobacter psychrophilum								42	27	24
Horse										
Actinobacillus spp.		40								
Escherichia coli (genital)	323	103	166	188	188	161	124	273	174	210
Rhodococcus equi	73	20			187					
Streptococcus zooepidemicus	301	174	163	150	185	175	174	180	159	152
Staphylococcus aureus										308
Dog										
Escherichia coli (urinary)	185	183	204	234	247	304	366	425	503	599
Pasteurella multocida					231					
Pseudomonas aeruginosa				234						261
Staphylococcus pseudintermedius	145	156	133	102	159	126	89	220	258	381
Cat										
Escherichia coli (urinary)			46	52	55	74	95	131	170	245

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SWEDRES | 2009

A Report on Swedish Antimicrobial Utilisation and Resistance in Human Medicine

Strama
Swedish Strategic Programme against Antibiotic Resistance

SMITTSKYDDSINSTITUTET
Swedish Institute for Infectious Disease Control

SMITTSKYDDSINSTITUTET
Swedish Institute for Infectious Disease Control

SMI, The Swedish Institute for Infectious Disease Control (SMI) is a government expert authority with a mission to monitor the epidemiology of infectious diseases among Swedish citizens and promote control and prevention of these diseases.

Strama

Strama, The Swedish Strategic Programme against Antibiotic Resistance was founded in 1995. The remit from the Government is to collaborate interdisciplinary on issues aiming to preserve the effectiveness of antibiotics.

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Content

1. Preface

2.1 Summary

Use of antibiotics

After several years of small changes, 2009 showed a marked decrease (5.5%) in sales of antibiotics. The number of prescriptions per 1000 inhabitants in outpatient care took a downturn in the last quarter of the year. The decrease encompasses all age group, all county and majority of antibiotics. The greatest reduction was seen in age group 0-6 years were the sale decreased with 17.2%. Several reasons have been suggested in the analysis of this decrease, one of the major being the increased awareness in infection control issues and hand hygiene evoked by the pandemic influenza 2009. Many daycare centers have also developed hygiene curricula after initial studies of the use of hand sanitizers showing promising results regarding less absence due to sickness.

30% of all children aged 0-6 years were treated with at least one course of antibiotics in 2009. In 10.3% of all purchases of antibiotics commonly used to treat respiratory tract infections in children aged 0-6 years, a repeated course within 14 days is seen during 2005-2009.

Beta-lactamase sensitive penicillins together with tetracyclines are the most commonly used antibiotics in outpatient care. Treatment of respiratory tract infections has been the subject of information campaigns last year and is reflected in the sale of antibiotics commonly used to treat respiratory tract infections. Doxycyclin is the most frequently used tetracycline and a substance mainly used to treat respiratory tract infections. The total sale of tetracyclines decreased in 2009 and the seasonal variation was less pronounced.

Treatment of lower urinary tract infections in women has been the subject of information campaigns for several years. The total proportion of the tow first line recommend substances increase for every year and represent nearly 70% of the sale of antibiotics commonly used to treat respiratory tract infections in 2009.

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 continues and is in fact even more pronounced in 2009. However, there are still large differences between counties in this aspect. Kommer ev till några rader.

Use of antifungals

During the past five years we have seen the arrival of many new antifungal drugs. The total amount of antifungals used in hospitals have only increased with 10%, but what we have started to see is a shift from narrow spectrum drugs such as flukonazole towards broadspectrum drugs like the echinocandins and late generation azoles. This development becomes even more evident if we also confer prescriptions of vorikonazol och posaconazole to hospital use. The total amount of antifungals in hospitals is still low, 55 DDD/106/day, but with increasing reports of resistance and a shift towards non albicans species it is important to closely monitor both resistance and consumption of antifungals, both at a national and a local level.

Antibiotic resistance

While a few forms of antibiotic resistance are notifiable under the Communicable Disease Act the vast amount of data on antibiotic resistance in Sweden is gathered by the voluntary reporting by Swedish clinical microbiology laboratories. All laboratories take part in the annual resistance surveillance and quality control (RSQC) programme, and three fourths of the laboratories also contribute with data on defined invasive isolates to the European Antimicrobial Resistance Surveillance System, EARSS, network database. For some microorganisms data are produced and presented by laboratories with referral functions and/or with special interest in certain species (e.g. Neisseria spp.). In this report the most recent data on antibiotic resistance is presented and analysed together with data from previous years.

Staphylococcus aureus: A total of 1480 cases of MRSA were notified in 2009, a 13% increase compared to 1307 cases in 2008. Almost half of the reported cases (48%, n=711) had acquired MRSA in Sweden, and one-third (35%, n=517) had acquired the infection abroad. Eight of the Swedish counties had an incidence of notified MRSA cases above the average country incidence of 15.8 cases/100 000 inhabitants. Community-acquired infections dominated among domestic cases (64%) but were less frequent among imported cases (38%). Hospital-acquired infections were comparatively more common in imported cases (41%) than among domestic cases (12%), indicating continued good compliance to basal hygiene principles.

Invasive isolates of MRSA were as few in 2009 (n=18) as in previous years and thus Sweden is still one of the few countries having less than 1% of MRSA among invasive *Staphylococcus aureus*, as reported in the European surveillance network EARSS.

Epidemiological typing of all MRSA isolates is performed primarily by spa-typing. The five most commonly encountered *spa*-types in 2009 were t008 (n=157), t044 (n=108), t002 (n=106), t019 (n=59) and t015 (n=58), comprising one third of all isolates. The prevalence of MRSA with PVL toxin was 34% and was present in all or a majority of isolates with the common *spa*-types t008, t044, and t019. Multiresistance among MRSA, defined as resistance to betalactam antibiotics and to three or more other categories of antibiotics, was a rare phenomenon. Most cases could be correlated to six different spa types, and the acquisition of such strains was often from abroad and associated with healthcare.

Staphylococcus aureus from skin and soft tissue infections (RSQC programme) were susceptible to antibiotics in > 95% of cases. The fusidic acid resistant strain causing bullous impetigo, which has spread all over Sweden during the last decade, seems to decline and the epidemiology is described in detail.

Streptococcus pneumoniae: In 2009 there were 446 notifications of PNSP (Streptococcus pneumoniae with MIC of penicillin > 0.5 mg/L) in Sweden, a decrease by 21% compared with 2008. PNSP have decreased in annual incidence rate per 100 000 population from around 10 in 1997 to values between 5 and 7 since 2007. Most cases were identified through nasopharyngeal culture. The majority of PNSP cases, independent of year observed, were found in the age group 0-4 years. In 14 cases the PNSP isolates came from invasive sites, i.e. blood and/or spinal fluid. Multiresistance (resistance to penicillin and at least two more antibiotics) was common among PNSP. The most commonly found serotypes among all PNSP were, in decreasing order, types 19F, 23F, 9V, 19A, and 6B.

For five antibiotics tested on *Streptococcus pneumoniae* in the yearly RSQC programme 2009 the rates of resistance were slowly increasing, and low rates of quinolone-resistant isolates have been seen since 2005.

Rates of non-susceptibility to penicillins in *Streptococcus pneumoniae* (=PNSP) were lower among invasive isolates than in the nasopharyngeal isolates from the RSQC programme, and in 2009 also resistance to macrolide antibiotics was lower, 3.2% compared to 4.6-5.7% in 2001-2008.

Enterococcus faecalis and *Enterococcus faecium*: Enterococci, and more specifically vancomycin-resistant enterococci (VRE), have been important causes of nosocomial outbreaks in many parts of the world, but have until 2007 been rare in Sweden. In 2007 there were 53 notified cases, in 2008 618 cases, and in 2009 402 cases of VRE. These high notification rates were attributable to the spread of *van*B-carrying *Enterococcus faecium* not only in Stockholm county, but also in the counties of Halland and Västmanland. Intensive infection control efforts, implementation of screening programmes, contact tracing, and also other measures undertaken have contributed to the reduction in new cases in 2009. The strain of *Enterococcus faecium* with the vanB gene, affecting all three counties, was a new strain according to epidemiological typing using PFGE.

There were only four new cases of invasive vancomycin-resistant *Enterococcus faecium* in 2009. Of those four, only one was reported from an "EARSS-laboratory", thus resulting in 0.8% as reported to EARSS. In this case there was no connection to the widely disseminated new Swedish strain, neither geographically nor by epidemiological typing. Among invasive isolates of both *Enterococcus faecalis* and *Enterococcus faecium* high-level resistance to aminoglycosides (HLAR) was more common with 20% and 25%, respectively.

Streptococcus pyogenes: Data was obtained on 134 invasive isolates in 2009 (data derived from eleven laboratories using ADBact laboratory information system). Three isolates (2.2%) were resistant to erythromycin and clindamycin, indicating MLSB type of resistance. Thirteen isolates (9.7%) were resistant to tetracycline, a marked decrease compared to 2008 when 14.6% of the isolates were resistant.

Streptococcus agalactiae: Data was obtained on 131 invasive isolates in 2009 (data derived from eleven laboratories using ADBact laboratory information system). Nine isolates (6.9%) were resistant to erythromycin and clindamycin, a figure similar to those from 2006-2008.

Haemophilus influenzae: Data was obtained in the RSQC programme in 2009 and was compared to results from 2008. In 2009 the high frequencies of resistance remained with 23.3% for penicillins (including both beta-lactamase producing strains, BLPAR, and chromosomally mediated resistant strains, BLNAR) and 18.4% for trimethoprim-sulfamethoxazole. The frequency of BLNAR alone had increased from 3% to 4.2%. Betalactam-resistant strains from all laboratories and from both 2008 and 2009 were selected for further analysis. Co-resistance between trimethoprim-sulfamethoxazole and betalactams was more frequent among BLNAR than among BLPAR strains. Preliminary data on epidemiological typing of these selected strains also indicated a wide variety of strains and not a clonal dissemination of one strain. Haemophilus influenzae was rarely found among blood isolates, only 49 cases in 2009 derived from eleven laboratories using ADBact laboratory information system. Ten of these (20.4%) were beta-lactamase producing, and seven were resistant to trimethoprim-sulfamethoxazole.

Enterobacteriaceae producing extended spectrum beta-lactamases (ESBL) were made notifiable by the laboratories from February 2007. A total of 3754 cases were notified during 2009. Reports came from all 21 counties of Sweden, corresponding to a national incidence of 40 cases per 100,000 inhabitants. When comparing the second halfs of 2008 and 2009, respectively, a 27% increase of ESBL cases was noted for 2009. The most commonly reported species was *Escherichia coli* with 82% of all cases, followed by *Klebsiella pneumoniae* with 7%. Most ESBLs were found in urine samples (69%). 186 cases of invasive infections with ESBL-producing bacteria were noted in 2009. Isolates with ESBLs, most often of CTX-M-type, were often multiresistant, i.e. resistant to several other antibiotics, seriously limiting the options for treatment.

Escherichia coli, mainly derived from urinary tract infections, has been included in the national surveillance program (RSQC) since 1996, and invasive isolates have been included in the EARSS network since 2001. Ampicillin resistance, caused by production of plasmid-mediated beta-lactamase (most often of TEM-type) was increasingly found in both blood isolates and urine isolates (33% and 30%) in 2009. The level of resistance to third generation cephalosporins among blood isolates has increased to 3%, and in the majority of these cases the resistance was caused by plasmid-mediated ESBLs of CTX-M type. This resistance was often accompanied by resistance to many other antibiotics, e.g. aminoglycosides and fluoroquinolones. Resistance to fluoroquinolones has increased every year and was almost the same in urine as in blood isolates (13.3 vs. 15.5%) in 2009.

Klebsiella pneumoniae has also been monitored in the RSQC programme and through the EARSS network since 2005. The rates of resistance to tested antibiotics were comparable between the two surveillance programmes. Almost 2% of

Klebsiella pneumoniae were cephalosporin resistant and ESBL-producing, thus no increase from 2008. In 2007 the first isolate of K. pneumoniae with KPC-2 (*K. pneumoniae* carbapenemase) was detected in Sweden. In 2008 one isolate with a KPC-3 betalactamase was identified, and in 2009 there were reports of three isolates in Stockholm, one identified as KPC-2 and two as KPC-3. All the cases were healthcare related.

Pseudomonas aeruginosa has been monitored in the RSQC programme and through the EARSS network since 2005. The rates of resistance to tested antibiotics were comparable between the two surveillance programmes, but carbapenem resistance was more frequent in invasive isolates (7.5%) than among "all" isolates in the RSQC surveillance (4%). Fluoroquinolone resistance was approximately 10%.

A national surveillance program for *Clostridium difficile* was initiated by SMI in 2009. The program included both a voluntary laboratory reporting system of all new cases and determination of resistance and epidemiological typing of collected isolates. On isolates from 25 laboratories, collected during weeks 11 and 39, susceptibility tests and PCR ribotyping was performed. Type 014 was most frequent followed by types 020, 001, 023, 078 and 012. One isolate of type 027 was detected; however this isolate was susceptible to moxifloxacin, which is otherwise a typical marker for the virulent type 027 that has spread world-wide. In summary, there was geographical clustering of certain *C. difficile* types that also were resistant to several antibiotics.

Helicobacter pylori have been monitored locally at a few laboratories, but consistent data was only retrieved from one laboratory (University Hospital MAS, Skåne). Following a steady increase since 1994 and a peak of 16% in 2006, the rate of resistance to clarithromycin was 10.6% in 2009. In *Campylobacter jejuni/coli* high levels of resistance were seen for fluoroquinolones (30-60%), tetracyclines (20-35%) and low but variable for erythromycin (1-7%) during the last ten years.

Neisseria gonorrhoeae. Gonorrhoea is a notifiable disease, and in 2009 611 cases of the disease were reported. Isolates from 387 of the notified clinical cases were completely characterised at the Swedish Reference Laboratory for Pathogenic Neisseria, Örebro University Hospital, and at the Division of Clinical Bacteriology, Karolinska University Hospital Huddinge, Stockholm, representing 63% of the notified cases. In 2009 44% of these isolates were beta-lactamase producing and ampicillin resistant, and 75% were resistant to ciprofloxacin.

Mycobacterium tuberculosis. The total number of new cases of TB diagnosed in Sweden 2009 were 642, an increase of 16% compared to 2008. The numbers of cases diagnosed with isoniazid resistant TB in 2009 were 38/515 (7,4%) and with MDR-TB 13/515 (2,5%).

Genetic typing with RFLP (restriction fragment length polymorphism) was completed on 50 of the 58 resistant strains of *Mycobacterium tuberculosis* or *M. africanum* and is ongoing on the remaining 8 Sixteen of the 50 examined isolates belong to 12 different clusters with two or more patients in each cluster.

2.2 Sammanfattning

Antibiotikaförbrukning

Efter flera år av små skillnader i antibiotikaförsäljningen minskade försäljningen markant under 2009. I öppenvården minskade antalet recept per 1000 invånare kraftigt under det sista kvartalet. Minskningen omfattar alla åldrar, alla län och de flesta preparaten. Barn 0-6 år är den åldersgrupp som uppvisar störst minskning (17.2%) av antibiotikaförsäljning under 2009. Många orsaker kan ligga bakom den minskade antibiotikaförsäljningen. En trolig orsak som diskuteras i analysen är den ökade medvetenheten om infektionsspridning som väckts av informationskampanjer under våren 2009 på grund av den nya influensan. Många förskolor har skaffat sig goda hygienvanor efter studier som visar på mindre sjukfrånvaro vid användning av handsprit.

30% av alla barn 0-6 år behandlades med minst en antibiotikakur under 2009. I 10,3% av alla köp av luftvägsantibiotika till barn 0-6 år köptes en ny kur av luftvägsantibiotika inom 14 dagar.

Betalaktamas känsliga penicilliner och tetracykliner är de antibiotika som oftast förskrivs på recept. Behandling av luftvägsinfektioner har varit i fokus för informationsaktiviteter senaste året vilket kan ses i försäljningsstatistiken. Doxycyklin är den tetracyklin som förskrivs mest och en substans som oftast används mot luftvägsinfektioner. Under 2009 minskade den totala försäljningen av tetracykliner och säsongsvariationen av doxycklin minskade kraftigt.

Behandling av nedre urinvägsinfektioner hos kvinnor har varit i fokus för informationsinsatser under flera år. Andelen av de två rekommenderade förstahandspreparaten ökar för varje år och utgör nästan 70% av förskrivningen av antibiotika som ofta används vid urinvägsinfektioner.

Senaste åren har antibiotikaanvändningen i slutenvården

växlat från ett stort användande av cefalosporiner till ett ökat användande av smalspektrum antibiotika. Trenden fortsätter och är under 2009 ännu tydligare. Trots detta ses en stor skillnad mellan länen ur detta perspektiv.

Förbrukning av svampmedel

Under de senaste fem åren har utbudet av systemiska läkemedel mot svampinfektioner ökat, och man har sett en ökad användning av främst echinocandinerna, men också av de nyare azolerna. Den totala förbrukningen har ökat med beskedliga 10 % sedan 2006, men det finns en tendens att smalspektrumantimykotika, dvs flukonazol minskar och att bredspektrumantimykotika tar motsvarande marknadsandel. Denna utveckling ses än tydligare om man även inkluderar receptförsäljning av vorikonazol och posakonazol i sjukhusdata, eftersom dessa läkemedel så gott som alltid förskrivs av sjukhusspecialister.

Den totala mängden av antimykotika på sjukhus är fortsatt låg med 55 DDD/106/dag. Det är dock viktigt att noga följa både resistens och konsumtionsdata på både lokala och nationell nivå för att tidigt upptäcka förändringar i resistensmönster eller i artfördelning.

Antibiotikaresistens

Vissa former av antibiotikaresistens anmäls enligt smittskyddslagen men den frivilliga rapporteringen av resistensdata från de svenska kliniskt mikrobiologiska laboratorierna utgör basen för resistensövervakningen. Alla laboratorier deltar i den årliga insamlingen av data till ResNet, och tre fjärdedelar av laboratorierna bidrar också med data avseende de invasiva isolat som definierats av EARSS. För vissa mikroorganismer sammanställs data av laboratorier med referensfunktion och/eller med speciellt intresse för dessa arter (till exempel Neisseria- arter). I denna rapport presenteras resistensdata från 2009 och analyseras tillsammans med föregående års data.

Staphylococcus aureus: Totalt 1480 fall av MRSA anmäldes 2009, en ökning med 13 procent från 2008 då 1307 fall noterades. Nästan hälften av fallen hade blivit smittade i Sverige (711 fall), och en tredjedel (517 fall) hade blivit smittade utomlands. I åtta län/regioner var incidensen av MRSA-fall högre än riksgenomsnittet (15.8 fall per 100 000 invånare). Antalet invasiva isolat av MRSA var lika få 2009 (n=18) som föregående år, vilket medför att Sverige fortfarande är ett av de få länder i Europa som ännu ej nått nivån 1 procent av alla invasiva *Staphylococcus aureus* enligt rapportering till den europeiska resistensövervakningen EARSS.

Från och med 2006 har spa-typning utgjort den primära typningsmetoden. De fem vanligast förekommande spa-typerna var t008 (n=157), t044 (n=108), t002 (n=106), t019 (n=59) och t015 (n=58). Förekomsten av MRSA med PVL-toxin var 34 procent och förekom hos alla eller hos majoriteten av de vanliga spa-typerna t008, t044 och t019, men dessutom hos ett flertal andra spa-typer. Multiresistens var sällsynt och förekom framför allt hos kända ”utländska” stammar som de med spa-typ t037. *Staphylococcus aureus* i sårinfektioner (data från ResNet) var i mer än 95 procent av fallen känsliga för antibiotika. Detta gällde även fusidinsyra, berorende på att den tidigare spridda fusidinsyra-resistenta stammen som orsakade bullös impetigo kraftigt har minskat.

Streptococcus pneumoniae: Under 2009 noterades 446 fall med nedsatt känslighet för penicillin (MIC av penicillin > 0.5 mg/L, definierade som PNSP). Incidensen PNSP/ 100 000 invånare har minskat från 10.1 1997 till 5-7 sedan år 2007. De flesta fallen identifierades genom nasofarynxodling. Majoriteten av PNSP-fallen var i åldersgruppen 0-4 år. I 19 fall påvisades PNSP från blod och/eller spinalvätska. Multiresistens (resistens mot penicillin och minst två ytterligare antibiotika) var vanlig hos PNSP. De vanligast förekommande serotyperna/grupperna var 19F, 23F, 9V,19A och 6B. Enligt data rapporterade i ResNet sågs en långsam ökning av resistens mot testade antibiotika. Frekvensen PNSP var lägre hos invasiva isolat än hos nasofarynx-isolat, och detta gällde även frekvensen makrolidresistens som var 3.2 procent jämfört med tidigare års 5-6 procent.

Enterococcus faecalis och *Enterococcus faecium*: Enterokocker, särskilt de med resistens mot vankomycin (VRE), har varit frekvent förekommande vid sjukvårdsrelaterade utbrott i många delar av världen och har ofta omfattat riskpatienter. Från att ha varit ovanliga i Sverige, indikerade ökningen av anmälda fall 2007 ett skifte. Under 2008 rapporterades 618 fall och 2009 402 fall. Det stora antalet fall kunde tillskrivas förekomst och spridning av en vanB-innehållande *Enterococcus faecium* som uppträdde inte enbart i Stockholm utan också i Halland och Västmanland. Intensiva vårdhygieniska åtgärder, kontaktspårning och screening är alla faktorer som har medverkat till att antalet nya fall 2009 ändå har minskat. Genom epidemiologisk typning med PFGE framkom att den aktuella VRE-stammen sannolikt inte hade förekommit i Sverige före 2007. Endast fyra invasiva VRE har noterats 2009, och av dessa var det bara ett som ingick i rapportering till EARSS 2009 vilket då gav 0.8 procent resistens. Hos invasiva isolat av både *Enterococcus faecalis* och *Enterococcus faecium* förekom också höggradig aminoglykosidresistens (HLAR), i 20 respektive 25 procent av isolaten.

Streptococcus pyogenes: Data för 134 invasiva isolat, erhållna från elva ADBact-laboratorier under 2009, visade något ökad förekomst av makrolid-resistens, 2.2 procent jämfört med 0.5 procent 2008. Tetracyklinresistensen var lägre 2009 (10 procent) än 2008 (15 procent).

Streptococcus agalactiae: Data för 131 invasiva isolat, erhållna från elva ADBact-laboratorier under 2009, visade att 7 procent var makrolid-resistenta, vilket var samma nivå som 2006-2008.

Haemophilus influenzae: Data från övervakningen i ResNet, som genomfördes 2008 och 2009 efter ett uppehåll på tre år, visade på en kraftigt ökad förekomst av betalaktamas-producerande (ampicillin-resistenta) isolat och också av trimetoprim-sulfa-resistenta isolat. Siffrorna är nu på nivån runt 20 procent.. Andelen cefalosporinresistenta (ej betalaktamas-producerande) utgjorde cirka 4 procent av alla betalaktamresistenta. Preliminära resultat på utvalda isolat som typats med

PFGE visar att det förekommer flera olika stammar av de resistenta isolaten, ofta med bara lokal spridning.

Haemophilus influenzae var ett sällsynt fynd bland invasiva isolat, och endast 49 fall fanns registrerade från de elva ADBakt-laboratorierna 2009. Tio av dessa var betalaktamasproducerande (20 procent), och sju var resistenta mot trimetoprim-sulfa.

Enterobacteriaceae som producerar betalaktamaser med utvidgat spektrum, så kallade ESBL, blev anmälningspliktiga i februari 2007. Totalt 3754 fall rapporterades under 2009. Samtliga landsting rapporterade, och den genomsnittliga incidensen i Sverige var 40 fall per 100 000 invånare. Vid jämförelse mellan andra halvåret 2009 med samma period 2008 noterades en 27-procentig ökning av fall 2009. De flesta isolaten återfanns i urinprover (69 procent) och var Escherichia coli (82 procent), och de hade oftast ESBL av CTX-M-typ. Multiresistens var ett vanligt fynd hos dessa isolat.

Escherichia coli huvudsakligen från urinvägsinfektioner, har övervakats enligt det nationella programmet (ResNet) sedan 1996, och blodisolat har inkluderats i EARSS sedan 2001. Ampicillinresistens, oftast orsakad av plasmidmedierad betalaktamasproduktion av TEM-typ, återfanns i ökande utsträckning både hos blodisolat och urinisolat 2009 (33 procent och 30 procent). Frekvensen blodisolat med resistens mot 3:e generationens cefalosporiner var 3 procent, och hos majoriteten av dessa var resistensen orsakad av plasmidmedierade ESBL av CTX-M-typ. De cefalosporin-resistenta stammarna var ofta resistenta mot andra antibiotikagrupper som t ex aminoglykosider och kinoloner. Resistens mot kinoloner har ökat årligen och var hos både blodisolat och urinisolat 13-15 procent 2009.

Andra gram-negativa bakterier som övervakats nationellt och/eller internationellt är *Klebsiella pneumoniae* och *Pseudomonas aeruginosa*. Resistensnivåerna hos respektive patogen var desamma oberoende av övervakningsprogram och typ av prov. Hos *K. pneumoniae* var cirka 2 procent resistenta mot cefalosporiner genom ESBL-produktion. Under 2007 identifierades det första isolatet med KPC-2 i Sverige, under 2008 ytterligare ett, och under 2009 har tre KPC-producerande isolat påträffats. I samtliga dessa fall fanns en bakomliggande historia med sjukvård i södra Europa.

Hos *P. aeruginosa* var karbapenemresistensen vanligare hos invasiva isolat (7.5 procent) än hos övriga (4 procent), och kinolonresistensen var generellt cirka 10 procent.

Salmonella (här saknas text)

Helicobacter pylori har övervakats regelbundet vid ett laboratorium. Resistens mot klaritromycin har ökat stadigt under flera år men från 2007 och framåt har en minskning skett till 11 procent 2009.

Hos *Campylobacter jejuni/coli* har kinolonresistensen under de senaste tio åren varit 30-60 procent, tetracyklinresistensen 20-35 procent, och erytromycinresistensen 1-7 procent.

Neisseria gonorrhoeae: Gonorré är en anmälningspliktig sjukdom och 2009 rapporterades 611 kliniska fall. Isolat från 387 (63 procent) av dessa har undersökts vid det svenska referenslaboratoriet i Örebro eller vid laboratoriet för klinisk bakteriologi, Karolinska Universitetssjukhuset Huddinge, Stockholm. 2009 var fyrtiofyra procent av isolaten beta-laktamasproducerande och därmed ampicillinresistenta, och 75 procent var resistenta mot kinoloner (ciprofloxacin testat).

Mycobacterium tuberculosis. Antalet anmälda nya fall av tuberkulos var 642 under 2009, en ökning med 16 procent från 2008. *M. tuberculosis* med resistens mot minst två antibiotika (MDR-TB) rapporterades hos 2.5 procent av alla odlingsverifierade fall(13/515). Epidemiologisk typning med RFLP av de resistenta TB-isolaten visade att de tillhörde 12 olika kluster med två eller fler patienter i varje.

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Data on antibiotic use in relation to number of admissions and number of patient days in somatic hospital somatic care during 2006-2008 have kindly been provided by pharmacists in local Strama-groups.

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Editors

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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 wherever 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. Most people living in nursing homes still get their medicines by prescription, and data on this consumption are managed as outpatient care. However, there are also nursing homes where medicines are bought by the institution and then dispensed to the residents. That consumption is not included in outpatient statistics but in hospital care. 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 of course the number of individuals in the same group.

In this report outpatient care includes primary care, open specialist surgeries and parts of nursing homes. Hospital care includes 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.

Total sales of antibiotics

Due to the large decrease of antibiotic use in outpatient care, the total use of antibiotics in Sweden was 5.5 percent lower in 2009 than in 2008, Table 3.1.1.

Outpatient care

Sales of antibiotics in outpatient care decreased with 7.4% in 2009. This is the greatest decrease since 1995 calculated as a percentage. The decrease encompasses all age groups and children aged 0-6 represent the age group with the greatest decrease, Figure 3.1.4.

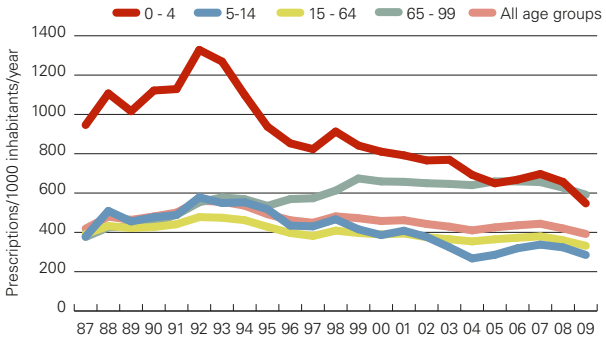

FIGURE 3.1.4. The sales of antibacterial drugs for systemic use in outpatient care 1987-2009, different age groups, prescriptions/1000 inhabitants.

Seasonal variations in antibiotic use have been less pronounced during the last years and this trend continues in 2009. This could be regarded as an indicator of good quality in prescribing, Figure 3.1.5.

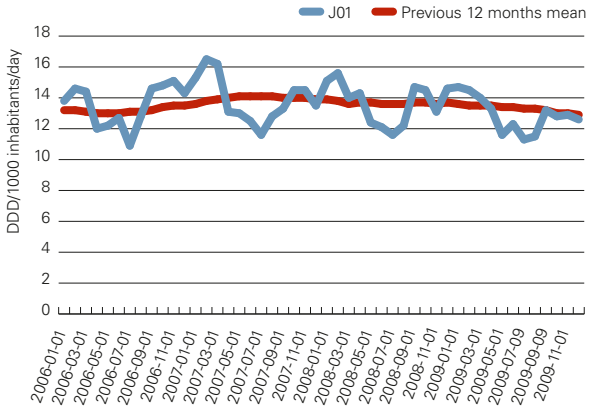

FIGURE 3.1.5. Antibiotics in outpatient care 2006-2009, DDD/ 1000 inhabitants/month. Monthly sale and 12 months mean.

The decrease in sales encompasses all antibiotic groups except nitrofurantoin and pivmecillinam. Penicillins with extended spectrum with the exception of pivmecillinam (J01CA) and

TABLE 3.1.1. Sales of antibiotics in outpatient and hospital care 2000-2009, DDD/1000 inhabitants and day.

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Out-patient care	13,7	13,8	13,3	13,0	12,8	13,1	13,5	13,9	13,7	12,9
Percent change from previous year		1%	-4%	-2%	-2%	3%	3%	3%	-1%	-6%
Hospital care	1,30	1,30	1,30	1,30	1,40	1,43	1,50	1,55	1,52	1,49
Percent change from previous year		0%	0%	0%	8%	2%	5%	4%	-2%	-2%

Antibiotic use in human and veterinary medicine

IN A GLOBAL PERSPECTIVE, bacteria in the environment are exposed to antibiotics from human medicines, veterinary medicines, foodstuffs and industrial products. Legislation in this area differs widely between countries and reliable data on use of antibiotics in the food industry is scarce. However, in this year's SWEDRES, an approach is done to somehow illustrate and relate the use of antibiotics in human and veterinary medicine to each other. Data collection and analysis has been done in collaboration between Strama and the corresponding programme for veterinary medicine and food, Strama VL.

The figures on total use of antibiotics sold for systemic use in humans were retrieved as defined daily doses and calculated to amounts of active substance. Figures on sales of antibiotics for use in animals (QJ01) are those presented in SVARM 2009. Sales for aquaculture are not included, nor are sales of medicines authorized for humans but sold for use in animals.

In 2009, around 64.5 tons of active substances from products classified as ATC J01 were sold for humans and around 15.2 tons of QJ01 to animals. Below are two diagrams showing a more detailed view of the relation between antibiotic use in humans and animals. Antibiotics that are used in both disciplines and which had a sales amount exceeding 1000 kg are included, Figures 3.1.1 and 3.1.2. Please note the difference in indexation of the x-axis.

Figure 3 displays the sales of beta-lactam antibiotics. These substances are by far the most used antibiotics in both human and veterinary medicine, but from an environment and resistance perspective they are relatively harmless. The substances presented in figure 2 are sold in much smaller quantities, but their impact on both antibiotic resistance and the environment is more pronounced due to their pharmacological and chemical properties.

Antibiotic use in relation to body weight in humans and animals is presented and discussed in SVARM 2009 (www.sva.se).

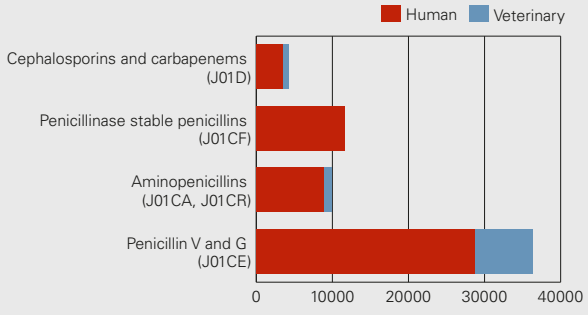

FIGURE 3.1.1. Amount of beta-lactam antibiotics in human and veterinary medicine, kg substance 2009.

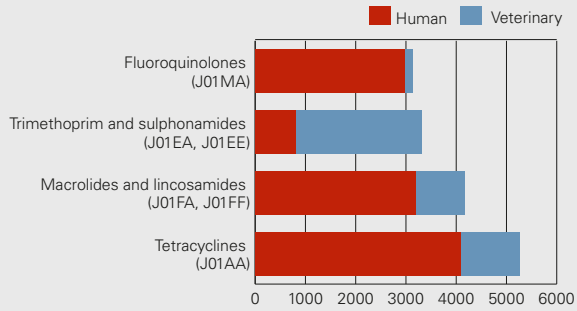

FIGURE 3.1.2. Amount of fluoroquinolones, macrolides, lincosamides, trimethoprim and sulphonamides and tetracyclines in human and veterinary medicine, kg substance 2009.

Human use makes up more than three quarters of all classes except trimethoprim and sulphonamides, where veterinary use represents 76 percent. An additional antibiotic group that is used in both disciplines is the aminoglycosides of which approximately 40 percent is used in human medicine.

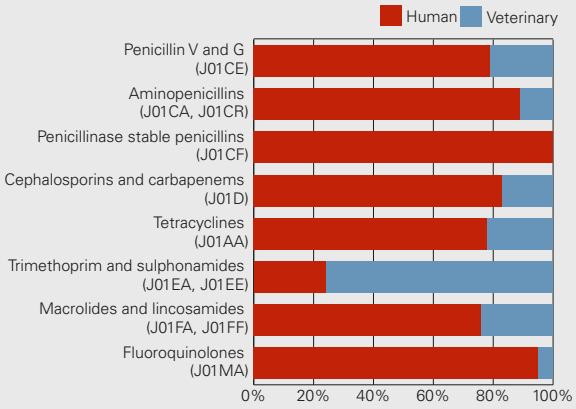

FIGURE 3.1.3. Proportions of certain antibiotic classes in human and veterinary medicine 2009.

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cephalosporins (J01DB-DE) are the two antibiotic groups with the greatest decrease expressed in percentage. Beta-lactamase sensitive penicillins (J01CE) together with tetracyclines (J01AA) are the most commonly used antibiotics in outpatient care 2009, Figure 3.1.6, and these groups show the largest decrease in absolute numbers.

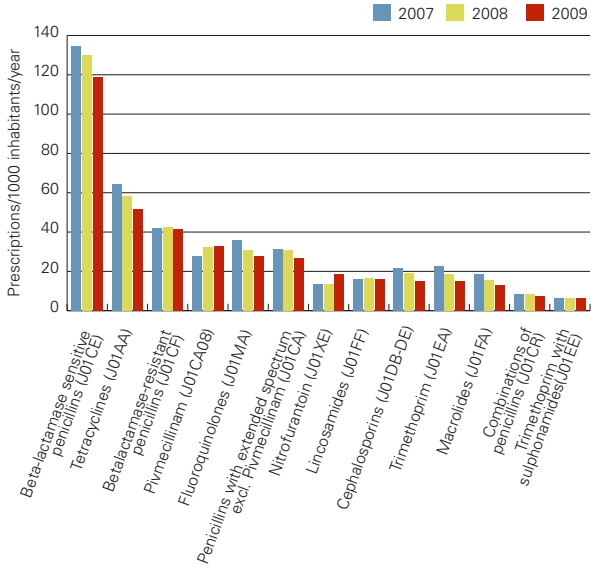

FIGURE 3.1.6. Antibiotics in outpatient care 2007-2009, Prescriptions/1000 inhabitants/ year.

Tetracyclines

Doxycycline is the most frequently used tetracycline measured as prescriptions/1000 inhabitants and stands for 75.6% of the sale of tetracyclines in 2009. This substance is mainly used to treat respiratory tract infections, which can be one explanation to the great seasonal variation. In Figure 3.1.7 the seasonal variation in use of tetracyclines during the period 2006-2009 is shown. However, during the winter 2009 the use of tetracyclines was less than earlier winter seasons. This may be an effect of the new treatment guidelines for respiratory tract infections launched by Strama and The Swedish Medicinal Products Agency in April 2008 and the distribution of these guidelines in a pocket format to all doctors in September 2008. Campaigns and information activities have been arranged ever since. Treatment with tetracyclines may give rise to photo sensibility which can be a contributing reason why the use decreases during summer. Antibiotic use for the indication acute bronchitis has also been debated in media and may have influenced the antibiotic prescribing pattern.

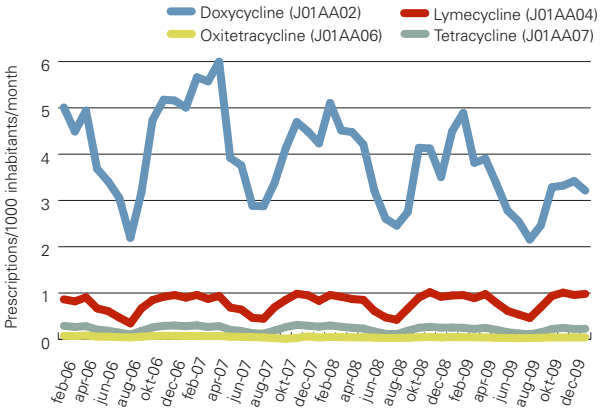

FIGURE 3.1.7. Seasonal variation of tetracyclines, outpatient care 2006-2009, prescriptions /1000 inhabitants/ month.

Sales of tetracyclines measured as prescriptions and DDDs decreased by 11% and 6% respectively in outpatient care in 2009. This indicates an increasing fraction of prescription with a larger number of DDDs. The reduction encompasses all age groups measured as prescriptions per 1000 inhabitants while measured as DDDs per 1000 inhabitants an increase in teenagers is seen, Table 3.1.2.

Teenagers, 13-19 years, are the age group with the highest use of tetracyclines measured as DDD per prescription. This is probably due to treatment of acne for which long-term treatment often is prescribed. The number of prescriptions of tetracyclines per 1000 teenagers range from 60 in Uppsala to 38 in Gotland. The diversity seems mostly relate to the substances commonly used to treat acne, Figure 3.1.8.

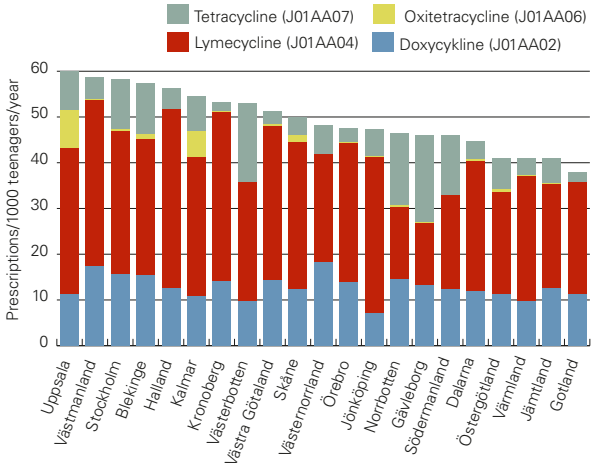

FIGURE 3.1.8. Tetracyclines in outpatient care per county, Prescriptions/1000 teenagers, 13 – 19 years/year.

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 commonly prescribed antibiotics. Among these substances we also find the greatest difference within the country in terms of number of prescriptions. The number of prescription range from 258 per 1000 inhabitants in Stockholm to 146 per 1000 inhabitants in Västerbotten, Figure 3.1.9.

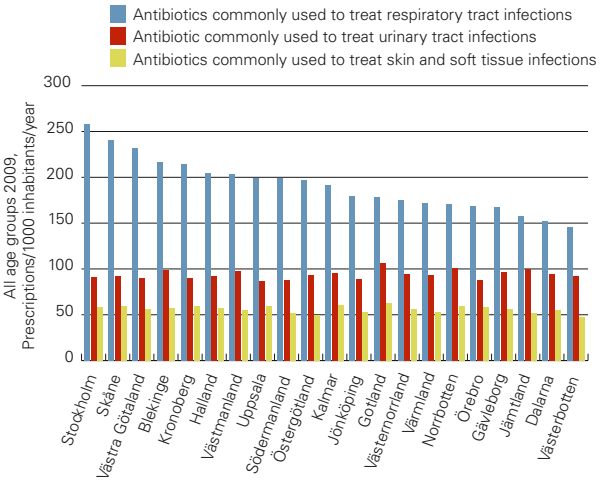

FIGURE 3.1.9. Antibiotics commonly used to treat respiratory tract infections (J01AA02, J01CE02, J01CA04, J01CR02, J01DB-DE and J01FA), urinary tract infection (J01CA08, J01 EA01, J01MA02, J01MA06 and J01XE01) and skin and soft tissue infections (J01FF01 and J01CF05) in outpatient care 2009, per county. Both sexes, all ages, prescriptions/1000 inhabitants/year.

New recommendations, launched by Strama and The Swedish Medicinal Products Agency in 2007, recommend pivmecillinam and nitrofurantoin over trimethoprim and prescribers are encouraged to minimize the use of fluoroquinolones for the treatment of lower urinary tract infections in women over 18 years. Sales of antibiotics commonly used to treat lower urinary tract infection have decreased every year since 2006. Nitrofurantoin and pivmecillinam are both recommended first-line drugs for the treatment of lower urinary tract infection in women and accounts for nearly 70% of antibiotics commonly used to treat lower urinary tract infections in women. Pivmecillinam is prescribed almost twice as often as nitrofurantoin.

In all, prescription of nitrofurantoin to women increased by 37% in 2009, while the number of DDDs only increased by 11%, Table 3.1.2. This can be explained by the introduction of a new package of nitrofurantoin containing fewer tablets in accordance to latest clinical guidelines for the treatment of lower urinary tract infections in women.

At the same time as the use of pivmecillinam and nitrofurantoin has increased the use of trimetoprim and fluoroquinolones has decreased drastically during the latest years, Figure 3.1.10.

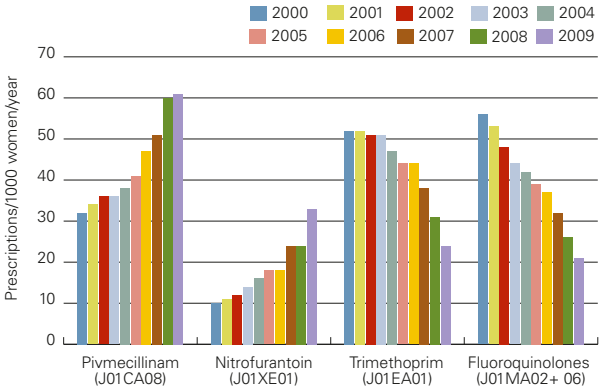

FIGURE 3.1.10. Antibiotics commonly used to treat lower urinary tract infections in women, 2000-2009, prescriptions/ 1000 women /year. County and municipalities data.s

County and municipality data

The fraction of people treated with any kind of antibiotic (users per 1000 inhabitants) has decreased by 6% in 2009, Table 3.1.2. However, the fraction of people treated with antibiotics varies within Sweden, from 255 users per 1000 inhabitants in Stockholm to 181 users per 1000 inhabitants in Västerbotten, Figure 3.1.11. A comparison of age and gender standardized sales data from the counties shows that the use is highest in the big cities and their surroundings.

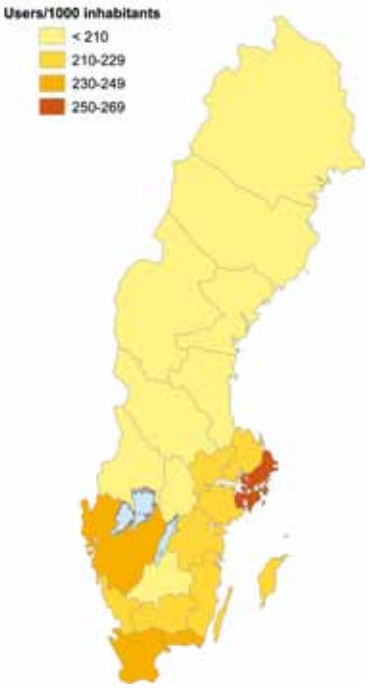

FIGURE 3.1.11. Fraction of people treated with at least one course of antibiotics (J01 excl. methenamine) in 2009, users/1000 inhabitants.

There are 290 municipalities in Sweden and Figure 3.1.12 presents the ten municipalities with the highest prescription of antibiotics and the ten with the lowest, in all age groups, in outpatient care 2009. Analyses of antibiotic prescriptions at municipality level generate even more pronounced differences within the country than analyses at county level. The number of prescriptions per 1000 inhabitants range from 485 in Upplands Väsby to 270 in Robertfors. A comparison of age and gender standardized data at municipality level shows no big differences regarding ranking. However data at municipality level are more sensitive for variation in the population's composition because of the small denominator.

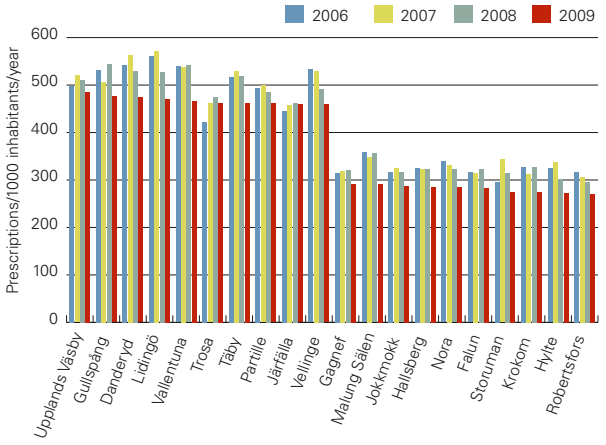

FIGURE 3.1.12. Swedish municipalities with highest and lowest prescription of antibiotics, age groups, in outpatient care 2009. Prescriptions/1000 inhabitants/year.

Antibiotic consumption in children

The fraction of children treated with any kind of antibiotic range from 342.3 users per 1000 children in Stockholm to 198.6 users per 1000 children in Jämtland, Figure 3.1.13. Taken together in Sweden the fraction of children treated with antibiotics was 298 users per 1000 children, which is 10% lower than in 2008, Table 3.1.2.

FIGURE 3.1.13. Fraction of children aged 0 to 6 years treated with at least one course of antibiotics (J01 excl. methenamine) in 2009, users/1000 children.

As seen in Table 3.1.3 prescriptions of antibiotics to children aged 0-6 years decreased with 17.2% in 2009. The great fall concerns all counties and all antibiotic groups except pivmecillinam, nitrofurantoin and lincosamides. Combinations of penicillins had the greatest decrease (27%) in number of prescriptions per 1000 children of all antibiotic groups, Table 3.1.2.

Different kinds of penicillins are the most commonly prescribed antibiotics. Amoxicillin-clavulanate, amoxicillin and penicillin V represent 75% of all antibiotics to children aged 0-6 years in outpatient care 2009.

Consumption of antibiotic to children varies greatly within the country. The number of prescriptions range from 606 prescriptions per 1000 children in Stockholm to 297 prescriptions per 1000 children in Jämtland, Figure 3.1.14. Even counties with the lowest numbers of prescriptions decreased to a great extent in 2009.

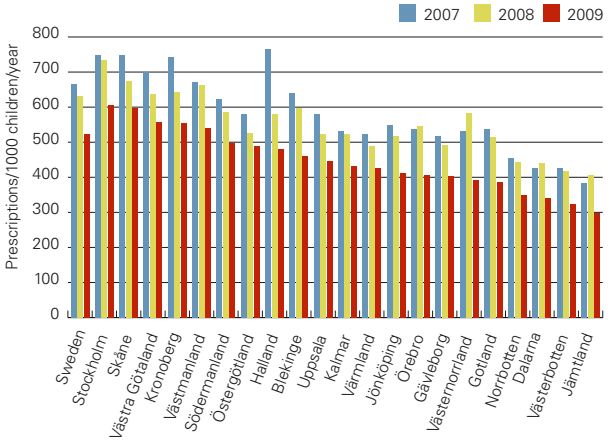

FIGURE 3.1.14. Antibiotics in outpatient care to children aged 0-6 years, per county 2007-2009. Prescriptions/1000 children/year.

Antibiotic use in children has been in focus of Strama's information activities the last year. The great reduction in sales of antibiotics may have several explanations. Hand hygiene has been the subject of many campaigns during 2009. One study has shown that using alcohol-based hand disinfection in preschools reduces absence from Swedish day care centers with 12%. Social insurance office reported a 7% less parental leave measured as days of parental leave per children aged 1-6 years in 2009. This may indicate fewer infections in children.

Dentists

Dentists account for approximately 20% of all antibiotic prescribing in outpatient care. After several years of increase, the prescription of antibiotics by dentists decreased by 7% in 2009. Penicillin V is the most commonly prescribed antibiotic and represents 80% of all antibiotics prescribed by dentists. Lincosamides is the antibiotic showing the highest increase last years, from 1 prescription/1000 inhabitants and year in 2000 to nearly 3 prescriptions/1000 inhabitants and year in 2009.

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Hospital care

As reported in earlier issues of Swedres, a more reasonable use of broad spectrum antibiotics has been one of Strama's objectives for a long time. The communication of this issue has been intensified in 2009 in accordance with the action plan to prevent ESBL resistance in enteric bacteria (see section 4). Penicillin V (J01CE02) is recommended by The Swedish Society of Infectious Diseases as first hand choice in community-acquired pneumonia and the Swedish Reference Group for Antibiotics has published a list of "substitutional" antibiotics to be used instead of cefuroxime which has been extensively used for a variety of indications.

The considerable decrease in the use of cephalosporins in

TABLE 3.1.2. Antibiotics in outpatient care, classes of antibiotics and age groups. DDD/1000 inhabitants/day and prescriptions/1000 inhabitants/year. 2004-2009. Users/1000 inhabitants/year.

Age group (years)	DDD/1000/day						Prescriptions/1000/year						Users/1000/year			
	2004	2005	2006	2007	2008	2009	2004	2005	2006	2007	2008	2009	2006	2007	2008	2009
Tetracyclines (J01AA)																
0-6	0.00	0.00	0.00	0.00	0.00	0.00	0.1	0.1	0.1	0.0	0.0	0.0	0.1	0.0	0.02	0.01
7-19	2.36	2.71	3.12	3.23	3.26	3.31	25.4	28.9	32.7	33.9	32.0	31.6	20.4	21.5	19.64	19.16
20-59	3.36	3.52	3.56	3.68	3.50	3.26	62.9	67.2	66.3	68.3	61.3	53.7	51.8	53.4	47.61	41.72
60-79	3.90	4.15	4.11	4.29	4.05	3.64	91.7	99.7	96.3	99.3	90.1	78.3	71.6	74.4	67.18	60.08
80 -	2.83	3.04	2.89	2.93	2.78	2.43	75.8	82.6	76.4	77.8	71.7	62.2	60.1	62.0	56.83	49.69
All age groups	3.06	3.26	3.33	3.44	3.29	3.08	58.6	63.2	62.6	64.3	58.3	51.7	46.9	48.6	43.7	38.82
Penicillins with extended spectrum (J01CA) excl. pivmecillinam																
0-6	1.25	1.41	1.59	1.74	1.71	1.52	84.7	85.0	86.9	95.2	90.8	72.7	64.6	70.5	66.74	56.31
7-19	0.32	0.38	0.45	0.46	0.43	0.39	10.8	12.5	14.1	14.5	13.6	11.8	12.4	12.8	11.54	10.08
20-59	0.64	0.72	0.72	0.77	0.75	0.66	16.8	18.3	18.4	19.4	18.7	16.5	16.0	16.7	15.1	14.15
60-79	1.43	1.56	1.59	1.62	1.63	1.52	39.3	41.2	41.4	42.0	41.3	37.9	32.3	32.9	29.9	30.05
80 -	1.65	1.80	1.81	1.79	1.83	1.76	45.3	47.5	47.3	46.8	46.5	44.0	38.3	38.0	32.87	35.39
All age groups	0.84	0.94	0.98	1.02	1.02	0.93	27.4	29.0	29.6	31.0	30.5	26.9	23.4	24.5	22.47	21.08
Pivmecillinam (J01CA08)																
0-6	0.01	0.01	0.01	0.01	0.01	0.01	0.3	0.4	0.5	0.5	0.7	0.8	0.4	0.5	0.61	0.74
7-19	0.14	0.15	0.17	0.19	0.24	0.24	7.4	8.7	10.7	12.4	15.5	16.1	9.6	11.0	13.58	13.89
20-59	0.32	0.31	0.34	0.36	0.43	0.44	15.4	16.9	20.1	22.2	26.9	27.3	17.3	19.0	22.52	22.99
60-79	0.72	0.70	0.71	0.74	0.84	0.85	33.4	36.2	40.3	43.0	49.5	49.9	31.2	33.1	37.3	38.09
80 -	2.05	1.90	1.84	1.84	1.95	1.92	97.4	100.0	106.7	109.3	116.6	115.8	80.1	81.8	85.14	83.94
All age groups	0.43	0.42	0.43	0.46	0.53	0.54	20.5	22.3	25.5	27.6	32.2	32.8	20.7	22.3	25.56	25.95
Beta-lactamase sensitive penicililns (J01CE)																
0-6	3.32	3.35	3.59	4.03	4.14	3.56	307.9	310.5	327.3	350.7	343.7	287.4	230.8	244.3	235.92	210.74
7-19	2.92	3.01	3.38	3.68	3.64	3.46	120.6	121.5	135.0	142.5	135.0	123.3	113.1	117.3	110.21	100.69
20-59	4.16	4.18	4.28	4.49	4.42	4.00	105.5	105.2	107.9	112.8	108.4	97.7	91.6	95.2	90.86	83.75
60-79	4.33	4.27	4.46	4.57	4.51	4.25	104.8	102.9	107.0	109.0	106.1	99.6	88.0	89.4	86.95	84.50
80 -	3.32	3.39	3.33	3.36	3.51	3.38	86.8	87.1	84.2	84.2	85.7	81.7	71.4	72.2	72.39	69.91
All age groups	3.90	3.92	4.09	4.30	4.26	3.96	122.6	122.5	128.1	134.3	130.0	118.6	104.0	108.1	103.74	95.96
Beta-lactamase resistant penicillins (J01CF)																
0-6	0.33	0.31	0.35	0.33	0.33	0.31	34.3	32.2	35.6	32.9	32.8	30.8	26.7	25.2	24.82	24.22
7-19	0.67	0.65	0.70	0.69	0.80	0.79	32.0	30.7	33.6	31.9	31.9	31.2	27.5	26.4	26.2	25.36
20-59	0.88	0.88	0.95	0.96	1.14	1.13	31.7	31.7	33.5	33.3	33.2	32.6	26.9	26.7	26.45	26.24
60-79	1.94	1.91	2.04	2.04	2.37	2.29	54.5	54.4	57.4	56.3	56.9	55.0	37.7	37.1	37.31	37.05
80 -	4.47	4.38	4.44	4.40	5.01	4.92	124.2	122.0	123.4	122.6	122.1	119.4	68.7	67.9	66.75	65.46
All age groups	1.18	1.18	1.25	1.25	1.46	1.45	40.9	40.5	42.9	42.2	42.3	41.7	31.2	30.7	30.52	30.11
Combinations of penicillins (J01CR)																
0-6	0.68	0.73	0.73	0.75	0.67	0.52	48.5	51.8	51.2	52.7	46.4	33.7	34.4	35.2	30.89	24.00
7-19	0.17	0.20	0.22	0.21	0.20	0.18	5.1	6.0	6.4	6.4	6.0	5.4	5.1	4.9	4.54	4.07
20-59	0.15	0.17	0.18	0.20	0.21	0.20	3.3	3.8	3.9	4.4	4.6	4.3	3.5	3.9	4	3.70
60-79	0.17	0.20	0.22	0.25	0.27	0.28	3.5	4.2	4.5	5.1	5.5	5.7	3.6	4.1	4.38	4.57
80 -	0.11	0.15	0.15	0.17	0.20	0.22	2.4	3.0	3.0	3.4	4.1	4.3	2.3	2.7	3.21	3.40
All age groups	0.19	0.22	0.24	0.26	0.26	0.24	6.9	7.8	8.0	8.5	8.3	7.2	6.1	6.5	6.26	5.53
Cephalosporins (J01DB-DE)																
0-6	0.53	0.50	0.52	0.52	0.46	0.36	49.7	46.4	49.0	49.7	43.6	34.1	37.6	38.0	33.86	28.12
7-19	0.30	0.29	0.30	0.29	0.27	0.21	20.9	19.6	20.6	20.2	18.4	14.9	17.4	17.2	15.71	12.64
20-59	0.30	0.30	0.29	0.28	0.25	0.20	16.9	16.6	16.8	16.2	14.5	11.4	14.2	13.7	12.2	9.77
60-79	0.48	0.47	0.46	0.40	0.36	0.29	23.6	23.1	22.6	20.2	17.7	13.8	17.1	15.5	13.49	10.66
80 -	0.79	0.77	0.73	0.65	0.54	0.41	42.6	42.3	40.5	35.4	29.4	22.7	30.9	27.4	22.86	17.88
All age groups	0.40	0.38	0.37	0.35	0.31	0.25	23.4	22.5	22.5	21.5	19.0	15.2	17.9	17.2	15.3	12.29

Age group (years)	DDD/1000/day						Prescriptions/1000/year						Users/1000/year			
	2004	2005	2006	2007	2008	2009	2004	2005	2006	2007	2008	2009	2006	2007	2008	2009
Trimethoprim (J01EA)																
0-6	0.12	0.11	0.12	0.12	0.10	0.09	15.6	14.8	16.0	15.4	14.0	12.6	11.1	10.6	9.82	9.67
7-19	0.21	0.20	0.21	0.18	0.15	0.11	12.4	11.9	12.4	10.9	8.9	7.0	10.8	9.5	7.75	6.02
20-59	0.36	0.33	0.33	0.29	0.24	0.18	18.7	17.3	17.4	14.6	11.8	8.7	14.7	12.4	9.89	7.25
60-79	0.92	0.86	0.84	0.76	0.64	0.52	44.6	41.7	40.7	35.2	29.2	23.1	29.7	25.6	20.97	16.65
80 -	2.48	2.28	2.19	1.91	1.58	1.30	136.0	125.6	120.1	104.5	84.7	69.6	73.3	61.6	49.08	38.59
All age groups	0.53	0.49	0.49	0.43	0.36	0.29	28.2	26.4	26.3	22.8	18.8	14.9	19.8	16.9	13.77	10.73
Trimetoprim with sulphonamides (J01EE)																
0-6	0.15	0.15	0.16	0.16	0.14	0.13	18.4	18.1	18.1	18.8	16.7	14.8	13.2	13.5	12.03	10.70
7-19	0.09	0.10	0.10	0.10	0.11	0.11	4.0	4.1	4.0	4.1	4.2	4.3	2.7	2.6	2.65	2.55
20-59	0.12	0.12	0.13	0.14	0.14	0.15	2.7	2.8	2.9	3.0	3.1	3.3	1.9	1.9	2.02	2.12
60-79	0.33	0.34	0.36	0.39	0.44	0.47	8.2	8.4	8.8	9.2	10.1	10.4	5.8	6.1	6.75	7.13
80 -	0.35	0.34	0.36	0.39	0.43	0.43	11.8	11.5	11.7	12.2	13.1	12.5	8.8	9.1	9.91	9.72
All age groups	0.18	0.18	0.19	0.20	0.21	0.22	6.2	6.2	6.3	6.4	6.5	6.6	4.0	4.1	4.25	4.25
Macrolides (J01FA)																
0-6	0.73	0.80	0.80	0.85	0.68	0.51	34.5	37.4	37.3	38.1	29.9	22.4	29.6	30.4	23.28	18.09
7-19	0.62	0.72	0.76	0.74	0.54	0.45	18.1	21.0	22.1	21.7	15.4	12.7	17.9	17.2	11.82	9.70
20-59	0.54	0.56	0.54	0.55	0.49	0.42	16.3	16.8	16.3	16.5	14.3	12.1	13.0	13.2	11.3	9.61
60-79	0.49	0.51	0.50	0.50	0.47	0.42	14.1	14.8	14.5	14.6	13.0	11.3	11.0	11.0	9.58	8.41
80 -	0.31	0.34	0.34	0.32	0.30	0.29	9.7	9.8	9.3	8.7	8.4	7.4	7.2	6.8	6.35	5.46
All age groups	0.55	0.59	0.58	0.59	0.50	0.43	17.3	18.4	18.2	18.4	15.3	12.8	14.4	14.4	11.74	9.85
Lincosamides (J01FF)																
0-6	0.02	0.02	0.02	0.03	0.02	0.02	4.1	4.5	5.0	5.3	5.0	5.2	3.6	3.9	3.67	3.84
7-19	0.09	0.10	0.11	0.12	0.12	0.12	6.5	6.9	7.8	8.3	8.4	8.2	6.2	6.7	6.85	6.57
20-59	0.24	0.25	0.28	0.29	0.30	0.29	12.6	13.0	14.3	15.6	15.6	15.0	11.1	12.2	12.21	12.00
60-79	0.51	0.53	0.55	0.55	0.57	0.57	21.1	22.1	23.7	24.4	24.6	23.8	15.3	15.9	16.26	16.40
80 -	0.71	0.77	0.75	0.74	0.76	0.72	30.0	32.2	32.6	32.8	33.2	31.0	18.1	18.6	19.21	18.79
All age groups	0.27	0.29	0.31	0.32	0.33	0.32	13.5	14.1	15.4	16.3	16.4	15.9	10.9	11.7	11.85	11.71
Fluoroquinolones (J01MA)																
0-6	0.01	0.02	0.01	0.01	0.01	0.01	0.4	0.8	0.8	0.8	0.7	0.7	0.4	0.4	0.39	0.36
7-19	0.12	0.12	0.12	0.13	0.12	0.12	5.5	5.5	5.5	5.5	4.8	4.3	4.7	4.4	3.85	3.51
20-59	0.81	0.81	0.80	0.76	0.69	0.63	33.1	31.9	30.2	27.8	23.8	20.9	22.0	20.3	17.33	15.43
60-79	2.07	2.08	2.05	1.93	1.75	1.67	88.0	84.6	80.2	73.7	63.9	58.6	52.7	48.7	42.73	40.22
80 -	3.14	3.13	3.00	2.74	2.41	2.25	158.4	149.4	136.8	119.7	98.5	88.2	92.5	81.5	68.14	61.43
All age groups	0.98	0.99	0.98	0.93	0.84	0.80	42.5	41.0	39.0	35.7	30.6	27.8	27.0	24.9	21.47	19.59
Nitrofurantoin (J01XE)																
0-6	0.07	0.07	0.07	0.07	0.06	0.06	6.9	6.4	6.3	6.3	6.2	6.9	4.2	4.2	4.15	4.93
7-19	0.11	0.12	0.12	0.14	0.13	0.15	4.9	5.3	5.2	6.7	6.6	9.2	4.4	5.8	5.78	7.89
20-59	0.17	0.19	0.20	0.24	0.23	0.26	7.4	8.5	8.5	11.0	10.6	14.7	7.0	9.1	8.84	12.16
60-79	0.29	0.34	0.36	0.46	0.47	0.53	11.7	14.1	14.6	19.4	20.6	28.1	10.7	14.3	15.19	20.82
80 -	0.68	0.78	0.78	0.97	0.95	1.05	31.0	36.5	37.2	46.7	47.7	61.7	24.0	30.3	31.17	40.29
All age groups	0.20	0.23	0.24	0.30	0.29	0.32	9.0	10.3	10.5	13.5	13.6	18.5	8.0	10.3	10.4	14.08
All agents (J01 excl. methenamine)																
0-6	7.23	7.49	7.98	8.62	8.34	7.12	605.9	608.8	634.7	666.8	630.8	522.4	335.6	348.5	330.34	298.02
7-19	8.13	8.76	9.79	10.18	10.02	9.66	274.1	283.4	311.1	319.8	301.4	280.8	204.5	208.1	195.83	182.14
20-59	12.09	12.37	12.63	13.04	12.82	11.84	344.2	350.9	357.6	366.1	348.0	318.9	223.9	228.7	217.78	204.07
60-79	17.66	18.02	18.34	18.58	18.46	17.37	541.0	550.0	554.5	553.7	531.0	497.7	288.8	289.6	279.04	269.55
80 -	23.01	23.20	22.74	22.33	22.37	21.18	856.3	854.2	833.3	807.9	765.1	723.5	379.4	372.5	356.15	340.11
All age groups	12.77	13.13	13.51	13.87	13.70	12.88	418.2	425.6	436.1	443.8	423.1	391.9	249.8	254.1	242.53	228.02

Strama's prescribing goal in outpatient care

OF ALL ANTIBIOTIC SALES 90 percent is prescribed in outpatient care including primary care, open specialist surgeries, dentists and parts of nursing homes. There is no medical reason to the wide regional variations in the use of antibiotics that are seen within the country. National studies show that antibiotic prescribing not always is done according to guidelines. Given the rapid and serious development of antibioticresistance Strama has proposed three goals for antibiotic use in outpatient care. The aim is to preserve the relatively favorable resistance situation in Sweden as long as possible.

Find more information about Stramas prescribing goals in outpatient care at Stramas webpage www.strama.se

The total number of antibiotic prescriptions in Sweden

Stramas prescribing goal at 250 prescriptions /1000 inhabitants and year is mainly estimated from an analysis of electronic patient records of visits for respiratory tract infections in primary care in Kalmar County. All patients diagnosed with respiratory tract infections between the year 2000 and 2005 were included. In addition, electronic patient records from 21 Health centres covering all visits diagnosed as an infection (respiratory tract infections, urinary tract infections and skin- and soft tissue infections) between the year 2007 and 2009 has been analysed (unpublished data). The management of all patient visits was compared to current indications for antibiotic treatment according to national recommendations.

In primary care, respiratory tract infections stands for approximately 60%, urinary tract infections 20% and skin- and soft tissue infections 15% of all antibiotic prescriptions. Since GPs prescribe approximately 60% of all prescriptions in outpatient care in Sweden, the number of prescriptions that should cover the need of antibiotic treatment according to current recommendations in outpatient care was estimated to be approximately 250 prescriptions/1000 inhabitants and year.

The total number of antibiotic prescriptions in Sweden shouldn't exceed 250 prescriptions per 1000 inhabitants and year by 2015. The goal includes all antibiotics for systemic use excluding methenamine (J01 excl. J01XX05). The goal cannot however be applied by a single care unit but it can provide a measure at the county level.

Calculations based on recent Swedish epidemiological data show that if common infections in outpatient care were treated according to current guidelines, the long-term overall national level of consumption could be 250 antibiotic prescriptions/1000 inhabitants and year. This level of prescribing of antibiotics in outpatient care is currently existing in the Netherlands. However, it is important to emphasize that still all patients benefiting from antibiotics should be treated according to current guidelines.

In 2009 the average use of antibiotics in outpatient care in Sweden was 392 prescriptions per 1000 inhabitants. Still, there are great regional differences within the country. Prescriptions per 1000 inhabitants range from 430 in Stockholm to 311 in Västerbotten. The use of antibiotics decreased in all counties in 2009, Figure 3.1.15.

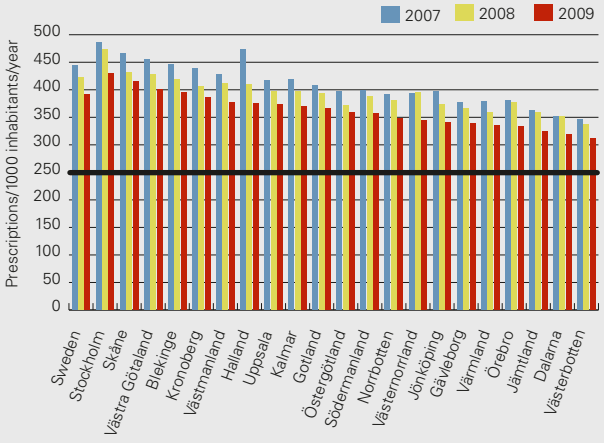

FIGURE 3.1.15 Sales of antibiotics in outpatient care 2007-2009, prescriptions/1000 inhabitants. The red line indicates the desired level for prescriptions in Sweden according to Strama of 250 prescriptions/1000 inhabitants in outpaitent care.

Further more Stramas' target is that:

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 (J01CE 02) and the denominator is amoxicillin (J01CA04), penicillin V (J01CE02), amoxicillin-clavulanate (J01CR02), cephalosporins (J01DB-DE) and macrolides (J01FA). This qualityindicator is also used by The National Board of Health and Welfare and the SALAR in their annual benchmarking of medical treatments and procedures.

In 2009 the proportion of penicillin V of antibiotics commonly used to treat respiratory tract infections in children aged 0-6 years was 64% on a country level and the proportion of penicillin V increased in the majority of all counties. Värmland had the greatest proportion, 78%, and Stockholm the lowest, 58%, Figure 3.1.16.

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

The total number of prescriptions of antibiotics commonly used to treat urinary tract infections in women 18-79 years was decreased by 1% in 2009 while the prescription of fluorquinolones decreased by 18%.

In Sweden the average proportion of fluorquinolones was 16.5% in 2009. Kronoberg was the county with the highest proportion (19.4%) and Jämtland was the county with lowest proportion (13,1%), Figure 3.1.17.

The Swedish Association for General Medicine (SFAM) has developed quality indicators. These indicators are primarily intended as tools for the individual physician or clinic/family

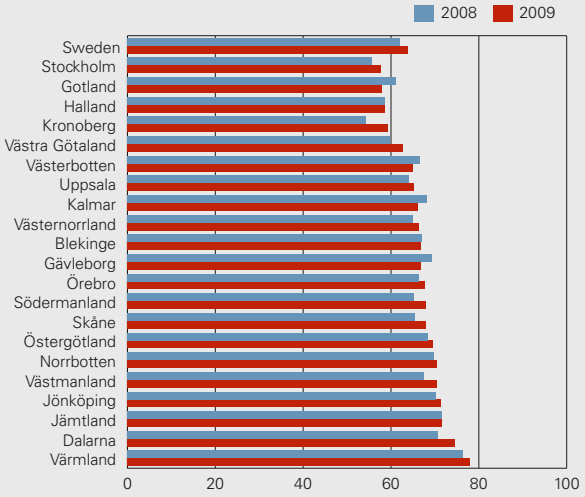

FIGURE 3.1.16. Proportion penicillin V of antibiotics commonly used to treat respiratory tract infections* in children aged 0-6 years, per county. Prescriptions in outpatient care. The red line indicates the relative goal for prescription of penicillins in outpatient care according to Strama. *Amoxicillin (J01CA04), penicillin V (J01CE02), amoxicilli-clavulate (J01CR02), macrolides (J01FA) and cephalosporins (J01DB-DE).

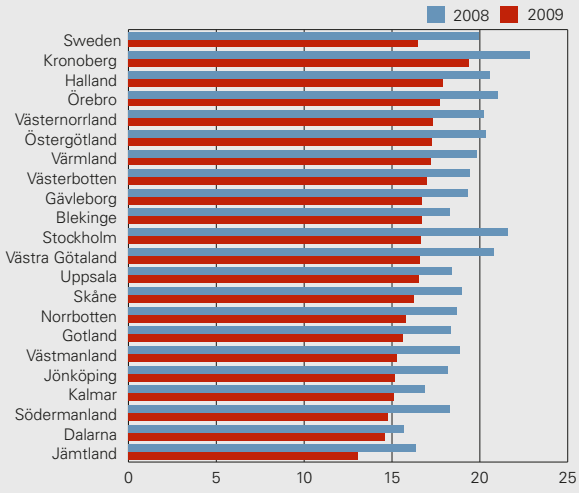

FIGURE 3.1.17. Proportion of fluoroquinolones of commonly used antibiotics in treatment of urinary tract infections* in women aged 18-79 years, per county in outpatient care. The red line indicates the maximum proportion of fluoroquinolones on 10% according to the Strama goals in outpatient care. * Fluoroquinolones (J01MA02+06), pivmecillinam (J01CA08), nitrofurantoin (J01XE01), trimethoprim (J01EA01).

doctors to review their own prescribing. One of these indicators is proportion of fluorquinolones and cephalosporins of antibiotics commonly used to treat lower urinary tract infections in women aged 18 years or older.

Of great importance when promoting a reduced use of antibiotics is to ensure that this does not bring about increased morbidity. Figure 3.1.18 shows the prevalence of pneumonia in relation to antibiotic prescribing in outpatient care and figure 3.1.19 shows the number of children with mastoiditis in Sweden 1987-2008. Despite the great decrease in antibiotic sales the last years, complications in bacterial infections have not increased attributable to less antibiotic treatment. No correlation between the decreasing use of antibiotics and the prevalence of pneumonia is seen.

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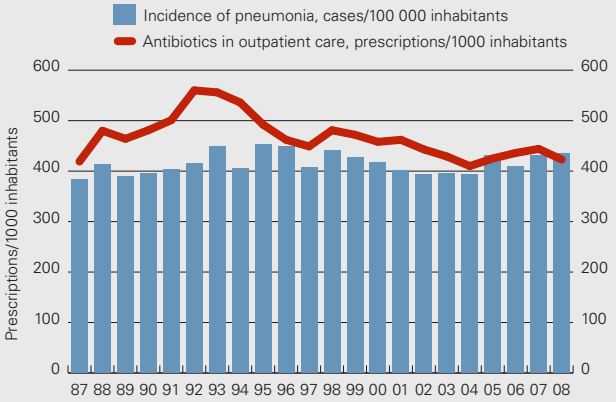


FIGURE 3.1.16. Proportion penicillin V of antibiotics commonly used to treat respiratory tract infections* in children aged 0-6 years, per county. Prescriptions in outpatient care. The red line indicates the relative goal for prescription of penicillins in outpatient care according to Strama. *Amoxicillin (J01CA04), penicillin V (J01CE02), amoxicilli-clavulate (J01CR02), macrolides (J01FA) and cephalosporins (J01DB-DE).

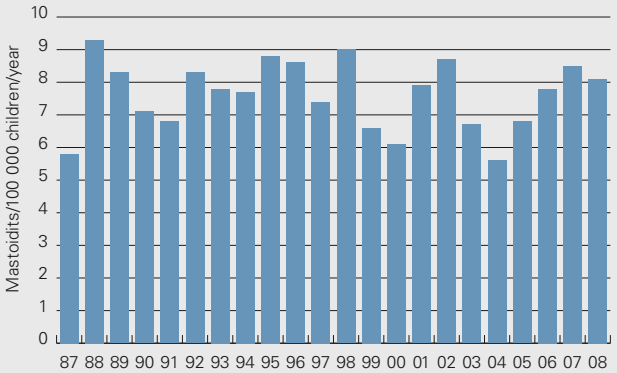


FIGURE 3.1.19. Hospitals admissions for mastoiditis in children aged 0-6 years, 1987-2008. Data from the national registry of diagnosis in hospital care.

the recent years seems to continue also in 2009, Figure 3.1.22. Initially, the decrease was partly explained by a shift from cefuroxime to cefotaxime. The latter has a lower prescribed daily dose in Sweden that is lower than WHO´s DDD, so comparison of DDDs showed a too large decrease in use. From 2007 to 2009 the sales of second generation cephalosporins, of which more than 90% was cefuroxime, decreased by 66%. Sales of third generation cephalosporins, mainly cefotaxime and ceftazidime, increased by 87% in the same period. Taken together, the overall decrease in DDDs for cephalosporins indicates that these substances are actually replaced by other antibiotics.

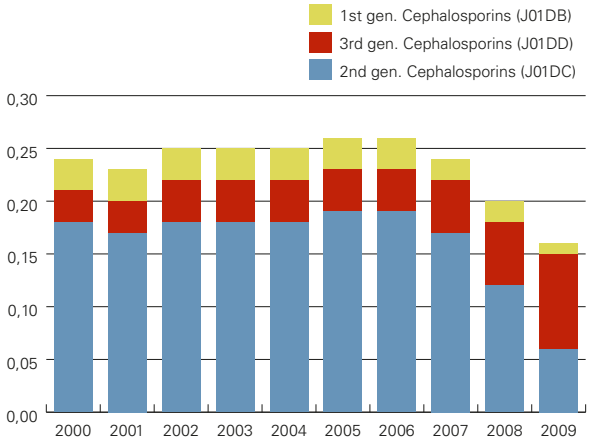


FIGURE 3.1.22. Cephalosporins to all patients, hospital care, DDD/1000 inhabitants/day 2000-2009.

As mentioned initially in this chapter, the analysis and interpretation of data regarding antibiotics to inpatients is complicated by the fact that these numbers reflect not only hospitals but also other types of caregivers, mainly nursing homes. This brings about several problems in the comparison of data regarding substances as well as between geographical regions and trends over time, Figure 3.1.23. shows the diversity within Sweden. The magnitude of the error of course varies between substance groups; certain antibiotics used in advanced medical care tend to be falsely low whereas antibiotics commonly used to treat lower urinary tract infections are falsely high. On the national level, the proportion of inpatient antibiotics actually used in hospitals is about 75%, and has been so for the last four years.

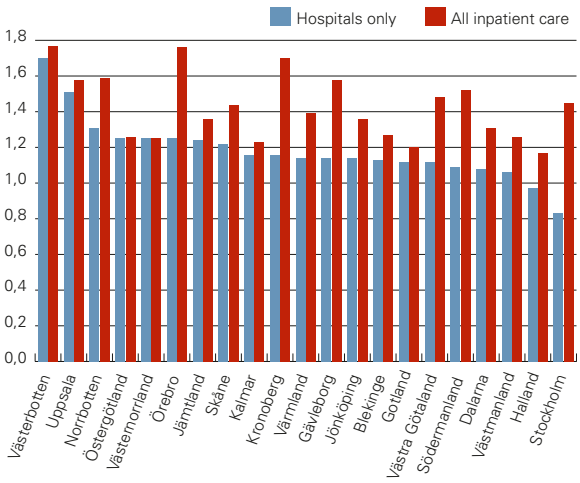


FIGURE 3.1.23. Antibiotic use in hospitals and in all inpatient care in the counties, DDD/1000 inhabitants and day 2009.

Despite the fact that several counties did initiate stock-piling of certain antibiotics to meet increased needs due to severe outbreaks of influenza, the overall sales of antibiotics to hospital care decreased a little between 2008 and 2009. Due to the recent rapid decrease (17% between 2007 and 2008, 21% between 2008 and 2009) in use of cephalosporins, the betalactamase-resistant penicillins (J01CF) are now the largest group of antibiotics in hospital care, Figure 3.1.24. This substance is largely used as prophylaxis before surgery. Another class of broad spectrum antibiotics, the fluoroquinolones (J01MA), is also decreasing in accordance with recommendations. Piperacillin with tazobactam still represents a small proportion of antibiotic use in hospitals, but it is increasing rapidly. Sales have increased by between 25 and 30 percent each year since 2006.

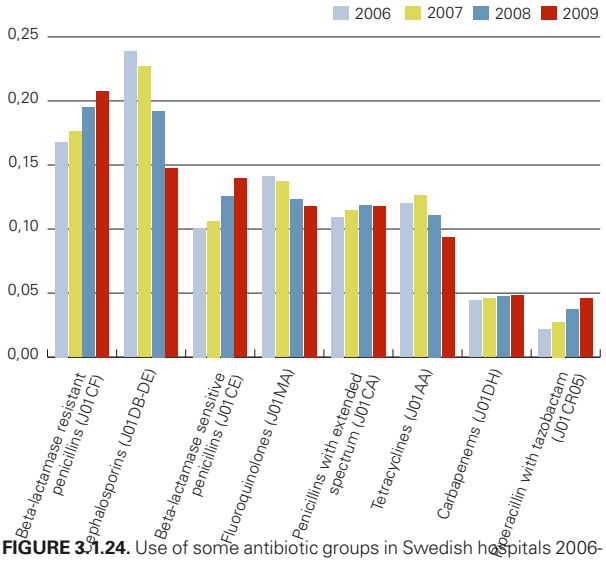


FIGURE 3.1.24. Use of some antibiotic groups in Swedish hospitals 2006-2009, DDD/1000 inhabitants and day.

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 J01CR, penicillins with enzyme inhibitors, has more than doubled over these four years. Around 80% of this group constitutes of piperacillin with tazobactam, the rest is amoxicillin with clavulanate. The increasing use of betalactamase sensitive penicillins is evident also with this denominator.

Taken together, the amount of antibiotics used per 100 patient-days or admissions to hospital remains quite stable since 2006 – the former increase by six percent and the latter decrease by three percent, Table 3.1.4 and 5. The major changes in antibiotic use in hospital care seem to lie in the shifts between substances.

TABLE 3.1.4. DDD/100 patient-days in somatic medical care 2006-2009.

	2006	2007	2008	2009*
Tetracyclines (J01AA)	5,5	5,7	5,5	4,7
Penicillins with extended spectrum (J01CA)	5,0	5,2	5,8	5,9
Betalactamase sensitive penicillins (J01CE)	4,6	4,8	6,2	6,9
Betalactamase resistant penicillins (J01CF)	7,7	8,0	9,6	10,3
Combinations of penicillins (J01CR)	1,3	1,6	2,3	2,8
Cephalosporins (J01DB-DE)	10,9	10,4	9,5	7,3
Carbapenems (J01DH)	2,0	2,1	2,3	2,4
Trimethoprim (J01EA)	1,3	1,2	1,2	1,0
Trimethoprim with sulphonamides (J01EE)	1,5	1,6	1,9	2,0
Macrolides (J01FA)	1,0	1,0	1,0	1,0
Lincosamides (J01FF)	1,5	1,5	1,7	1,7
Aminoglycosides (J01GB)	0,7	0,7	0,9	1,0
Fluoroquinolones (J01MA)	6,5	6,3	6,1	5,9
Glycopeptides (J01XA)	0,6	0,6	0,7	0,8
Imidazole derivatives (J01XD)	1,6	1,5	1,5	1,3
Methenamine (J01XX05)	0,9	0,9	0,8	0,7
Linezolid (J01XX08)	0,1	0,1	0,1	0,1
All agens (J01)	53,2	53,8	57,6	56,2

*Denominator data from 2008.

TABLE 3.1.5. DDD/100 admissions in somatic medical care 2006-2009.

	2006	2007	2008	2009*
Tetracyclines (J01AA)	28,8	29,9	26,5	22,5
Penicillins with extended spectrum (J01CA)	26,2	27,1	28,2	28,4
Betalactamase sensitive penicillins (J01CE)	24,2	25,2	30,0	33,5
Betalactamase resistant penicillins (J01CF)	40,3	41,8	46,4	49,9
Combinations of penicillins (J01CR)	6,7	8,2	11,0	13,6
Cephalosporins (J01DB-DE)	57,2	53,9	45,8	35,4
Carbapenems (J01DH)	10,6	10,8	11,3	11,6
Trimethoprim (J01EA)	6,7	6,3	5,8	4,8
Trimethoprim with sulphonamides (J01EE)	7,7	8,3	9,1	9,7
Macrolides (J01FA)	5,4	5,3	4,7	4,7
Lincosamides (J01FF)	7,8	8,0	8,2	8,0
Aminoglycosides (J01GB)	3,8	3,8	4,2	4,9
Fluoroquinolones (J01MA)	33,9	32,5	29,4	28,4
Glycopeptides (J01XA)	3,4	3,4	3,4	3,7
Imidazole derivatives (J01XD)	8,4	7,9	7,4	6,5
Methenamine (J01XX05)	4,7	4,5	3,8	3,2
Linezolid (J01XX08)	0,3	0,3	0,3	0,3
All agens (J01)	278,4	279,8	278,0	271,4

*Denominator data from 2008.

When comparing geographical regions, data on patient-days and admissions to hospital are subject to changes that are not easily retrieved and thus difficult to incorporate in the analysis. To minimize the risk for error caused by unreliable denominator data, the figures below display sales of certain substances as proportions of all antibiotics in hospital care in each county.

The proportion of broad and narrow spectrum antibiotics used in hospitals varies greatly between counties, as seen in Figures 3.1.25 and 3.1.26. Only 6% of systemic antibacterials in hospitals in Uppsala County are penicillins V or G, whereas in Värmland County these substances represent more than one-fifth. Less variation is seen in sales of one of the most common broad spectrum substances, the fluoroquinolones, which constitute between 9 and 14% of all antibiotics in the counties. After several years of decreasing use, the cephalosporins make up only six percent of antibiotics in Gotland, Södermanland and Västmanland Counties. In Gävleborg County the proportion is more than three times higher.

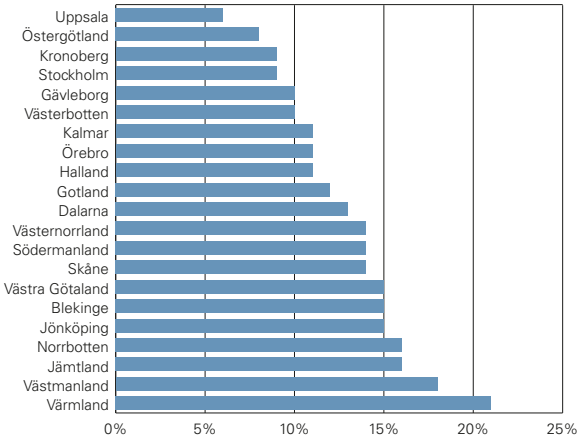


FIGURE 3.1.25. Percentage of narrow spectrum penicillins (penicillin V and G, J01CE) of all antibiotics in Swedish hospitals 2009, per county.

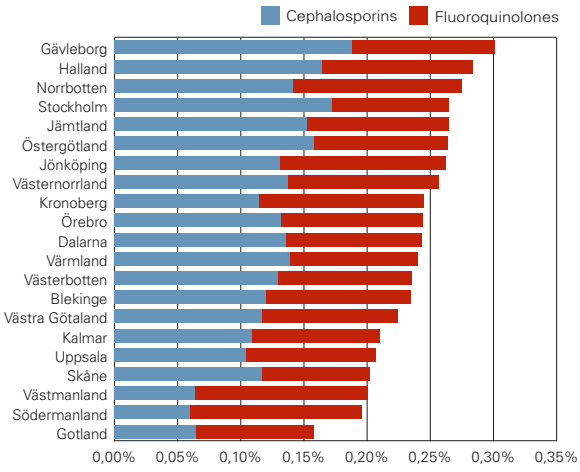
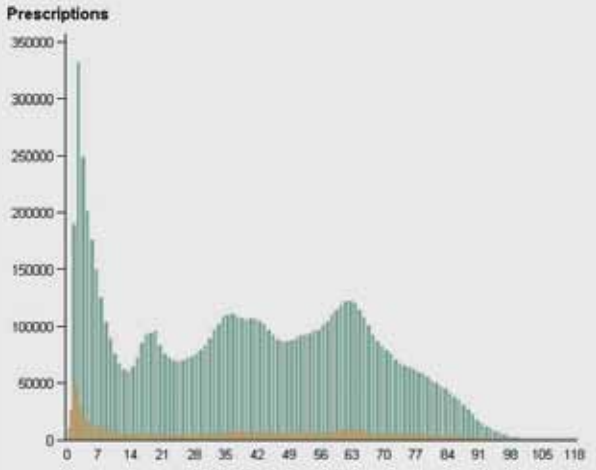


FIGURE 3.1.26. Percentage of broad spectrum antibiotics (cephalosporins, J01DB-DE and fluoroquinolones, J01MA) of all antibiotics in Swedish hospitals 2009, per county.

Respiratory tract infections – repeated courses in outpatient antibiotic use

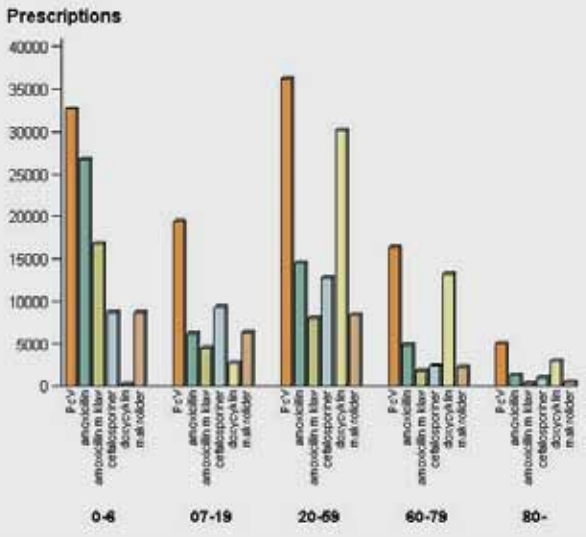
THE PURPOSE OF THIS STUDY was to investigate the treatment of respiratory tract infections and to what extent repeated treatments occur within two weeks. Data from the Swedish Prescribed Drug Register were analyzed with respect to 1) what kind of antibiotic that was used prior to a further purchase, 2), the choice of antibiotic in a supplementary purchase and 3) the time between purchases.

Children have the highest occurrence of prescription purchases of antibiotics used to treat respiratory tract infections and the largest fraction of repeated courses of antibiotics within 14 days. In the age group 0-6 years, the proportion of prescriptions with supplementary purchases for the same individual within 2 weeks is 10.3% of the total number of prescriptions on antibiotics used to treat respiratory tract infections (other age groups 5.4-6.6%).



FIGUR 3.1.20. Users treated with antibiotics used to treat respiratory tract infections in outpatient care during the period Sep 2005 – Aug 2009 versus patient age. The different colors indicate the prescriptions with no supplementary purchase for the same individual within 2 weeks (green) and the prescriptions followed by a further purchase within 2 weeks (brown). Antibiotics commonly used to treat respiratory tract infections (Strama): Amoxicillin-clavulanate (J01CR02), cephalosporins (J01DB-DE), doxycycline (J01AA02), macrolides (J01FA), amoxicillin (J01CA04), penicillin V (J01CE02). As medical cause of drug therapy not is indicated in the register, some recipes for other indications than respiratory tract infections may be included.

Many prescriptions are followed by a new course of the same antibiotic within 14 days (46% of 583 049 prescriptions), Figure 3.1.20. Penicillin V is the most commonly prescribed respiratory tract antibiotic in ages below 60 years, more than half of the repeated purchases are made after penicillin V. The choice of antibiotic that follow after penicillin V varies among different age groups. Figure 3.1.21 illustrates the choice of antibiotic that follows after penicillin V.



FIGUR 3.1.21. The choice of new antibiotic within 2 weeks after penicillin V in different age groups. The bars show the contribution of each sort of antibiotic (all formulations) to the total number of prescriptions that follow after purchases of penicillin V in each age group.

The number of days between purchases within 2 weeks varies with the type of antibiotic that was preceding the new course and the age of the patient. After use of penicillin V in children aged 0-6 years, new purchases of antibiotics often occur after just one day. This pattern has remained unchanged for the last 4 years. Among the other age groups there is a more even spread of purchases over time.

A new course of antibiotics commonly used against respiratory tract antibiotic within a 14-days period may have many explanations including unsuitable formulation (oral suspension, tablets) or unappreciated taste by young children, allergy, relapsed infection or lack of effect (viral or mycoplasma etiology).

One tenth of the prescriptions for antibiotics commonly used to treat respiratory tract infections in young children is followed by a new course within 14 days. The key to improvement might be in the prescribing situation or at the pharmacy for example; advice on how to ease the intake, discuss formulation alternatives, motivate parents of young children, involve the child in drug therapy to ease intake, etc.

The reason why nearly half of all repeated prescriptions results in an additional recipe for a course of the same antibiotic must be further investigated in the ambition to reduce ineffective antibiotic therapy.

Pinelopi Lundquist, National Board on Health and Welfare

Trends in antibiotic use in Swedish Intensive Care Units (ICUs)

Eleven year (1999-2009) report from ICU-Strama and Swedish ICU registry

The ICU-Strama programme was developed eleven years ago and used for regular audit of antibiotic use, antibiotic resistance and infection control procedures in Swedish ICUs. It is a joint project between the Strama-ICU and the Swedish Intensive Care Registry. The purpose of this report is to provide a trend analysis of antibiotic consumption in Swedish ICUs. Regarding data collection see Apppendix 3.

Total antibiotic consumption in Swedish ICUs increased from 1216 DDD1000 1999 to 1425 DDD1000 2009 ($p<0.001$). Antibiotic consumption varied widely between different units during 2009, ranging between 680 and 2698 DDD1000 with a median of 1354 DDD1000. Trend analyses of usage of different classes of antibiotics were performed and showed increased consumption of aminoglycosides, betalactam sensitive penicillins, carbapenems, piperacillin-tazobactam, triazoles and vancomycin ($p<0.01$). There was no significant (ns) change in consumption of cephalosporins for the eleven year period but a trend towards decreased consumption the last three years. No significant correlations between antibiotic consumption and standardised mortality rates were shown for 2008 or 2009.

The four-fold variation in consumption between ICUs can be explained by different case mix, but there were also great variations between ICUs of the same type. The high antibiotic consumption concurs with figures from European and US ICUs in general, but like a few ICUs in our programme, relatively low antibiotic consumption has been reported from The Netherlands and Switzerland. The lower antibiotic consumption suggests that it is possible to reduce antibiotic consumption in the critically ill, but it has to be accompanied with a quality control system to make sure that it does not compromise patient outcomes. There was no significant correlation between antibiotic consumption and standardised mortality rates in our study.

Morgan Edström, Hans Gill, Sten Walther, Håkan Hanberger, ICU-Strama and the Swedish ICU registry

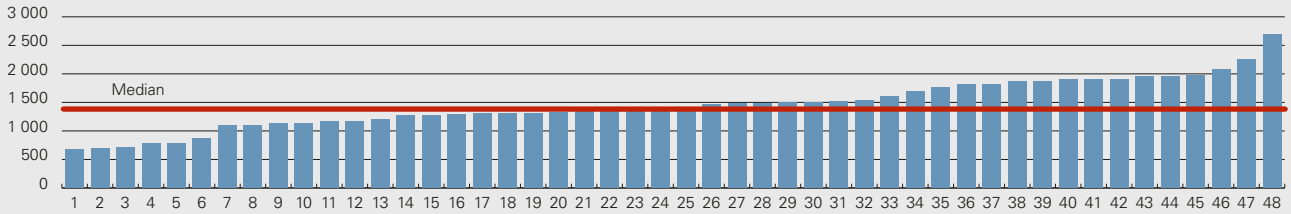


FIGURE 3.1.28. Antibiotic consumption in individual Swedish ICUs 2009

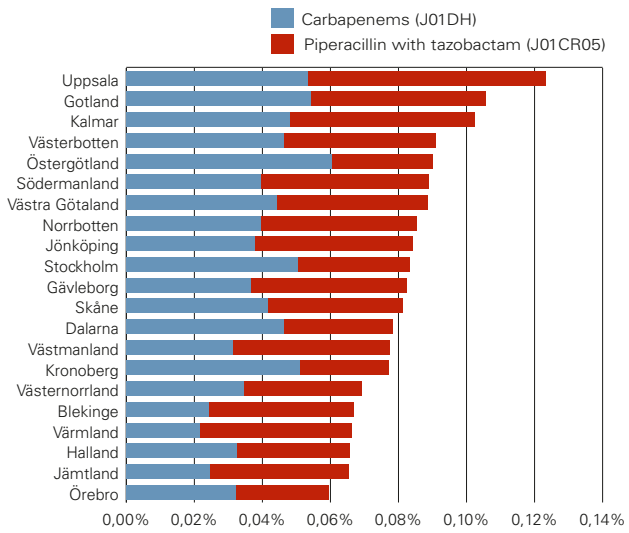


FIGURE 3.1.27. Percentage of carbapenems, J01DH, and piperacillin with tazobactam, J01CR05, of all antibiotics in Swedish hospitals 2009, per county.

As seen in Figure 3.1.27 newer broad spectrum antibiotics 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 over ten percent in others. The proportion of carbapenems of all antibiotics in hospitals varies threefold, from 2% in Jämtland, Värmland and Blekinge Counties to 6% in Östergötland County. Concerning piperacillin with tazobactam, sales vary from 3% in several counties to 7% in Uppsala County.

Ulrica Dohnhammar, Jenny Hellman

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, 2005–2009, were analysed for various groups of agents. The follow-

ing organ system groups received most reports related to the use of systemic antibiotic drugs (J01): skin- and subcutaneous tissue disorders (n=513), hepato-biliary disorders (n=210), gastrointestinal disorders (n=206), general disorders (n=140), musculoskeletal disorders (n=98), blood disorders (n=123), and neurological reactions (n=120). The majority of the reports (62%) concern female patients. 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 3.1.6. A newcomer in this top-ten-list is amoxicillin.

Table 3.1.6. Most reported antibiotic agents to the Swedish Medical Products Agency 2005–2009

Antibiotic	Total number of ADR reports 2005 to 2009	Number of 'serious' reports	Number of fatal cases (causal relationship possible)
Ciprofloxacin	167	93	4
Flucloxacillin	111	70	4
Nitrofurantoin	102	52	1
Fenoxymethylpenicillin	87	40	0
Clindamycin	75	35	0
Trimethoprim	71	29	0
Doxycylin	70	21	2
Sulphamethoxaxol + trimethoprim	65	38	1
Cefuroxime	51	27	1
Amoxicillin	42	16	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 was reflected in a decrease in reported adverse events. In recent years the reporting rate has been stable. For nitrofurantoin which was increasingly prescribed a slight 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 3.1.7.

TABLE 3.1.7. Number of most frequently spontaneously reported adverse events for fluoroquinolones and nitrofurantoin, during the period 2005 - 2009

	2005	2006	2007	2008	2009	2005-2009
Fluoroquinolones						
Total no of reports	56	45	55	35	34	225
Number of reactions						
Musculoskeletal	24	11	15	9	9	68
tendinitis	13	6	7	2	3	31
tendon rupture	5	3	2	5	3	18
Skin- and subcutaneous tissue	11	4	13	4	8	40
Psychiatric disorders	10	8	4	2	1	25
Nitrofurantoin						
Total no of reports	15	20	22	24	21	102
Number of reactions						
Respiratory system	8	12	3	7	9	39
dyspnoea	2	4	0	1	2	9
interstitial pneumonia	2	2	2	2	3	11
pulmonary fibrosis	0	2	0	0	0	2
Skin- and subcutaneous tissue	1	7	8	7	6	29
General disorders	7	8	7	6	7	35
fever	6	4	3	4	4	21

Charlotta Edlund, Ulf Persson

3.2. Use of antifungals

Hospital care

Despite the arrival of several new compounds to treat antifungal infections systemically in the past few years, the total amount of antifungals in hospital care has not increased proportionally. From 2006 until 2009 there has been a 10% increase from 50, 4 DDD/10^6/day to 55, 0 DDD/10^6/day.

Flukonazol which is a narrow spectrum antimycotic with effect towards candida species (excluding among others *C. krusei* and some strains of *C. glabrata*) stands for approximately 75% of all consumption. It is a fungiostatic drug that is indicated for treatment of invasive 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; vorikonazol which is regarded as treatment of choice for proven or probable aspergillosis, and posaconazol, 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 as well as in other parts of the world. This is a possible result of the widespread use of flukonazol, both as prophylaxis and as treatment.

The use of voriconazol is still low in absolute numbers (2.49 DDD/10^6/day), but the downward trend that was seen in hospital use last year has been reversed and the use increased

by 9%. The total use in outpatient settings is three times higher and the absolute majority of voriconazole therapy is 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.

Voriconazol is the only broadspectrum antifungal drug that can be given orally and is therefore often used when the initial iv 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 and as prophylaxis, so it is mainly used as prophylaxis in hematologic units. The total use increased by 63% in 2009.

Since 2005 there has been a small but steady increase in the use of the echinocandins. This is a new group of antimycotics with a fungicidal effect. The first drug in this group, caspofungin has been available in Sweden since 2002, and has now been joined by two more compounds anidulafungin and mikafungin. (The latter has not been used much in Sweden due to preclinical reports of an increased incidence of liver tumors in rats.) The echinocandins have a more potent effect against candida species and are also effective against *Aspergillus 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 different agents but the antifungal spectrum is similar. As a class the echinocandins have increased in use by 11% during 2009.

Amfotericin 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 amfotericin B is now mostly used in its liposomal form, which improves tolerability. The use remained at the same level as last year.

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

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

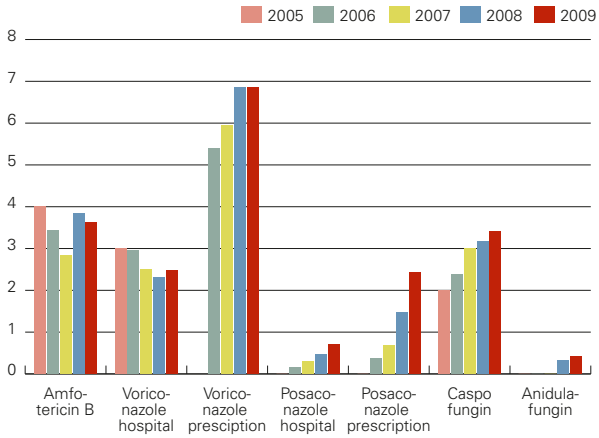


FIGURE 3.1.29. Use of broadspectrum antifungals in hospital care, 2005-2009, DDD/10^6/day.

Outpatient care

70% of all systemically administrated antifungal drugs are sold on prescription. The majority of those prescriptions took place in primary health care. The most commonly prescribed drug is flukonazole, mainly for mucocutaneal infections.

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

Jesper Ericsson

4. Antimicrobial resistance

SURVEILLANCE of antimicrobial resistance is normally based on testing of clinical samples and samples taken according to screening programmes. Each part of the Swedish surveillance program is based on data collected from all the clinical microbiology laboratories. In these laboratories testing of clinical isolates for antibiotic susceptibility is routinely performed using the standardized disk diffusion method (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 ESBL-producing *Enterobacteriaceae* are notifiable according to the Communicable Disease Act, regardless of whether it was judged to be a clinical infection or colonisation without infection. MRSA, PNSP and VRE require notifications by laboratories as well as by the diagnosing clinicians, whereas ESBL require laboratory notification only.

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

Under the heading **Data on invasive isolates reported to EARSS,** 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 EARSS/ECDC via the Swedish coordinator at SMI.

Eleven of these laboratories also deliver data on invasive isolates from all positive blood cultures (Appendix 5). For bacterial species other than those reported to EARSS, data on resistance is presented under the heading **Surveillance of invasive isolates in addition to EARSS**.

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 in the laboratories to be analysed for screening 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 2009 22 of 28 laboratories provided data on MRB- screening.

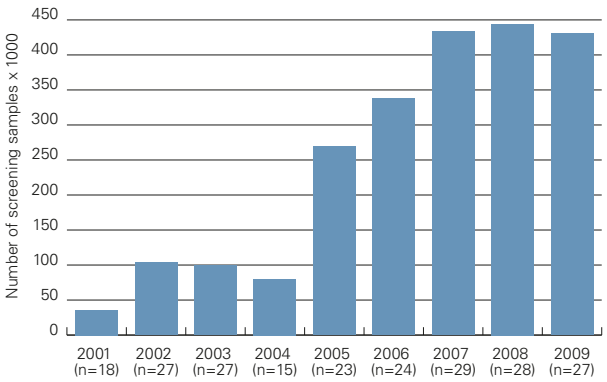


FIGURE 4.1. Annual number of recorded screening samples for multiresistant bacteria, 2001-2009. n refers to the number of participating laboratories.

TABLE 4.1. Compilation of responses, from 24 responding laboratories, of an inquiry concerning sampling series, sampling and positivity numbers for screening/contact tracing samples for 2009. n refers to the number of responding laboratories.

	Total number of analyses	Number of sampled persons	Total number of positive tests	Number of persons with, at least, one positive sampling
MRB	69 217 (n=11)	13 814 (n=7)	1 603 (n=8)	313 (n=6)
MRSA	286 802 (n=19)	62668 (n=15)	4253 (n=19)	1728 (n=19)
VRE	65 292 (n=17)	24730 (n=15)	749 (n=19)	341 (n=17)
ESBL	14 620 (n=14)	15089 (n=13)	1877 (n=16)	1788 (n=16)
Other	851 (n=1)	126 (n=1)	2 (n=1)	2 (n=1)

Staphylococcus aureus including MRSA

Notifications of MRSA according to the Communicable Disease Act

MRSA was made mandatory notifiable in the year 2000. Infection control programmes have been developed and implemented locally under supervision by 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 web-based notification system "SmiNet 2" as recorded at the county level. During the last four 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 2009 a total of 1480 cases of MRSA were notified, an increase by 13% compared with the 1307 cases 2008, Figure 4.2.

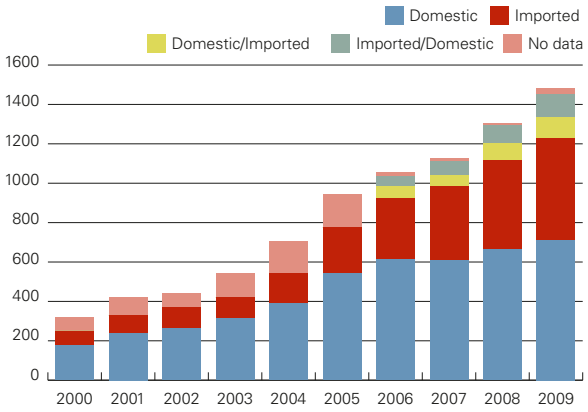


FIGURE 4.2. Number of MRSA notified annually by country of infection, Sweden 2000-2009. "Domestic/Imported" and "Imported/Domestic" indicate several mentioned countries of infection with the most likely mentioned first.

In 2009, eight of the Swedish counties, marked by colour in Table 4.2, (Stockholm, Jönköping, Kalmar, Skåne, Västra Götaland, Örebro, Västmanland, Västernorrland), had a higher incidence than the average national incidence of 15.8 cases/100 000 inhabitants, Table 4.2. (Föreslår att de åtta länen gråmarkeras i tabellen hellre än att tabellen sorteras om. De behöver då inte räknas upp ovan./BL).

During 2009, 48% (n=711) of all reported MRSA cases

TABLE 4.2. MRSA notified in 2000-2009 by county according to the Communicable Disease Act

	2000		2001		2002		2003		2004		2005		2006		2007		2008		2009	
County	**No**	**Inc ***	**No**	**Inc ***	**No**	**Inc ***	**No**	**Inc ***	**No**	**Inc ***	**No**	**Inc ***	**No**	**Inc ***	**No**	**Inc ***	**No**	**Inc ***	**No**	**Inc ***
Stockh olm	97	5.3	166	9,0	205	11.1	228	12.3	277	14.8	315	17.1	356	18.9	351	18,0	342	17.3	375	18.6
Uppsala	19	6.5	17	5.7	10	3.3	12	4,0	26	8.6	28	9.2	24	7.9	33	10.2	40	12.2	33	9.9
Södermanland	2	0.8	1	0.4	4	1.5	2	0.8	8	3.1	11	3.8	9	3.4	26	9.8	20	7.5	23	8.5
Östergötland	2	0.5	7	1.7	7	1.7	14	3.4	14	3.4	101	24.3	48	11.5	49	11.6	43	10.2	45	10.5
Jönköping	7	2.1	6	1.5	5	1.5	24	7.3	14	4.3	40	12.1	44	13,0	17	5.1	20	6.0	66	19.6
Kronoberg	1	0.6	0	0,0	4	2.3	5	2.8	17	9.5	11	6.1	14	7.8	13	7.2	19	10.4	26	14.2
Kalmar	3	1.3	5	0.9	5	2.1	6	2.6	16	6.8	23	9.7	26	11.1	36	15.4	29	12.4	42	18,0
Gotland	1	1.8	10	17.5	3	5.3	2	3.5	1	1.7	10	17.3	4	6.9	8	14,0	6	10,5	6	10.5
Blekinge	7	4.7	1	0.7	3	2,0	2	1.3	3	2,0	9	5.9	4	2.7	16	10.5	10	6.6	11	7.2
Skåne	22	1.9	76	6.7	68	5.9	104	9.1	128	11.3	162	13.9	179	15.5	166	13.8	273	22.5	284	23.1
Halland	10	3.6	26	9.4	13	4.7	13	4.6	9	3.2	21	7.4	23	8.1	18	6.2	16	5.5	45	15.2
Västra Götaland	114	7.6	56	3.7	48	3.2	63	4.2	118	7.8	125	8.1	177	11.6	178	11.5	245	15.7	258	16.4
Värmland	9	3.3	7	2.6	6	2.2	11	4,0	18	6.6	9	3.2	13	4.8	32	11.7	22	8.0	33	12.1
Örebro	8	2.9	7	2.6	16	5.9	8	2.9	11	4,0	16	5.8	35	12.8	25	9.1	46	16.6	45	16.1
Västmanland	3	1.2	8	3.1	6	2.3	11	4.2	12	4.6	35	13.4	48	18.4	54	21.7	23	9.2	46	18.3
Dalarna	0	0,0	5	1.8	1	0.4	2	0.7	3	1.1	6	2.1	11	4,0	15	5.4	23	8.3	28	10.1
Gävleborg	2	0.7	1	0.4	12	4.3	5	1.8	5	1.8	24	8.6	17	6.1	12	4.4	26	9.4	12	4.3
Västernorrland	14	5.7	12	4.9	7	2.9	10	4.1	5	2,0	4	1.6	9	3.7	22	9,0	35	14.4	43	17.7
Jämtland	0	0,0	0	0,0	2	1.6	5	3.9	1	0.8	8	6.2	4	3.1	24	18.9	31	24.4	18	14.2
Västerbotten	3	1.2	17	6.7	10	3.9	13	5.1	16	6.2	10	3.8	7	2.7	23	8.9	22	8.5	28	10.8
Norrbotten	3	1.2	5	2,0	7	2.8	9	3.6	7	2.8	8	3.1	5	2,0	10	4.4	16	6.4	13	5.2
Total	327	3.7	429	4.8	442	4.9	549	6.1	709	7.8	975	10.8	1057	11.7	1128	12.3	1307	14.1	1480	15.8

* = Incidence (cases/100 000 inhabitants)

were domestically acquired and 35% (n=517) were acquired abroad. China (54 cases), Philippines (44 cases), Iraq (33 cases), Vietnam (32 cases) and USA (27 cases) made up the five most common countries for imported MRSA infection during 2009. In 15% 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 three most common countries were still the same (China 55 cases, Philippines 48 cases and Iraq 47 cases), whereas Thailand (35 cases) became number four followed by Vietnam (34 cases). The country for acquisition was reported as "unknown" in 24 cases and in seven cases no country of acquisition was listed.

Among the domestic MRSA cases, an increased incidence was seen in the age group 0-6 years during 2009, Figure 4.3. In contrast, a decrease in incidence was seen for domestic cases 80 years and older. Since 2006, the incidence in age groups between 7 and 79 years has remained stable.

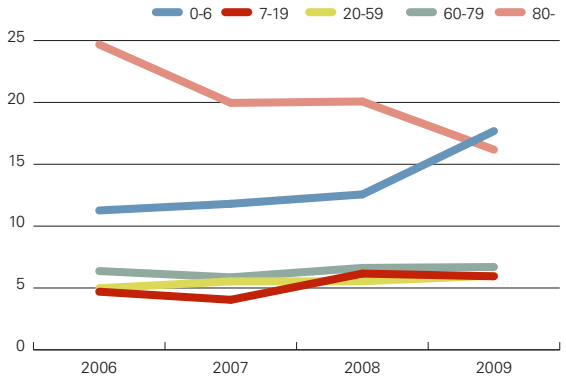


FIGURE 4.3. Age group adjusted incidence of notified domestic MRSA cases (n=711), Sweden 2006-2009.

In 2009, 57% of the domestic cases were identified through contact tracing or targeted screening, and 42% presented with clinical symptoms (Figure 4.4). For imported cases in 2009 the corresponding figures were 65% and 35%. Only twenty-two cases with invasive MRSA infection were reported. Eighteen of those were new cases 2009, and four cases were previously known to carry MRSA.

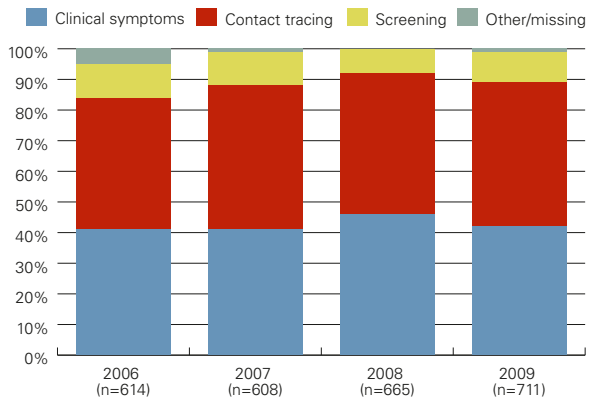


FIGURE 4.4. The reasons for detection of domestic MRSA cases in Sweden 2006-2009. n refers to the number of reported cases.

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.

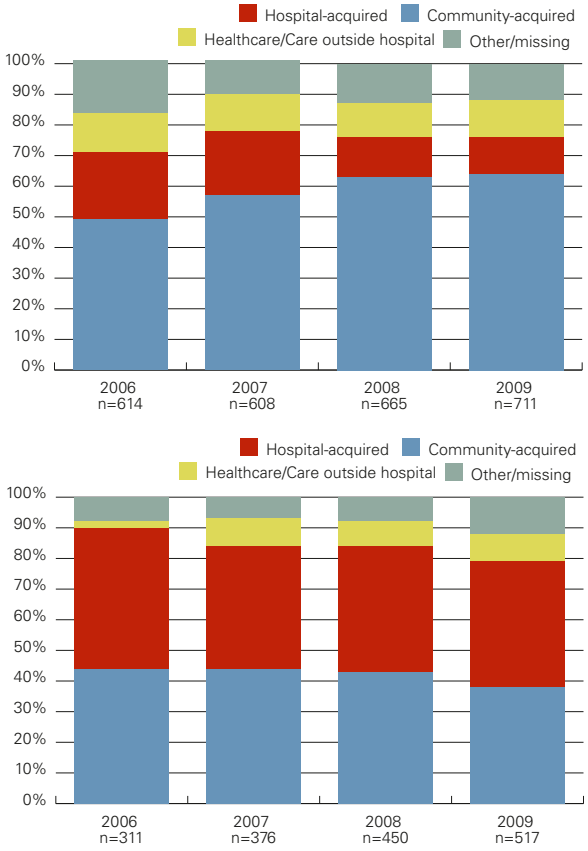


FIGURE 4.5. A and B. Epidemiological classification of the acquisition of domestic (a. top) and imported (b. bottom) MRSA, Sweden 2006-2009.

Community-acquired infections dominated among domestic cases 2009 and comprised 64% (n=458) of all domestic cases. There has been a continuous increase of the proportion of community acquired cases since 2007, and in Sweden today MRSA is acquired primarily in the community. Among the imported cases the proportion of community acquired infections was 38% (n=198). Community acquisition was reported for two thirds of the cases for which it was uncertain whether MRSA was acquired domestically or imported (n=258, not presented graphically).

Hospital acquired MRSA was comparatively more common in imported cases, 41% (n=212), than among domestic cases, 12% (n=85). Among imported cases a similar proportion of hospital acquired MRSA was seen in 2007 and 2008, but for domestic cases the proportion of hospital acquired MRSA was lower in 2008 and 2009 (12%) than in 2006 and 2007 (20%).

During 2009 only minor outbreaks were reported from the Swedish healthcare system and from long-term care facilities. They were reported from several counties.

The diversity in MRSA types reported (see below) and the low numbers of multiresistant MRSA found further support that MRSA in Sweden were primarily community acquired.

Typing of MRSA

DNA-based methods have been used for typing of all MRSA isolates in Sweden since the year 2000. During 2000-2005 pulsed field gel electrophoresis (PFGE) was the standard method. It was replaced by *spa*-typing in 2006 and this is now the primary typing method. *spa*-typing is based on sequencing of the polymorphic X-region of the *S. aureus* species-specific protein A gene, spa, and the Ridom StaphType® software is used for analysis.

The ten most common *spa*-types among notified cases in 2009 were t008 (n=157), t044 (n=108), t002 (n=106), t019 (n=59), t015 (n=58), t437 (n=53), t223 (n=46), t127 (n=44), t032 (n=38), and t037 (n=27) (Table 4.3). The five most common of these types comprised one third, and all ten most common types comprised almost 50% of all cases. The total number of spa types identified in 2009 was 245, indicating the good discriminatory power of this typing method.

The ten most common *spa*-types during the last three years are shown in Table 4.2. The most dramatic changes seen were on the one hand the decrease in prevalence of t032 (often equivalent to strain EMRSA-15 or UK E15 according to the Swedish PFGE nomenclature), which is a typically healthcare related strain, and on the other hand the rise and dominance of the PVL-positive, most often community associated strains with spa types t008, t044 and t019.

TABLE 4.3. Ten most common *spa*-types in 2007-2009 listed in decreasing order per year.

2007	2008	2009
t032	t002	t008
t008	t008	t044
t044	t044	t002
t002	t019	t019
t037	t032	t015
t015	t127	t437
t437	t437	t127
t690	t024	t223
t024	t015	t032
t019	t037	t037

As in the previous two years, isolates with *spa*-types t015, t032, t037 and t223 were always negative for the PVL-toxin, whereas isolates with *spa*-type t044 were always positive. Among isolates of the other common spa types both PVL-positive and –negative ones were found. In total, 491 (34%) of all tested isolates from 2009 were PVL-positive. This was in line with results from the last couple of years, when PVL-positive isolates have represented more than 30% of all MRSA cases. Among the PVL-positive isolates, those of spa type t008 were most frequently encountered in 2009, followed in decreasing order by t044, t019, t437, t002, t355, t852, t024, t657 and t318.

Since 2006 there has been focus on the zoonotic potential of MRSA and especially occurrence of the livestock associated MRSA belonging to clonal complex CC398 as reported from several European countries (see also SVARM). However, in humans in Sweden 2006-2009, only few cases of MRSA with spa types correlating to CC398 were found. These were five cases with t011, two cases with t108, five cases with t034, and two cases with t571, all of them PVL-negative. An additional twelve cases of PVL-positive t034 have been identified, but they seem to be unrelated to the livestock associated MRSA. The epidemiological information on these cases is however scarce, and only in one case the connection between animal (horse) and man has been confirmed.

Antibiotic resistance in MRSA

All MRSA isolates were investigated with regard to resistance to antibiotics other than betalactam antibiotics, Table 4.3. Out of 1158 isolates tested (MRSA from all counties except Skåne and Örebro), 508 (44%) had no other resistance marker than the *mec*A gene defining them as MRSA. Among the other strains, concomitant resistance to erythromycin and clindamycin was still most frequently seen. These resistance markers were found in strains of many different spa types, indicating that macrolide resistance is a widespread phenomenon. Resistance to ciprofloxacin was the second most common resistance marker, followed by resistance to fusidic acid, resistance to gentamicin, and to a lesser degree resistance to rifampicin or to mupirocin. The general trend described in SWEDRES 2008 was still valid.

The decreased proportion of multiresistant MRSA probably reflected the transition from hospital- or healthcare-associated strains to community associated strains. When defining multiresistance as resistance to at least three different categories of antibiotics apart from the betalactam antibiotics, there were only 84 strains meeting these criteria. The antibiotic categories were fluoroquinolones (ciprofloxacin tested), macrolides (counting erythromycin and clindamycin as one category), fusidic acid, aminoglycosides (gentamicin tested), and rifampin. Six different spa types were frequently found to be multiresistant and are described in Table 4.4.

Table 4.4. Characteristics of the six most frequent spa types among multiresistant MRSA 2009

Spa type	No of strains	Acquisition	Route of transmission	Antibiogram[a]	CC/ST[b]
t037	27	Sweden/ abroad	Healthcare	CDEFGR CDEG	CC8 /ST239, worldwide
t041	7	Abroad	Healthcare	CDEG	CC5 /ST228, Germany, Italy
t189	6	Sweden/ abroad	Healthcare/ Community	CDEG	ST188, worldwide (also as MSSA)
t062	5	Sweden/ abroad	Healthcare/ Community	CDEG	CC5 /ST5
t149	5	Abroad	Healthcare/ Community	CDEG	CC5 /ST5, Europe
t1081	7	Sweden/ abroad	Healthcare	CDEG	CC45 /ST45, Europe

[a] C = ciprofloxacin, D = clindamycin, E = erythromycin, F = fusidic acid, G = gentamicin, R = rifampicin. [b] Information retrieved from Ridom SpaServer (www.spaserver.ridom.de).

Is the epidemic of fusidic acid resistant *Staphylococcus aureus* causing bullous impetigo over?

SINCE THE MID-1990s there has been an increased incidence, later described as a clonal spread, among Swedish children of a *Staphylococcus aureus* strain resistant to fusidic acid. This strain caused bullous impetigo in small children, necessitating treatment. Fusidic acid ointment has long been used in Sweden, but this use was questioned when the epidemic potential of the resistant strain was understood. Not only Sweden but also other northern European countries have witnessed this epidemic.

In Sweden this epidemic has been thoroughly investigated regarding both its epidemiology and microbiology, and its effect on the sales of fusidic acid ointments has also been studied. In previous SWEDRES reports we have briefly commented upon the epidemic in relation to the yearly prevalence studies on antibiotic resistance in *S. aureus*.

In 2009 it was feasible for those counties providing information to the previous two studies to once again retrieve microbiological data on fusidic acid resistance in *S. aureus* from children (0-12 years) compared to adults (13-99 years). In Figure 4.7 it is clearly shown that the frequencies of resistance among children are decreasing in all counties and are approaching the levels around 10% seen throughout in the adult population. The sales statistics of fusidic acid to children 0-12 years are presented in Figure 4.8.

It is assumed that the resistance levels should be back at "normal" levels in a year or two, and that the voluntary ban on the use of fusidic acid ointment could then be withdrawn.

Gunnar Kahlmeter, National Reference Laboratory for Antibiotic Resistance; Barbro Olsson-Liljequist, Swedish Institute for Infectious Disease Control

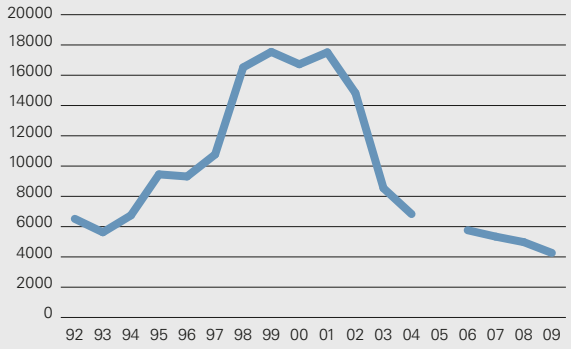


FIGURE 4.8. Sales statistics of fusidic acid to children 0-12 years in Sweden 1992-2009.

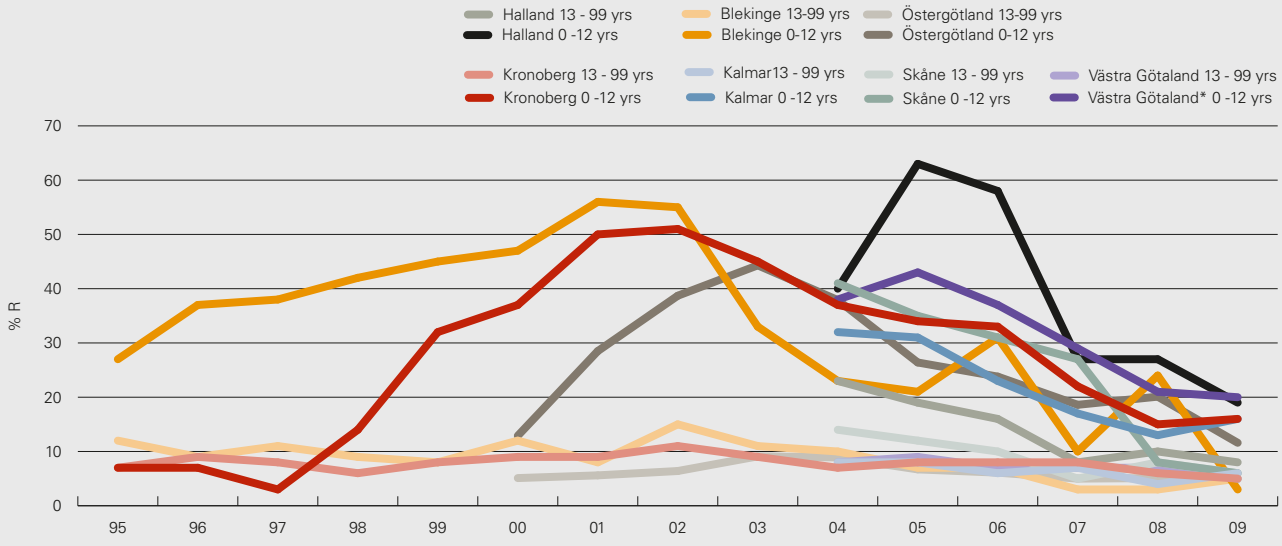


FIGURE 4.7. *Staphylococcus aureus* with fusidic acid resistance in patients 0-12 years and 13-99 years in 7 Swedish counties 1995-2009.

Annual Resistance Surveillance and Quality Control (RSQC) programme

Staphylococcus aureus from wound infections has been included in the annual RSQC programme since 2001 (Appendix 5). Twenty-eight laboratories regularly provide data on consecutive isolates using the disk diffusion method for cefoxitin (from 2004 used as screening disk for detection of MRSA), clindamycin, fusidic acid, aminoglycoside (gentamicin or tobramycin) and vancomycin. Erythromycin (group representative for macrolide antibiotics) and a fluoroquinolone (ciprofloxacin or norfloxacin) have also been tested since 2004. The average resistance rates, as retrieved from ResNet, are shown in Figure 4.6.

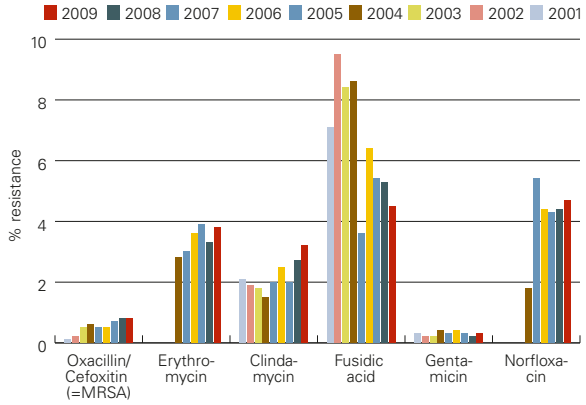


FIGURE 4.6. Resistance rates for *Staphylococcus aureus* 2001–2009 (data from the annual RSQC programme, approximately 3000 isolates per year). In 2005 resistance rates were recorded in *S. aureus* isolated from skin and soft tissue infections from elderly (> 65 years) people only.

The frequency of MRSA in skin and soft tissue infections (SSTI) (cefoxitin used as test compound) has increased slowly but the level in 2009 still remained below 1%. The resistance rate for erythromycin (3.8%) was only slightly higher than that for clindamycin (3.2%). The simultaneous increase in clindamycin and erythromycin resistance indicated a shift towards an increased prevalence of erm genes (constitutively or inducibly expressed) among the clinical isolates. The level of fusidic acid resistance was reduced to below 5%. The story of the fusidic acid resistant clone causing bullous impetigo in children is described in detail, see HIGHLIGHT. Almost no resistance to aminoglycosides was seen in bacteria from SSTI. Fluoroquinolone resistance was stable at 4-5%.

Data on invasive isolates reported to EARSS

In 2009, 0.9% of the invasive *S. aureus* isolates were MRSA (identified by the cefoxitin screen disk test and confirmed by detection of the mecA gene), Table 4.5. This low level has remained during the nine years of mandatory reporting, indicating that infection control measures to prevent MRSA from spreading in the hospital environment have been successful. Fifteen spa types were identified among the 18 newly discovered invasive MRSA isolates in 2009, indicating that these cases were sporadic.

TABLE 4.5. *Staphylococcus aureus* susceptibility results (number of strains and percentage) in blood isolates by the disk diffusion method and by confirmation of the mecA gene. Data reported from SMI to EARSS.

Year	S	R
2001	1618 (99.1%)	14 (0.9%)
2002	1830 (99.4%)	12 (0.6%)
2003	1839 (99.1%)	16 (0.9%)
2004	1891 (99.3%)	14 (0.7%)
2005	1756 (99%)	18 (1.0%)
2006	1849 (99.1%)	16 (0.9%)
2007	2162 (99.5%)	11 (0.5%)
2008	2408 (99.3%)	16 (0.7%)
2009	2621 (99.1%)	18 (0.9%)

Johan Struwe, Tomas Söderblom, Gunnar Kahlmeter, Barbro Olsson-Liljequist

Streptococcus pneumoniae

Background

S. pneumoniae with reduced susceptibility to penicillin, MIC > 0.5 mg/L (PNSP) 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 2009 there were 446 notifications of PNSP in Sweden, Figure 4.11, a decrease by 21% compared with 2008. Fifty-three percent of the cases had been infected domestically and 16% of the cases in a foreign country. In the remaining 138 cases no country for acquisition was given.

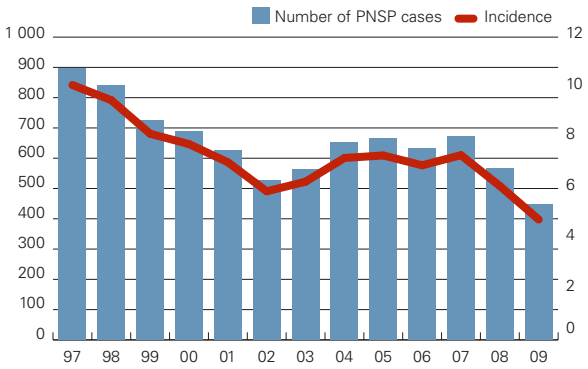


FIGURE 4.11. Number of cases of *S. pneumoniae* with reduced susceptibility to penicillin, MIC ≥ 0.5 mg/L (left) and cases per 100 000 inhabitants (right), Sweden 1997-2009. (Rubriker på axlarna ska skrivas in, Number of PNSP cases till vänster, och Cases per 100 000 inhabitants till höger)

The PNSP incidence in Sweden was 4.8 cases per 100 000 inhabitants 2009. Previous analysis has 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

Staphylococcus aureus among blood isolates: proportions and types

CONSECUTIVE DATA on blood isolates are obtained from 20 laboratories taking part in the Swedish EARSS Network. These laboratories deliver data on seven pathogens, namely *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. From eleven of these 20 laboratories information is available on all their positive blood cultures (one isolate per patient), allowing for analysis on more microorganisms than the seven "EARSS"-bacteria. These sets of data are complete from 2005 and onwards and have been used to gather information on for instance Streptococcus pyogenes and Streptococcus agalactiae to previous SWEDRES reports.

However, the two most frequently found pathogens in blood cultures were *E. coli* and *S. aureus*, save for the commonly isolated coagulase negative staphylococci. We investigated the proportions of these two bacterial species in relation to the total numbers of positive cultures and also looked for trends. The total numbers of blood cultures taken (pairs of bottles) increased every year in all of the eleven laborartories as can be seen in Figure 4.9. This might indicate a general awareness of infectious diseases and an increased adherence to guidelines. However, the percentage of positive blood cultures did not change during these five years. It ranged between 7.6% and 7.9% in 2006-2009.

The proportions of *S. aureus* (this chapter) were further analysed for geographical differences or changes over time. In Figure 4.10 is shown the percentage of *S. aureus* of all positive blood cultures per laboratory and year. A rough estimate of the overall average was 11%.

There were small differences between laboratories/counties, but there were only few examples of trends within laboratories/counties. One laboratory (Lab 11) had a proportion above 11% during all five years, whereas the other ten varied around 11% through the years. In one laboratory (Lab 2) there was a continuous rise in the proportions of *S. aureus*, whereas in the other laboratories / counties the levels fluctuated between the years.

Invasive *Staphylococcus aureus* – a snapshot of *spa*-types

Molecular typing methods are only rarely applied on *S. aureus* isolates, invasive or others. However, one recent European overview of invasive *S. aureus* isolates was performed through an initiative by the EARSS network together with Seqnet.org. National EARSS-representatives agreed to create a working group of *S. aureus* reference laboratories across Europe. This working group supported a structured survey for the identification of the strain composition of *S. aureus* isolates that cause invasive infections in Europe. During a 6 month period 2006-2007, 2890 methicillin-susceptible *S. aureus* (MSSA) and methicillin-resistant *S. aureus* (MRSA) isolates from invasive infections of patients treated in 450 European healthcare institutions from 26 European countries have been systematically collected and analysed by spa-sequence typing. This collection provides a genetic snapshot of the *S. aureus* population causing invasive disease in Europe including MSSA as well as MRSA strains (Grundmann et al. 2010). In the report there is a mapping platform providing a widely applicable research tool for geographic tracking of strains/clones with particular public health importance. It enables viewing the spatial distribution of spa types across the EARSS network.

Sweden contributed information and spa typing results on 200 isolates, 5 of which were MRSA. These five had spa types t002, t021, t032, t041 and t455. Among the 195 MSSA a total of 93 spa types were identified. The ten most common of these were, in decreasing order, t015, t084, t012, t021, t002, t160, t050, t026, t005 and t008. These spa types are also commonly found among MRSA isolates both in Sweden and in Europe.

Byline

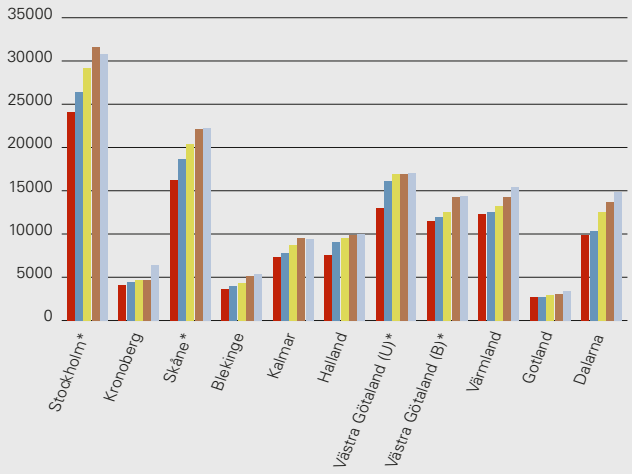


FIGURE 4.9. Number of blood cultures per laboratory 2005 - 2008.

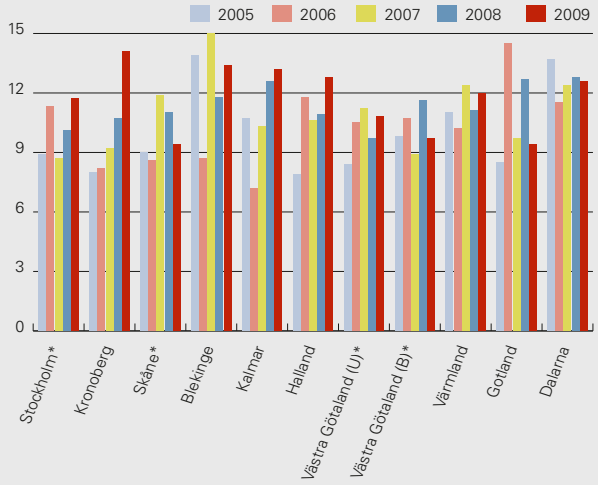


FIGURE 4.10. Proportions of *S. aureus* among positive blood cultures from eleven laboratories representing counties or parts of counties (*) 2005-2009.

group 0-4 years, Figure 4.12. Compared with 2008 the decrease in 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 sex.

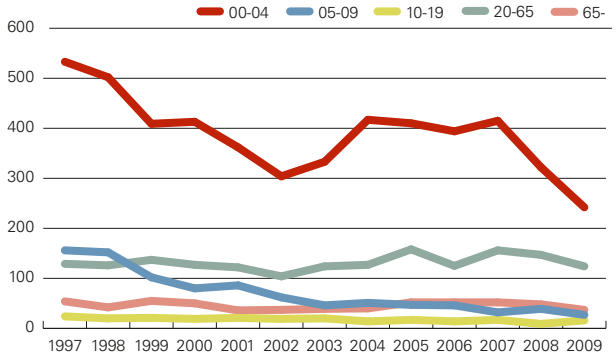


FIGURE 4.12. Age-group distribution among all cases reported with PNSP in Sweden 1997-2009.

PNSP were reported from all 21 counties with Stockholm (144 cases) and Skåne (135 cases) accounting for 63% of all notifications. In these two counties, the notifications have decreased by 22% and 38%, respectively. Remaining counties reported 1-36 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 incidence rates is not meaningful.

The majority, 82% of all notifications of PNSP, were found in cultures from nasopharynx. In 43% of all cases the detection of PNSP was due to clinical infection, and in 28% due to targeted screening including contact tracing. In the remaining cases another reason for sampling was stated or the information was missing. Of all PNSP cases during 2009, 53% (n=236) were domestic cases and 16% were imported. Information was missing in 135 cases.

In 2009, 14 cases were reported to have invasive PNSP infections, 14 cases in blood and in one of those also in cerebrospinal fluid. For 11 of these cases the serotypes were reported, and six had serotype 9, two serotype 14, and one each had serotypes 6, 23 and 35. The most commonly found serotypes among all PNSP were, in decreasing order, type 19F (29%), followed by type 23F (12%), 9V (9%), 19A (7%), 6B (7%), and non-typeable 7%. The distribution of serotypes has thus changed and serotype 9V was less dominant. Based on these results the potential coverage rates of the 7-, 10- and 13-valent vaccines were 64%, 64% and 77%, respectively.

Annual Resistance Surveillance and Quality Control (RSQC) programme

The isolates collected during the RSQC surveys are mainly derived from nasopharyngeal cultures. Approximately 3000 consecutive isolates per year from all the clinical laboratories have been tested for susceptibility to penicillin (by means of oxacillin 1 µg screen disk), erythromycin, clindamycin (from 2004), tetracycline, trimethoprim-sulfamethoxazol, and norfloxacin (from 2005, used as indicator for fluoroquinolone resistance) using the disk diffusion method. The national summary of the results is shown in Figure 4.13. For all tested antibiotics except norfloxacin there has been a steady increase in rates of resistance every year.

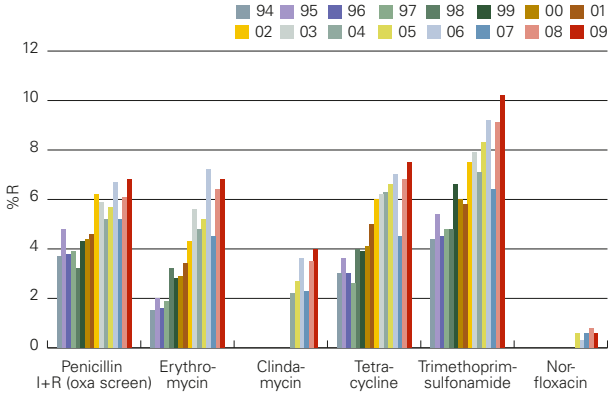


FIGURE 4.13. Resistance rates for *Streptococcus pneumoniae* 1994-2009 (data from the annual RSQC programme, approximately 3000 isolates per year).

Data on invasive isolates reported to EARSS

The Swedish data on susceptibility to penicillin and erythromycin among invasive isolates for 2001-2009 are given in Table 4.6. Levels of resistance were lower among invasive isolates than in the nasopharyngeal isolates from the RSQC programme. Also, there has been no increased resistance among invasive isolates, neither for penicillin nor erythromycin, contrary to the nasopharyngeal isolates.

TABLE 4.6. Invasive isolates of *Streptococcus pneumoniae* reported to EARSS.

Penicillin * (I+R = PNSP)				
Year	**S%**	**I%**	**R%**	**Total**
2001	97.2	2.3	0.5	788
2002	97.5	2.4	0.1	783
2003	95.0	5.0	0	920
2004	96.8	2.8	0.4	955
2005	96.4	3.1	0.5	1017
2006	97.9	2.1	0	936
2007	97.1	2.9	0.1	1029
2008	98.0	1.6	0.4	1213
2009	97.2	2.8	0	1098
Erythromycin				
Year	**S%**	**I%**	**R%**	**Total**
2001	95.4	0.2	4.4	653
2002	94.7	0.1	5.2	700
2003	94.9	0.1	5.0	736
2004	94.7	0.1	5.2	869
2005	94.3	0.3	5.4	924
2006	94.8	0.4	4.8	813
2007	94.9	0.1	5.2	926
2008	94.4	0.4	5.2	1123
2009	96.8	0.1	3.1	1098

* S < 0.12 mg/L; I 0.12-1.0 mg/L; R > 1.0 mg/L

Johan Struwe, Tomas Söderblom, Birgitta Henriques Normark, Gunnar Kahlmeter, Barbro Olsson-Liljequist,

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 immunosuppressed 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 also mandatory.

Notifications of VRE according to the Communicable Disease Act

From 2000 to 2006 low numbers of VRE-cases were reported (18-35 per year), and in 2007 53 cases were notified. Beginning late autumn 2007, reports came from Stockholm County about an increase in the number of VRE-cases. An increased dissemination of VRE was also reported from other counties and continued during the whole of 2008, adding up to a total of 618 cases. In 2009, the number of cases was 402, a reduction from the previous year with 35%. Reports on VRE came from 13 of the 21 Swedish counties, but the majority of cases (92%) were from the three counties with previously reported outbreaks, Stockholm (n=179), Västmanland (n=133) and Halland (n=59). An additional 31 cases were reported from the remaining 18 counties. The national incidence of VRE was 4.3 cases per 100 000 inhabitants. In the three affected counties the incidence had decreased in Stockholm from 21.1 to 8.8 and in Halland from 29.3 to 19.9, but increased in Västmanland from 33.2 to 53. Also Gotland, with five reported VRE cases, reached above the national incidence with 8.7 cases per 100 000 inhabitants. The mean age for all cases was 72 years with an even distribution between the sexes.

In 26 cases the VRE was acquired abroad and 16 different countries were stated. For 21 of the cases the acquisition was healthcare-related and for the remaining five cases information was missing.

During 2009, 394 cases had *Enterococcus faecium*. Of these, 326 carried the vanB gene and 61 the *van*A gene. Information was missing for seven cases. In one case a double infection was reported with *Enterococcus faecium* with either *van*A or -vanB. *Enterococcus faecalis* was reported in six cases and all had the *van*A-gene. Three cases were reported with both *Enterococcus faecalis* and *Enterococcus faecium*.

According to the first laboratory notifications for each case the majority of isolates were from faeces (90%), whereas 2.5% each of the isolates were from rectum and urine. Invasive VRE infections, all from blood, were reported in 5 cases. Four of those were new cases and one case was known from previous years. The findings of VRE in faeces or rectum in more than 90% indicated that most of the cases were detected by screening.

Epidemiological typing

For enterococci PFGE was used as the standard typing method. All isolates from the counties of Halland and Västmanland were analysed and found to have one variant each of the strain causing epidemic spread in these counties. Only a minor set of strains from Stockholm County was available for analysis, but exchange of information indicated that the majority of cases of *Enterococcus faecium* with the *van*B gene in Stockholm also belonged to this strain.

Comparisons with older isolates of *Enterococcus faecium* with the vanB gene in the national strain collection and database indicated that this strain had not been detected before 2007. Several smaller outbreaks in Sweden during 2000 – 2006 were caused by strains of different PFGE-types.

Sporadic cases with *Enterococcus faecium* with the *van*A gene have been notified since 2000. PFGE analyses of those indicate that the majority are single cases with unique PFGE patterns.

Data on invasive isolates reported to EARSS

Enterococcus faecalis and *Enterococcus faecium* have been reported to EARSS 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% of all), and in 2004 three isolates were found (1.2%), Tables 4.7 and 4.8. Molecular typing of these vancomycin-resistant isolates indicated relatedness only between two of them from the same hospital. In 2006 two resistant blood isolates were found, in 2007 none, in 2008 six isolates of *Enterococcus faecium* with vanB, and in 2009 two isolates. The six isolates from 2008 all showed the same PFGE pattern as the recent epidemic strain described in the highlighted section (page xx).

HLAR was more prevalent in *Enterococcus faecium* (27.4%) than in *Enterococcus faecalis* (19.6%) in 2009. This shift was seen already in 2008. From 2006 and onwards all laboratories who reported HLAR used gentamicin (GEN) as test disk for detection.

Table 4.7. Resistance among invasive isolates of *Enterococcus faecalis* reported to EARSS 2001-200

Year	Vancomycin-R (%)	HLAR (%)	Total number (number tested for HLAR by GEN)
2001	0	12.7	395 (212)
2002	0	17	430 (235)
2003	0	17.5	593 (440)
2004	0	15.4	592 (533)
2005	0	18.7	567 (492)
2006	0.4	19.9	579 (563)
2007	0	16.1	651 (632)
2008	0	20.1	720 (703)
2009	0	19.6	718 (627)

The nationwide outbreak of a vancomycin-resistant *Enterococcus faecium* with *van*B – an update

VANCOMYCIN-RESISTANT *Enterococcus faecium* and *Enterococcus faecalis* (VRE) in infection as well as colonization, have been mandatory notifiable according to the Swedish Communicable Diseases Act since year 2000. Mandatory contact tracing was implemented 2004. The basic epidemiological information of the notified cases has been given in chapter *Enterococcus faecalis* and *Enterococcus faecium*. In this highlighted area we describe the rise and decline of this widespread dissemination in more detail.

The recognition of the outbreak situation in 2007 lead to intensive contact tracing and screening activities and also to other infection control measures. Since August 2007 until the end of 2009 altogether 1057 cases of VRE were found and reported from 17 counties. Of these, 11 counties reported 986 cases as acquired domestically, and a majority of these (95%, n=941) were healthcare-related. Among the domestic cases only 7% had clinical symptoms. 73% were identified through contact tracing, 13% by screening, and for 7% the indication for sampling was unknown. According to the first laboratory notifications of the domestic cases 88% (n=868) were isolated from faeces, 3.5% (n=35) from urine, 3.5% (n=34) from wounds, and 4 cases (0.4%) isolated from blood.

Typing and antibiotic resistance of the epidemic VRE

Verification by PCR of species and vancomycin resistance mechanism showed that 856 of the domestic cases were E. faecium with *van*B gene, 125 E. faecium with *van*A gene and in five cases the resistance gene was not reported. E. faecalis were reported for only 9 cases during the whole period, six with vanA gene and in three cases the resistance gene was not reported. The species and resistance genotype distribution per county for the 941 domestic cases reported as healthcare-related are presented in Table 4.9.

TABLE 4.9. Species and resistance genotype for the domestic, healthcare-related VRE cases, August 1st 2007 to 31st December 2009.
Efm = *Enterococcus faecium*, Efs = *Enterococcu s faecalis*. The numbers per county of species and resistance genotype do not always match exactly with the total number of cases due to double infections or missing information of resistance genotype.

County	No of cases	Efm, *van*A	Efm, *van*B	Efs, *van*A	Efs, *van*B
Stockholm	571	110	463	2	-
Västmanland	211	2	207	1	-
Halland	138	2	136	-	-
Uppsala	9	-	8	-	-
Gotland	4	-	3	1	-
Skåne	4	-	4	-	-
Västra Götaland	2	-	2	-	-
Värmland	1	-	1	-	-
Västerbotten	1	-	1	-	-

Epidemiological typing of the *E. faecium* isolates with vanB gene was performed by PFGE. The results showed that all examined isolates from Västmanland and Halland, as well as the majority of the isolates from Stockholm County, had closely related PFGE patterns, suggesting dissemination of the same strain in these counties. Preliminary, but still incomplete, data indicate that this pattern has not been seen in VRE isolates reported before 2007 in Sweden. Moreover, this PFGE pattern could not be recognised in a large collection of recent VRE isolates from Germany (G Werner, personal communication).

The isolates of the epidemic strain were typically resistant to vancomycin (MICs 8-64 mg/L) but susceptible to teicoplanin (MICs 0.125-1 mg/L), and they were also resistant to ampicillin, imipenem, ciprofloxacin and macrolides but showed only low-level resistance to gentamicin.

The epidemic curve for the domestic, healthcare-related cases of *E. faecium* with *van*B (n=825) is presented in Figure 4.14.

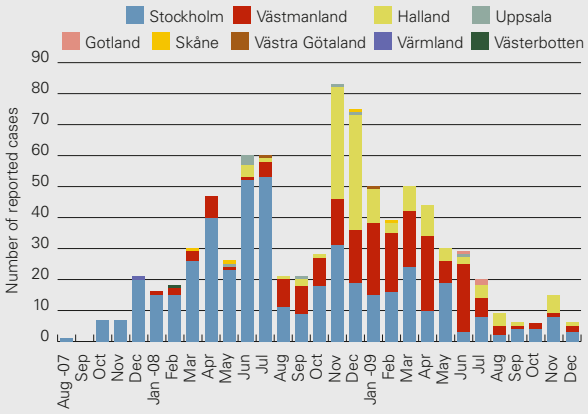


FIGURE 4.14. Epidemic curve for spread of healthcare-related domestic *Enterococcus faecium* with vanB.

Conclusions

Intensive efforts have been made in the respective regions, with support from national authorities, to control the outbreaks and disseminations of VRE. Control measures and interventions have consisted of increased awareness of hand hygiene, not only for staff but also for patients, withdrawing of food buffets from the hospital wards, extensive cleaning of the patient environment, and use of probiotics (Lactobacillus rhamnosus GG). At the end of 2009 there was a dramatic decrease in the number of newly detected cases, but it is too early to state that this will be a permanent situation. A central field epidemiology group was recruited for an assessment of the management of the outbreaks. Based on its report and on expertise presented at a timely workshop in December 2008, a new nation-wide action-programme will soon be launched.

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Table 4.8. Resistance among invasive isolates of *Enterococcus faecium* reported to EARSS 2001-2009

Year	Vancomycin-R (%)	HLAR (%)	Total number (number tested for HLAR by GEN)
2001	0	9.1	169 (99)
2002	0	6.3	181 (96)
2003	2.2	11.2	231 (170)
2004	1.2	7	260 (227)
2005	0	4.3	253 (211)
2006	0.3	14	286 (286)
2007	0	14.4	279 (263)
2008	1.5	24.8	333 (331)
2009	0.8	27.4	311 (274)

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Streptococcus pyogenes

Annual Resistance Surveillance and Quality Control (RSQC) programme

Streptococcus pyogenes was not included in the RSQC programme in 2009.

Surveillance on invasive isolates additional to EARSS data

Data on consecutive blood isolates were obtained from 11 laboratories. One hundred and thirty-four of 11.416 (1.2%) were *Streptococcus pyogenes* (GAS). This was in the same order of magnitude as in the previous two years with 1.8 and 1.2% GAS, respectively. All GAS isolates were susceptible to penicillin. Three isolates (2.2%) were resistant to erythromycin and clindamycin, indicating that they possessed erm genes (MLSB type of resistance). This was an increase compared with 0.5% in 2008. Thirteen isolates (9.7%) were resistant to tetracycline which was a decrease from 2008 (14.6%) but yet higher than in 2007 when 8% of the isolates were resistant. A majority of the isolates were retrieved from adults (> 50 years), and only 3% of the isolates were from children 0-9 years.

Streptococcus agalactiae

Surveillance on invasive isolates additional to EARSS data

131/11.416 (1.1%) of consecutive blood isolates from the participating 11 laboratories were *Streptococcus agalactiae* (GBS). This was in the same order of magnitude as the previous two years with 1.0 and 1.3% GBS, respectively. All GBS isolates were susceptible to penicillin/ampicillin. Nine of the isolates (6.9%) were resistant to erythromycin, but only five were resistant to clindamycin. This indicates, but has not been confirmed, that the isolates harbour either erm genes (MLSB type of resistance affecting both erythromycin and clindamycin) or mef genes (efflux-mediated resistance affecting only erythromycin). The figure for 2009 (6.9%) was comparable to those from 2008 (6.5%) and 2007 (8.8%). A majority of the isolates were retrieved from adults (> 50 years), but 12 (9.2%) were isolated from children less than 2 months. None of the isolates from newborns were resistant to erythromycin.

Haemophilus influenzae

Annual Resistance Surveillance and Quality Control (RSQC) programme

Haemophilus influenzae was included in the RSQC programme on antibiotic resistance in 2009 as a follow-up to 2008 when a marked increase in rates of penicillin-resistant and trimethoprim-sulfamethoxazole-resistant isolates was seen (Figure 4.15).

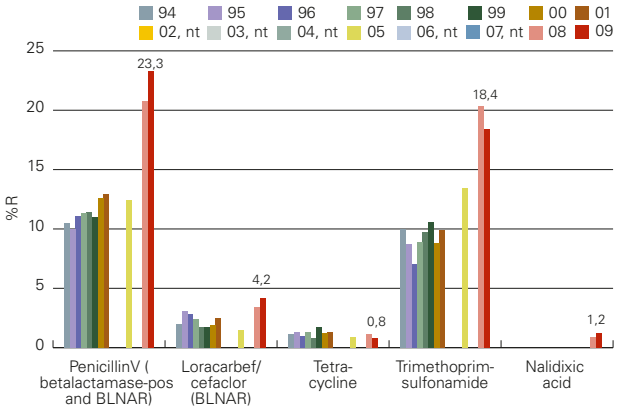

FIGURE 4.15. Resistance rates for *Haemophilus influenzae* 1994-2009 (data from the annual RSQC programme, approximately 3000 isolates per year).

In 2009 the high rates of resistance remained for both types of antibiotics, with an even higher figure for penicillin V (23.3% compared to 20.8%) but a slightly lower for trimethoprim-sulfamethoxazole (18.4% compared to 20.3%). It should be noted that the figures for penicillin V represent both betalactamase-producing strains and strains with chromosomally mediated resistance (BLNAR = betalactamase-negative ampicillin-resistant). The frequency of BLNAR alone, as interpreted from the cefaclor screening disk, had increased from 3% to 4.2%.

Tetracycline resistance in *H. influenzae* was still rare (approximately 1%). A few isolates with fluoroquinolone resistance, detected by the nalidixic acid screening disk, were found.

Typing of betalactam resistant *Haemophilus influenzae*

From each of the clinical laboratories the first six betalactam-resistant isolates during the respective study periods in 2008 and 2009 were sent to SMI for further testing. A total of 242 isolates were collected, consisting of 177 betalactamase-positive (BLPAR) and 65 BLNAR isolates. They were analysed by disk diffusion and MIC testing, and were typed by PFGE to

identify clusters of isolates which might explain the increased rate of resistance.

Resistance to trimethoprim-sulfamethoxazole was found in both groups but more frequently among BLNAR (36/65; 55%) than among BLPAR (55/177; 31%). Preliminary analysis of PFGE results showed at least 15 different patterns among BLPAR strains and 5-10 different patterns among BLNAR strains. Several of the patterns were restricted to 2-5 isolates each, which often originated from the same laboratory but sometimes from several laboratories. Only a few large clusters of betalactamase-producing isolates were identified, and they always originated from several laboratories.

In summary, in this selected material of betalactam resistant *H. influenzae* there was a wide variety of strains based both on their antibiotic susceptibility patterns and on their genetic relationship. The increased rates of *H. influenzae* with penicillin resistance which have been noted during the last couple of years could probably not be explained by the expansion of one single strain. Further analysis is needed in order to make a more precise statement.

Surveillance on invasive isolates additional to EARSS data

Of data on consecutive blood isolates from the participating 11 laboratories 49/11.416 (0.4%) were *Haemophilus influenzae*. Three of these isolates were from cerebrospinal fluid. Ten isolates (20.4%) were betalactamase-producing and ampicillin-resistant. This is comparable to 2008 when 25% of the isolates were resistant, and it corresponds to the increase seen in respiratory tract isolates (see above). None of the blood isolates had chromosomally mediated beta-lactam resistance (BLNAR). Seven isolates (14.3%) were resistant to trimethoprim-sulfamethoxazole, comparable to the results in 2008.

A majority of the isolates were retrieved from adults (> 50 years), but 3 were isolated from children 0-9 years.

Barbro Olsson-Liljequist, Gunnar Kahlmeter

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, information on ESBL 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 of limiting ESBL-producing *Escherichia coli* and *Klebsiella pneumoniae* in blood isolates to a maximum of 1% and that ESBL-producing bacteria should not affect 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, also including plasmid-mediated AmpC variants and carbapenemases. All Swedish clinical microbiology laboratories were requested to report ESBL according to the new definition from January 2010. Already during 2009, a few cases were reported according to this new definition.

Notifications according to the Communicable Disease Act

A total of 3754 cases were notified during 2009. Reports came from all 21 counties of Sweden, corresponding to a national incidence of 40 cases per 100 000 inhabitants (Figure 4.16). In May and June 2008 a strike in the health-care sector may have affected the sampling frequency and the number of reported cases, thus comparisons of these periods or the entire years are difficult to make. When comparing the second half of the two years, a 27% increase of ESBL cases was noted for 2009.

Almost all Swedish counties had an increased incidence, the highest incidence found in Jönköping 2009. In Uppsala the incidence continued to decrease from 57 to 46 cases per 100,000 inhabitants in 2009. This was most probably due to the extensive infection control and screening programme launched to control the large ESBL outbreak that was discovered in 2005. It indicates that an outbreak situation with ESBL-producing *K. pneumoniae* may be reversed when a combination of control measures is undertaken.

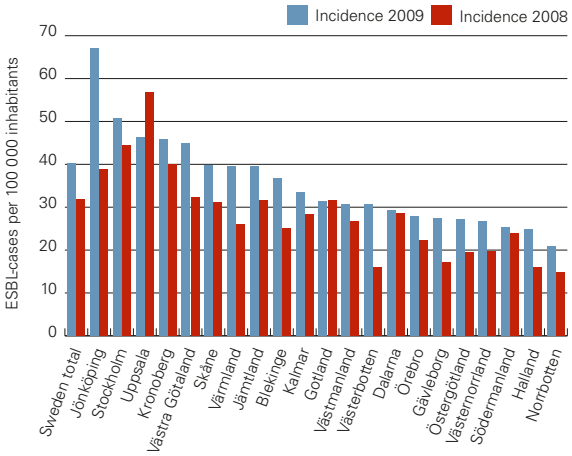

FIGURE 4.16. The incidence of ESBL in Swedish counties 2008-2009, arranged according to incidence 2009.

The most commonly reported species was *E. coli*, accounting for 82% of all cases, followed by *K. pneumoniae* with 7%, Table 4.10.

TABLE 4.10. Distribution of species among cases with ESBL-producing bacteria 2009.

Escherichia coli	3164
Klebsiella pneumoniae	290
Proteus mirabilis	29
Citrobacter species	28
Salmonella species	15
Other *Enterobacteriaceae*	105
Species not reported	243
Total number of reported species	3874*

* In 105 cases 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 69% of the cases according to the first laboratory notification. The second most common source was faecal samples with 12%. Isolates from rectum and wound samples constituted 4% each of the first notifications and blood isolates 3.5% of the first notifications. Invasive infections with ESBL-producing bacteria, all in blood, were notified in 186 cases during 2009. Among these, 168 were new cases for 2009 and 18 were known carriers of ESBL, notified during the previous year.

The incidence in age groups and gender differed between species.and is shown in Figures 4.17 and 4.18. ESBL-producing *E. coli* were derived from women in 67% of cases. They had a median age of 54 years compared to 63 years for men.The *K. pneumoniae* ESBL cases were equally distributed between sexes, with median ages of 62 years for women and 58 years for men. Compared with 2008 the mean age had decreased with 9 years for men due to several cases among newborns.

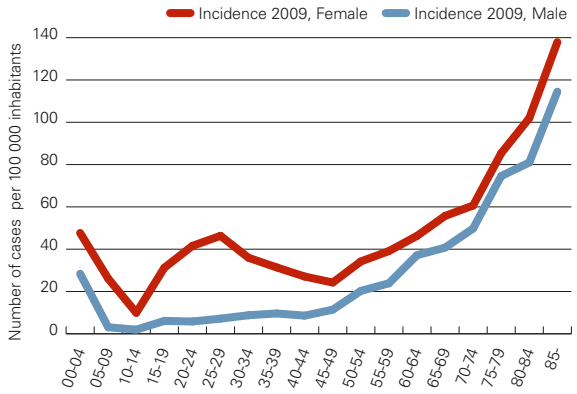

FIGURE 4.17. Age and gender distribution of *E. coli* ESBL cases 2008.

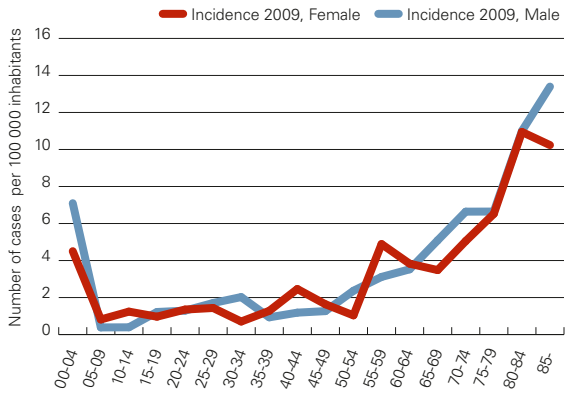

FIGURE 4.18. Age and gender distribution of *K. pneumoniae* ESBL cases 2009.

The nation-wide problem with ESBL-producing bacteria in Sweden has proven to be a larger problem than 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.

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 several times 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 achieve data that would be statistically more valid for trend analyses. The average resistance rates to ampicillin have increased yearly, from 17 up to 30% (Figure 4.19). A similar trend has been seen for trimethoprim, for which the rates have increased from 10 to 20%. Fluoroquinolone resistance, detected by the nalidixic acid screening disk since 2002, has also increased during this period and exceeded 13% in 2009. Resistance to cephalosporins (cefadroxil tested), although much less prevalent than ampicillin resistance, has continued to increase and reached 3.5% in 2009. This mirrored the increasing incidence of ESBL-producing bacteria as seen from the notified cases (above) and reports to EARSS (below). Also for nitrofurantoin there was an increase, although from a much lower level than for the other antibiotics. Nitrofurantoin resistance is associated with some strains of ESBL-producing *E. coli*, thereby explaining the concomitant increasing resistance rates.

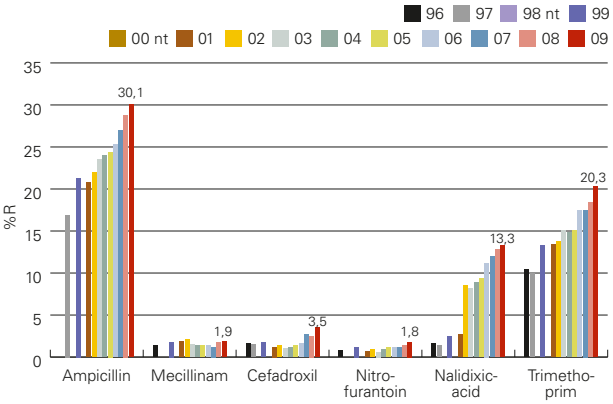

FIGURE 4.19. Resistance rates for six antibiotics 1996-2009. Between 1996-2001 fluoroquinolone resistance was detected with norfloxacin, from 2002 and onwards with nalidixic acid.

In 2009 the RSQC programme was performed as usual, but a follow-up of the extended survey from 2007 was done in parallel. All laboratories were asked 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. A total of 370 *E. coli* and 20 *K. pneumoniae* were collected and tested with phenotypic and genotypic methods. Preliminary results for *E. coli* showed that among isolates with verified ESBL-activity (inhibition by clavulanic acid) the ESBLs of CTX-M subgroup 1 dominated (74%), followed by CTX-M subgroup 9 (22%). Nineteen isolates (7%) harboured plasmid-mediated AmpC-enzyme of the type CIT (originating from Citrobacter species). A majority of the ESBL-producing isolates were multiresistant as was also

Escherichia coli in blood and urine – relation to antibiotic use

CONSECUTIVE DATA on blood isolates are obtained from 20 laboratories taking part in the Swedish EARSS Network. These laboratories deliver data on seven pathogens, namely *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. From eleven of these 20 laboratories information is available on all their positive blood cultures (one isolate per patient), allowing for analysis on more microorganisms than the seven "EARSS"-bacteria. These sets of data are complete from 2005 and onwards and have been used to gather information on for instance Streptococcus pyogenes and Streptococcus agalactiae to previous SWEDRES reports.

However, the two most frequently found pathogens in blood cultures were *E. coli* and *S. aureus*, save for the commonly isolated coagulase negative staphylococci. We investigated the proportions of these two bacterial species in relation to the total numbers of positive cultures and also looked for trends.

The total numbers of blood cultures taken (pairs of bottles) increased every year in all of the eleven laborartories (Figure 4.9, page xx). This might indicate a general awareness of infectious diseases and an increased adherence to guidelines. However, the percentage of positive blood cultures did not change during these five years. It ranged between 7.6% and 7.9% in 2006-2009.

The proportions of *E. coli* (this chapter) were further analysed for geographical differences or changes over time. In Figure 4.20 is shown the percentage of *E. coli* of all positive blood cultures per laboratory and year. A rough estimate of the overall average was 20%.

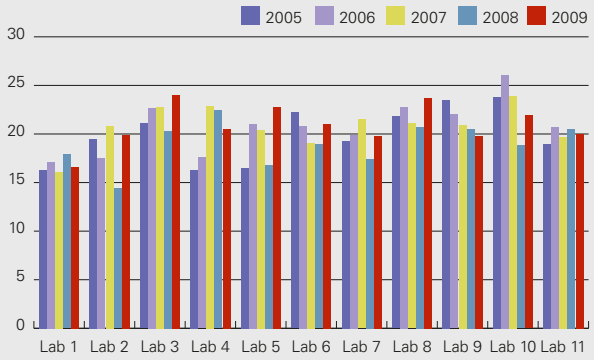

FIGURE 4.20. Proportions of *E. coli* among positive blood cultures from eleven counties 2005-2009.

There were only small differences between laboratories/counties as to their proportions of *E. coli* among invasive isolates. There were no obvious trends and no relation with either size or geographical location of the counties could be seen. In one county (skriv) the proportion seemed stable around 16%, and in others (skriv vilka) it was stable around 20%.

Escherichia coli from UTI and consumption of UTI antibiotics

In three regions antimicrobial resistance in *E. coli* isolated from UTI in relation to age was analysed (Figure 4.21 a – d). For mecillinam (a) and nitrofurantoin (c) resistance was low in all age groups and in all three counties and appeared lowest in the really young (0–2 years). For nalidixic acid (b) as a marker for quinolone resistance and trimethoprim (d) resistance was high in all age groups although trimethoprim resistance appeared to be lower among the elderly.

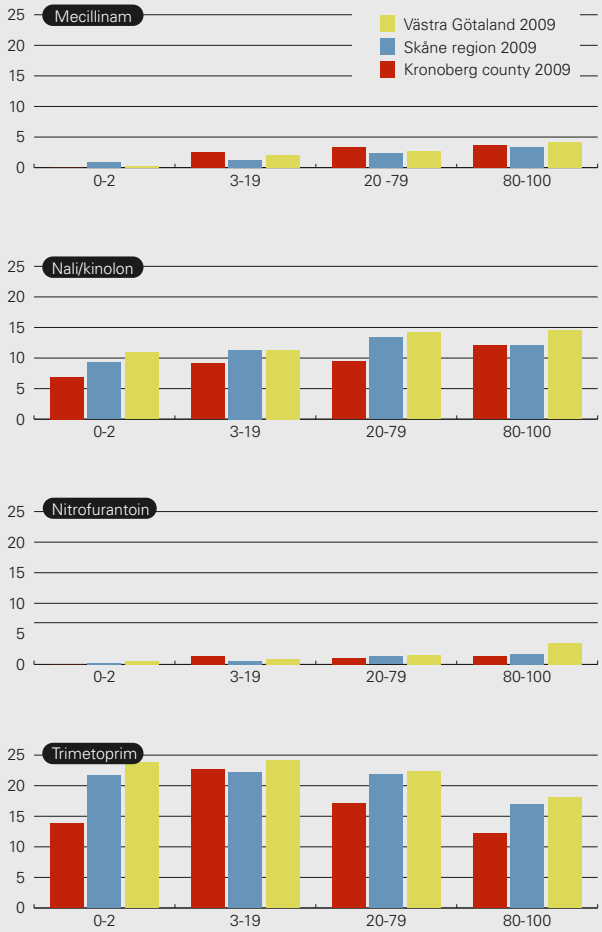

FIGURE 4.21. Resistance rates in different age groups to four antibiotics for treatment of urinary tract infections 2009; a) mecillinam, b) nalidixic acid, c) nitrofurantoin, d) trimethoprim. Data collected from three regions in Sweden.

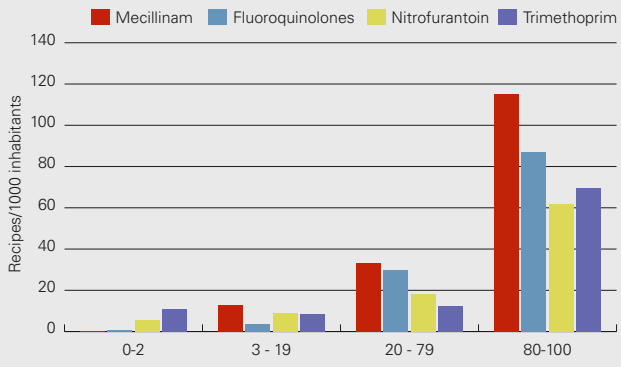

FIGURE 4.22. Prescriptions 2009 of four antibiotics for treatment of urinary tract infections to different age groups.

Författare???

noted in the study from 2007. A complete report of all results from 2007 and 2009 will be presented and distributed to laboratories and other interested parties.

Data on invasive isolates reported to EARSS

Escherichia coli derived from invasive infections (blood isolates) have been part of the European Antimicrobial Resistance Surveillance System (EARSS) since 2001. The surveillance system has focused on resistance to beta-lactam antibiotics, especially ESBL, and on resistance to aminoglycosides and fluoroquinolones. Results for 2001-2009 are presented in Table 4.11.

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, 33% versus.30%. However, the data for blood isolates was incomplete since one third of participating laboratories did not include ampicillin in susceptibility testing of invasive isolates. 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 was 3% in 2009, thus an increase from 2.3% in 2008. In the majority of the cefotaxime-R isolates resistance was attributed to the presence of ESBLs of CTX-M type.

Aminoglycoside resistance in *E. coli* has shown an increasing trend for the last couple of years and reached 3.7% in 2009. Resistance genes coding for aminoglycoside resistance often co-exist with genes coding for ESBL enzymes and other resistance markers which make these bacteria multiresistant.

Reduced susceptibility and resistance to fluoroquinolones (I+R) has increased from 5.5% in 2001 and reached 15.5% in 2009. These increasing trends of resistance in blood isolates were the same as those in urine isolates from the RSQC programme shown in Figure 4.19.

TABLE 4.11. *Escherichia coli* from blood cultures in Sweden 2001-2009, reported to EARSS/ECDC.

Year	Ampicillin-R (%) *	Cefotaxime-R (%; ESBL/other mechanism)	Aminoglycoside-R (%) **	Fluoro-quinolone-I/R (%) ***	Total number of isolates
2001	26.5	0.5	1	5.5	2627
2002	24.9	0.5	0.6	7.1	3062
2003	28.5	0.4	1	8.3	3300
2004	23	0.5 / 0.6	1.5	11.1	3336
2005	26	0.9 / 0.4	1.5	8.9	3212
2006	28.1	1.3 / 0.1	1.7	8.7	3514
2007	32.9	1.6 / 0.6	2.3	13.3	3745
2008	31.9	1.9 / 0.4	2.2	14.3	4028
2009	32.8	3	3.7	15.5	4423

*Only 55-60% of isolates were tested against ampicillin; **gentamicin or tobramycin, *** ciprofloxacin

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 since 2005.

As for E. coli, the RSQC 2009 programme for *K. pneumoniae* was mainly focused on urine samples, Figure 4.23. Resistance to commonly prescribed oral antibiotics for treatment of urinary tract infections was tested in 2009. The results indicated an increased resistance only to trimethoprim, whereas the rates of resistance to both cefadroxil and fluoroquinolones were the same or slightly lower than in 2008.

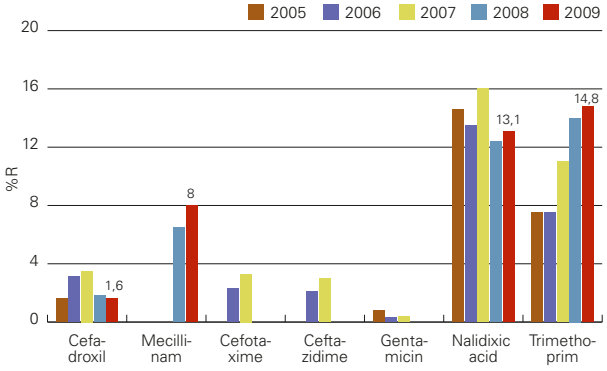

FIGURE 4.23. Resistance rates (resistant isolates in percent of all *Klebsiella pneumoniae* Isolates) for four groups of antibiotics 2005-2008.

Also for *K. pneumoniae* the RSQC programme was performed as usual in 2009, but as for *E. coli* a follow-up of the extended survey from 2007 was done in parallel. All laboratories were asked to collect consecutive cefadroxil-resistant (R < 13 mm) isolates during a one-month period and send them to SMI for further analysis. A total of 20 *K. pneumoniae* were collected and tested with fenotypic and genotypic methods. Preliminary results for this small collection of *K. pneumoniae* showed that 16 isolates had verified ESBL-activity (inhibition by clavulanic acid) which most commonly was CTX-M subgroup 1. A majority of the ESBL-producing isolates were multiresistant.. A complete report of all results from 2007 and 2009 will be presented and distributed to laboratories and other interested parties.

Data on invasive isolates reported to EARSS

Since July 2005, participants in the EARSS network have contributed with data on blood isolates of *K. pneumoniae*. In 2009 the number of isolates was lower than in 2008, 755 VS 826 as shown in Table 4.12. All cephalosporin resistance was caused by ESBLs of CTX-M type. The rate of fluoroquinolone resistance is slowly increasing.

TABLE 4.12. *Klebsiella pneumoniae* from blood cultures in Sweden 2005-2008, reported to EARSS. *gentamicin or tobramycin, **ciprofloxacin
The data for 2005 represent six months from 20 laboratories. From 2006 and onwards the data represent the whole years from 20 laboratories.

Year	Cefotaxime-R (%; ESBL/other mechanism)	Aminoglycoside-R (%) *	Fluoroquinolone-I/R (%) **	Total number of isolates
2005 (half year)	0.7 / 0.7	1.4	9.8	281
2006	1.0 / 0.5	0.3	8.5	610
2007	1.1 / 0.3	1.1	10.8	649
2008	2.3 / 0	1.1	12.9	826
2009	1.8 / 0	1.0	12.2	755

Isolates with new resistance mechanisms

In 2007 the first isolate of *K. pneumoniae* with KPC-2 (*K. pneumoniae* carbapenemase) was detected in Sweden. In 2008 one isolate with a KPC-3 betalactamase was identified, and in 2009 there were reports of three isolates in Stockholm, one identified as KPC-2 and two as KPC-3. The cases were healthcare related and further investigations will elucidate the origin of the infections.

Johan Struwe, Tomas Söderblom, Karin Tegmark Wisell, Christian Giske, Gunnar Kahlmeter, Barbro Olsson-Liljequist

Pseudomonas aeruginosa

Annual Resistance Surveillance and Quality Control (RSQC) programme

Pseudomonas aeruginosa was reentered in the RSQC programme on antibiotic resistance in 2009.

Laboratories were asked to test 100 consecutive isolates of *P. aeruginosa* with the exclusion of respiratory isolates. Resistance rates to all tested antibiotics showed similar or even lower levels of resistance compared to previous years, Figure 4.24.

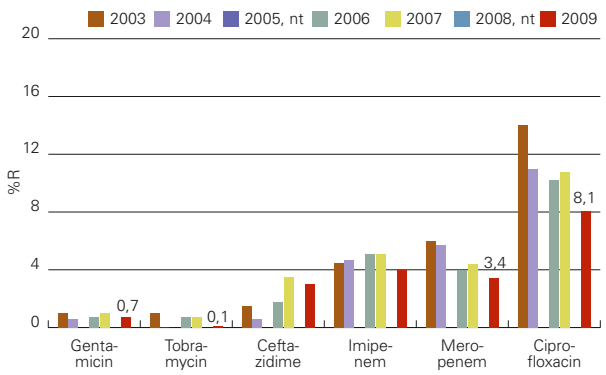

FIGURE 4.24. Resistance rates (resistant isolates in percent of all *Pseudomonas aeruginosa* isolates) for four groups of antibiotics 2003-2009.

Data on invasive isolates reported to EARSS

Since July 2005, participants in the EARSS network have been asked to contribute with data on blood isolates of *P. aeruginosa*. From Sweden a total of 149 isolates from 20 laboratories were tested during the second half of 2005, and these data are compared to complete data sets for 2006-2009 in Table 4.13. The levels of resistance to beta-lactam antibiotics (ceftazidime and carbapenems) were in the range 3-7% for all four years. No change in resistance rates had occurred for either aminoglycosides (0%) or fluoroquinolones (10.1%).

TABLE 4.13. *Pseudomonas aeruginosa* from blood cultures in Sweden 2005-2008, reported to EARSS.
* imipenem, meropenem, ** gentamicin, tobramycin, *** ciprofloxacin

Year	Ceftazidime-R (%)	Carbapenem-R (%) *	Aminoglycoside-R (%) **	Fluoroquinolone-I/R (%) ***	Total number of isolates
2005 (half year)	4.7	Insufficient data	0	9.0	149
2006	2.6	4.4	0.5	10.4	296
2007	4.5	7.0	0	10.4	342
2008	5.1	4.0	0	8.1	282
2009	3	7.5	0	10.1	352

Barbro Olsson-Liljequist, Gunnar Kahlmeter

Clostridium difficile

A national surveillance program for *Clostridium difficile* was initiated by SMI in 2009. The program included both a voluntary laboratory reporting system of all new cases and determination of resistance and epidemiological typing of collected isolates.

The laboratory reporting in SmiNet2 was launched in October and by the end of the year about half of the laboratories participated. The case definition for reporting of new cases was the detection of *C. difficile* cytotoxin B, regardless of method (direct positive by ELISA or ELISA-positive on a cultured isolate). At least 8 weeks was requested between positive samples from the same patient. During November-December these laboratories reported approximately 700 cases.

Isolates were collected and sent from 25 of the 28 Swedish laboratories during weeks 11 and 39. Susceptibility testing was performed by Etest for moxifloxacin, erythromycin, clindamycin, metronidazole and vancomycin. A total of 387 *C. difficile* isolates were typed by PCR ribotyping.

The most common types are presented in Figure 4.25. Type 014 was most frequent followed by types 020, 001, 023, 078 and 012. Type 014 consists of two subtypes according to the Swedish nomenclature, SE21 and SE21a, but these are not distinguished by the international type nomenclature. Increased numbers of types 078 and 023 were seen between weeks 11 and 39. These strains carry the so-called "binary toxin" and are commonly found in other European countries. One isolate of type 027 was detected, but this isolate was

susceptible to moxifloxacin – a typical marker for the virulent type 027 that has spread world-wide. For types 012, 017 and 046 geographical clusters were detected, Figure 4.26.

In summary, there was geographical clustering of certain *C. difficile* types that also were resistant to several antibiotics.

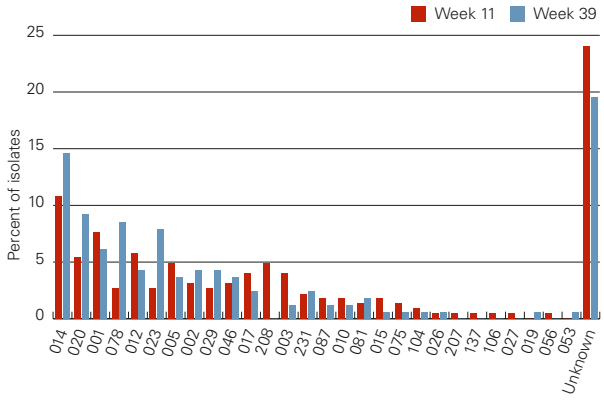

FIGURE 4.25. PCR ribotypes of *Clostridium difficile* in Sweden collected during two weeks 2009.

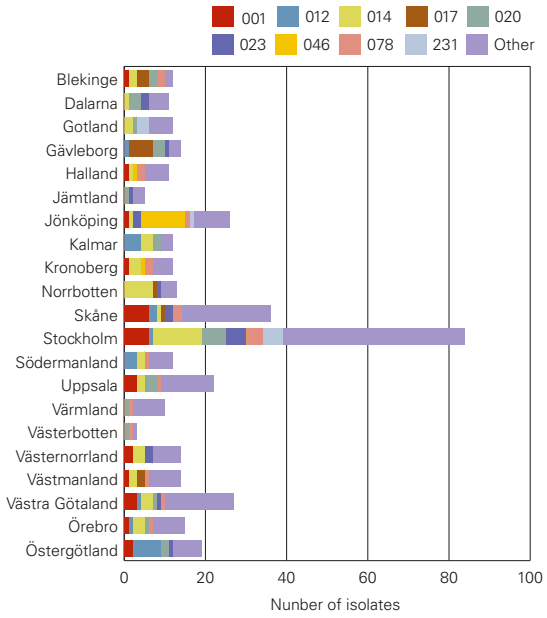

FIGURE 4.26. Distribution per county of the most common PCR ribotypes 2009.

Tomas Åkerlund, Karin Tegmark-Wisell, Johan Struwe

Helicobacter pylori

Annual Resistance Surveillance and Quality Control (QCRS) programme

Helicobacter pylori derived from gastric biopsies was not included in the annual RSQC programme until 2001 but has been monitored locally at a few laboratories. In vitro resistance to metronidazole has been reported in 10-40% of Scandinavian isolates. Resistance to clarithromycin is less common (3%) but is increasing and has locally at one laboratory reached over 10% for three years in a row. Resistance to tetracycline is less than 1% and resistance to amoxicillin has only been described in a few strains and only outside Scandinavia. Frequencies of resistance to clarithromycin and metronidazole in clinical isolates from southwest of Sweden, representing a population of approximately 300 000, are presented in Table 4.13.

Table 4.13. Helicobacter pylori University Hospital MAS, Malmö, Sweden1996-2009, %R

Year	Total number	Clarithromycin %R	Metronidazole %R
1994	536	1.0	29.0
1995	588	2.9	32.1
1996	381	3.9	35.2
1997	331	7.7	39.8
1998	116	6.7	34.3
1999	149	6.1	33.1
2000	216	7.8	30.5
2001	188	8.8	40.2
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

* Molecular biology technique from 2005

Mats Walder

Salmonella and *Shigella* spp.

Annual Resistance Surveillance and Quality Control (QCRS) programme

Salmonella spp. and *Shigella* spp. derived from faecal cultures were not included in the annual RSQC programme until 2002 but 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. Noteworthy is that fluoroquinolone resistance was high, 20-25%, among *Salmonella* strains, and 15-20% among *Shigella* spp.

Antibiotic resistance in domestic Salmonella spp 2009

To get a more comprehensive picture of the situation in Sweden we analysed the antibiotic susceptibility of a selection of domestic *Salmonella* spp. The isolates were chosen from the collection of domestic isolates sent to SMI in 2009 (n=593). More than 80 different serotypes were represented in this collection, but the ten most common were Typhimurium (n=172), Enteritidis (n=93), subspecies I (n=68), Agona (n=17), Infantis (n=13), Java (n=12), Stanley (n=12), Poona (n=11), Thompson (n=11) and Virchow (n=10). Together they constituted more than 70% of the total number. Susceptibility test-

ing by disk diffusion was performed according to recently developed European guidelines (EUCAST) on 200 faecal isolates, chosen to represent the ten most common serotypes but also with regard to geographical location of patients and time of isolation. The tested antibiotics were chosen because of clinical and epidemiological relevance but also with regard to the panel of antibiotics tested by the veterinarians (SVARM report), in order to make data comparable. We included ampicillin, cefotaxime, nalidixic acid, ciprofloxacin, gentamicin, streptomycin, chloramphenicol, tetracycline, trimethoprim and sulphonamides.

In summary we showed that 56% of the selected isolates were susceptible to all tested antibiotics. 88 isolates were resistant to one or several antibiotics and multiresistance (resistance to three or more antibiotic classes) was found in 61 of those. The most common resistance pattern was ampicillin/streptomycin/sulphonamides/tetracycline (n=26) and this pattern combined with quinolone resistance in an additional 21 isolates. Two isolates were resistant to cefotaxime and were comfirmed to have ESBLs of the type plasmid-mediated AmpC. The disk diffusion method for tetracycline was sensitive enough to separate resistant isolates of S. Typhimurium DT104 (inhibition zones 9-12 mm) from other resistant isolates (6 mm) (Figure 4. 27), and to show the almost complete correlation between nalidixic acid resistance (6 mm) and reduced zones for ciprofloxacin (25-33 mm) (Figure 4.28).

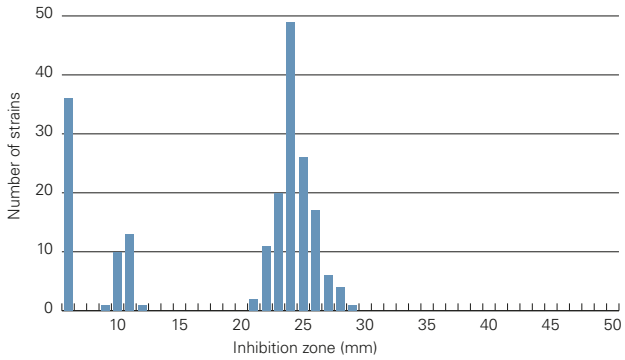

FIGURE 4.27. Inhibition zones of tetracycline 30 ug disk on 200 isolates of *Salmonella* spp.

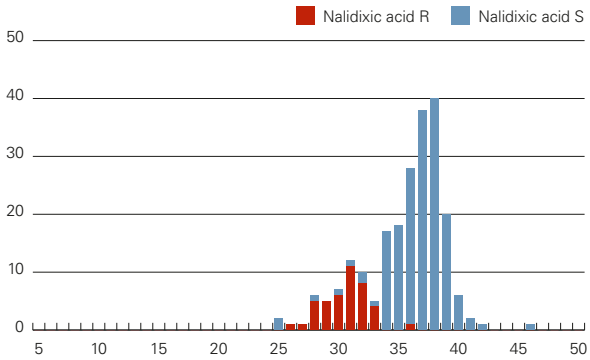

FIGURE 4.28. Inhibition zones of ciprofloxacin 5 ug disk on 200 isolates of *Salmonella* spp. and correlation to susceptibility (S) or resistance (R) to nalidixic acid.

Barbro Olsson-Liljequist, Cecilia Svensson, Mats Walder

Campylobacter spp

Annual Resistance Surveillance and Quality Control (QCRS) programme

Campylobacter spp. derived from patients with diarrhoea were not included in the annual RSQC programme until 2001 but has been monitored locally at a few laboratories. 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 quinolone resistance among *Campylobacter* isolates noticed a few years ago has now regained the former level of about 50%. When screening for fluoroquinolone resistance using nalidixic acid disks was introduced in Sweden in 2001, it was expected to influence the resistance rates dramatically. The data for nalidixic acid and ciprofloxacin in parallel show, however, that the two disks are equally able to detect quinolone resistance in *Campylobacter*, Table 4.14.

TABLE 4.14. *Campylobacter jejuni/coli* University Hospital MAS, Malmö, Sweden1995-2009 %R .

Year	Nalidixic acid	Cipro-floxacin	Tetracycline	Erythro-mycin
1995		22	27	4
1997		23	30	3
1998		34	33	2
1999		45	35	1
2000		55	45	1
2001	32	30	28	1
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

Mats Walder

Neisseria gonorrhoeae

Notifications according to the Swedish Communicable Diseases Act

Gonorrhoea is a notifiable disease/infection and in 2009, 611 cases 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 Malmoe, respectively. Clinical isolates are in the present report described from the Swedish Reference Laboratory for Pathogenic Neisseria (an external body of the Swedish Institute for Infectious Disease Control [SMI]), Department of Laboratory Medicine, Clinical Microbiology, Örebro University Hospital, Örebro; the Division of Clinical Bacteriology, Department of Laboratory Medicine, Karolinska University Hospital Huddinge,

TABLE 4.15. Antibiotic resistance rates (%) and β-lactamase production of Swedish Neisseria gonorrhoeae strains from 2003 to 2009.

	2003 (n=130)*	2004 (n=149)*	2005 (n=497)*	2006 (n=352)*	2007 (n=406)*	2008 (n=447)*	2009 (n=384)*
β-lactamase pos.	22	26	23	30	30	28	44
Ampicillin	22	26	23	30	30	28	44
Cefixime**	0	<1	0	0	<1	1	5
Ceftriaxone	0	0	0	0	0	<1	0
Azithromycin**	<1	0	<1	5	7	13	6
Ciprofloxacin	56	51	49	61	70	63	75
Spectinomycin	0	0	0	0	0	0	0

* From 2003 to 2004, only data from the Swedish Reference Laboratory for Pathogenic Neisseria, Örebro University Hospital, Örebro, Sweden were reported. From 2005 to 2008, also data from the Division of Clinical Bacteriology, Department of Laboratory Medicine, Karolinska University Hospital Huddinge, Stockholm, Sweden were reported. In 2009, in addition data from Department of Clinical Microbiology, Malmö University Hospital, Malmö, Sweden are included.

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

Stockholm; and the Department of Clinical Microbiology, Malmö University Hospital, Malmö, Sweden.

In 2009, isolates from 387 of the notified clinical cases were completely characterised at these laboratories, representing 63% of the notified cases. In total, 384 different *N. gonorrhoeae* strains were cultured from these cases (n=387).

Susceptibility testing was performed according to standardized methodology using Etest for MIC determination of ampicillin, cefixime, ceftriaxone, azithromycin, ciprofloxacin, and spectinomycin. The used SIR-breakpoints have been determined by The Swedish Reference Group for antibiotics (SRGA; http://www.srga.org). Production of beta-lactamase was examined by using Nitrocefin discs. Results for 2009 are compared with those from 2003 to 2008 in Table 4.15. Notable, the levels of resistance to all antimicrobials used in the traditional gonorrhoea treatment are exceedingly high. The levels of resistance to azithromycin and cefixime have substantially increased the recent years.

Magnus Unemo, Hans Fredlund

Neisseria meningitidis

Notifications according to the Swedish Communicable Diseases Act

Invasive meningococcal disease is a notifiable disease and in 2009 65 clinical cases of the disease were reported. A total of 45 clinical isolates from blood or cerebrospinal fluid were analysed at the Swedish Reference Laboratory for pathogenic Neisseria (an external body of the Swedish Institute for Infectious 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% defibrinated horse blood for determination of MICs of bensylpenicillin, cefotaxime, meropenem, ciprofloxacin, chloramphenicol and rifampicin. Production of beta-lactamase was examined by Nitrocefin discs.

None of the isolates produced beta-lactamase. Eight isolates (17%) had reduced susceptibility to bensylpenicillin (MIC>0.064 mg/L). All isolates had MICs of cefotaxime £0.008 mg/L except one with 0.032, and all had MICs of ciprofloxacin £0.008 mg/L. MICs of meropenem varied between 0.002 and 0.064 mg/L. MICs of chloramphenicol varied between 0.25 and 1 mg/L, and MICs of rifampicin were £0.032 mg/L.

Per Olcén

Mycobacterium tuberculosis

During 2009 a total number of 642 new cases of tuberculosis (TB) were diagnosed in Sweden compared to 554 cases in 2008, an increase of 16%. The number and proportion of culture confirmed cases were 515 (80%) in 2009 compared to 436 (79%) in 2008. *Mycobacterium tuberculosis* was identified in 509 cases, *Mycobacterium africanum* in one patient and *Mycobacterium bovis* in five patients. The numbers of cases diagnosed with isoniazid resistant TB in 2009 were 38/515 (7,4%) and with MDR-TB 13/515 (2,5%).

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 52 patients corresponding to 10% of the 510 with culture confirmed TB, see Table 4.16. The five isolates of *M. bovis* were not included since these strains are naturally resistant to pyrazinamid. As always, resistance to isoniazid was most commonly found. Among the patients born in Sweden 5/89 (5,6%) had resistant TB and they were all resistant to isoniazid only. In the largest group of patients with TB in Sweden, immigrants from Somalia, 17/159 (10.7%) had some kind of resistant TB, four of which had MDR-TB (2,5%). Among patients born in the rest of the world 36/262 (13,7%) had TB with some kind of resistance, nine of which had MDR-TB (3,4%).

Of the 510 culture confirmed cases, 31 (6%) had a history of previous treatment for TB after 1949, the time when effective medication was made available. Of these 31 cases, 7 (23%) had strains resistant to anyone of the first line drugs including 4 with MDR-TB. The corresponding figures for cases with no reported previous treatment were 51/479 (11%), nine of which (2%) with MDR-TB. None of the 13 cases with MDR-TB were born in Sweden. They had all lived in Sweden

for less than 6 years and 7 of them came to Sweden during 2009. In total 7 of the 13 cases had pulmonary manifestations but only two were smear positive.

Genetic typing with RFLP (restriction fragment length polymorphism) was performed on 50 of the 58 resistant strains so far. Typing of the remaining eight is ongoing. This is done to help detect clusters which could indicate ongoing spread of resistant strains. Sixteen of the 50 examined strains belong to 12 different clusters with two or more patients in each cluster. For two patients there is a close geographical connection and for two others a close family connection. Several of the clustered 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 an annual average of 5% during the 1990ies to 9% in the period 2000–2006 and then to 12.7% in 2007. In 2009 the proportion was slightly lower(51/510, 10%). In parallel the annual proportion of MDR-TB increased from 0,8% in 2006 to 4% in 2007 and dropped to 2,5% (13/510) in 2009. We have seen a marked increase in the number of cases from Somalia but the proportion of resistant TB in this group has been smaller than among immigrants from the rest of the world during 2009. This was not the case in 2008 when resistant TB was more common among Somalis as compared to other immigrants.

Sven Hoffner, Jerker Jonsson

TABLE 4.16. Drug resistant tuberculosis in Sweden, 2001-2009.

Year of diagnosis	2001		2002		2003		2004		2005		2006		2007		2008		2009	
Culture confirmed *M. tuberculosis* or *M. africanum*	354		346		345		368		448		395		361		434		510	
	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%
Any resistance	38	10,7	36	10,4	32	9,3	43	11,7	52	11,6	43	10,9	49	13,6	57	13,1	58	11,4
Isoniazid	31	8,8	34	9,8	26	7,5	35	9,5	46	10,3	38	9,6	46	12,7	51	11,8	51	10,0
Rifampicin	6	1,7	4	1,2	10	2,9	6	1,6	5	1,1	6	1,5	15	4,2	15	3,5	14	2,7
Ethambutol	3	0,8	1	0,3	5	1,4	3	0,8	3	0,7	1	0,3	7	1,9	6	1,4	7	1,4
Pyrazinamid	6	1,7	4	1,2	7	2,0	12	3,3	6	1,3	6	1,5	11	3,0	18	4,1	15	2,9
Isoniazid + rifampicin (MDR)	4	1,1	4	1,2	8	2,3	5	1,4	4	0,9	3	0,8	15	4,2	14	3,2	13	2,5

Appendix 1. Abbreviations

ABU	Asymptomatic bacteriuria
AST	Antibiotic susceptibility testing
ATC	The Anatomical Therapeutic Chemical classification system
BLNAR	Betalactamase negative ampicillin resistant
CDCDC	County Department for Communicable Disease Control
DDD	Defined daily dose
DST	Drug susceptibility testing
EARSS	European Antimicrobial Resistance Surveillance System
ESBL	Extended spectrum beta-lactamase
GAS	Group A streptococci or *Streptococcus pyogenes*
GBS	Group B streptococci or *Streptococcus agalactiae*
ICU	Intensive care unit
MDR	*Multidrug* resistance
MIC	Minimal Inhibitory concentration
MRB	Multiresistant bacteria
MRSA	Methicillin-resistant *Staphylococcus aureus*
PFGE	Pulsed field *gel electrophoresis*
PNSP	Penicillin non-susceptible pneumococci, MIC ≥ 0,5 mg/L
PVL	Panton-Valentine leukocidin
RSQC	Resistance Surveillance and Quality Control Programme
RTI	Respiratory tract infection
SRGA-M	The Swedish Reference Group of Antibiotics - subcommittee on Methodology
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 2008.

	0-6 years	7-19 years	20-59 years	60-79 years	+80 years	All ages
Stockholm	182 229	300 712	109 0681	322 732	84 909	198 1263
Uppsala	26 915	52 300	174 505	58 550	14 918	327 188
Södermanland	20 650	43 282	131 119	57 362	15 111	267 524
Östergötland	32 449	67 253	217 530	82 396	23 541	423 169
Jönköping	26 712	56 013	167 395	65 259	19 867	335 246
Kronoberg	14 118	28 792	91 911	36 395	110 08	182 224
Kalmar	15 715	36 440	113 456	52 704	150 82	233 397
Gotland	3 755	9 112	28 325	12 501	3 311	57 004
Blekinge	11 345	22 893	75 015	33 730	9 276	152 259
Skåne	98 238	185 204	635 007	230 639	65 670	1 214 758
Halland	23 942	48 779	145 348	59 137	16 366	293 572
Västra Götaland	123 505	243 969	817 719	290 304	82 633	1 558 130
Värmland	18 702	42 445	135 132	59 929	17 166	273 374
Örebro	20 980	44 273	139 641	56 585	16 253	277 732
Västmanland	18 645	39 806	125 332	52 240	13 951	249 974
Dalarna	19 478	43 746	134 100	61 105	17 438	275 867
Gävleborg	19 450	42 753	135 349	61 517	16 839	275 908
Västernorrland	18 018	37 080	118 577	54 828	14 869	243 372
Jämtland	9 333	19 384	62 813	27 215	8 152	126 897
Västerbotten	19 070	40 470	133 585	51 016	13 671	257 812
Norrbotten	17 060	38 795	125 057	55 683	13 082	249 677
Sweden	740 309	1 443 501	4 797 597	1 781 827	493113	9 256 347

TABLE APP 2.2. Population in Sweden 2000-2009. Numbers represent the population by December 31st the previous year.

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Population	8861265	8882831	8909322	8940744	8975669	9011391	9047803	9113297	9182923	9256347

TABLE APP 2.3. Number of admissions and patient-days in somatic medical care, 2008. Numbers represent production by hospitals in the counties.

	Patient-days	Admissions
Stockholm	1 108 000	261162
Uppsala	312 621	59091
Södermanland	200 899	37712
Östergötland	285 391	62987
Jönköping	246 566	52769
Kronoberg	142 195	25003
Kalmar	170 728	38269
Gotland	41 774	9455
Blekinge	120151	20951
Skåne	925 417	186580
Halland	218 536	44309
Västra Götaland	1 233 362	245484
Värmland	191 085	38807
Örebro	229 033	49197
Västmanland	201 154	38738
Dalarna	210814	47587
Gävleborg	198 161	41774
Västernorrland	194 053	39645
Jämtland	97 736	18674
Västerbotten	277 850	49716
Norrbotten	185 225	38 348
Sweden	679 0751	1 406 258

TABLE APP 2.4. Denominator data from the microbiological laboratories. NP = test not performed. NA = data not available.

	Number of analyses 2009									Number of positive cultures 2009				
Laboratory	**Blood (pair of bottles)**	**Cerebro-spinal fluid (CSF)**	**Nasopharynx**	**Throat**	**General culture**	**Screen MRB**	**Urine**	**Faeces SSYC**	**Faeces *Clostridium difficile* (toxin)**	***Staphylococcus aureus***	***Streptococcus pneumoniae***	***Streptococcus pyogenes***	***Escherichia coli***	***Clostridium difficile* (toxinpositive)**
Borås	14 344	201	2 823	4 305	10 885	1 391	26 892	6 628	1 874	4489	682	779	7491	151
Eskilstuna (Unilabs)	8906	142	5 897	4 354	8 279	950	24 629	3 793	1 978	3728	665	903	678	241
Falun	15 404	391	3 069	1 722	10 217	3 816	26 836	3 816	1 829	4355	550	602	7 184	331
Gävle	11 212	187	2 071	1 152	9 450	2 048	23 183	3 470	2 191	3701	342	329	7 046	485
Göteborg	28 473	1 055	3 263	4 022	16 444	38 762	70 712	11 906	4 772	13058	799	1 065	17 892	NA
Halmstad	10 023	132	2190	2 169	8 826	33 081	24 050	4 435	1 836	3442	468	527	6 586	187
HS Stockholm	33 579	576	12 306	5 338	36 728	104 300	81 199	11 623	6 212	13449	1713	1 823	20 691	792
KS Stockholm	30 856	2 050	18 587	6 017	38 624	64 351	71 793	10 284	7 011	13224	2 089	1 490	18 688	263
Jönköping	16 211	185	3 689	3 616	14 370	16 667	36 558	7 080	2 950	6040	1110	650	9 610	530
Kalmar	9 458	148	3 391	2 461	7 853	2 185	25 677	3 966	1 471	4032	517	524	7 185	224
Karlskrona	5 330	115	1 148	1 858	5 220	1 240	15 435	2 671	1 558	1854	214	356	4 207	361
Karlstad	15 476	208	1 409	2 621	12 280	5 992	32 287	4 328	1 940	5661	286	812	8 049	143
Linköping	17 093	911	5 633	3 428	18 620	5 580	37 325	7 060	3 769	6484	788	812	9 540	822
Lund*	38 380	1 467	16 093	11 730	34 294	20 480	98 766	18 670	6 587	16470	3 015	2 402	25 451	710
Malmö	22 270	348	5 613	6 280	12 817	47 410	60 537	11 364	4 109	8422	1 656	1 399	15 670	589
Aleris Medilab	NP	NP	9 656	4 536	8 755	9 547	35 878	8 168	940	3811	1 043	1 055	8 178	42
St:Göran (Unilabs)	7 599	125	5 577	8 512	13 779	32 713	31 343	7 415	2 946	5388	560	946	9 840	168
Skövde (Unilabs)	9 402	189	6 784	4 170	10 203	3 953	39 735	5 016	3 336	4252	421	573	8 870	249
Sunderby, Luleå	8 196	142	1 694	2 993	8 084	1 734	26 530	3 292	1 421	3116	329	563	7 581	292
Sundsvall	9 969	127	2 357	1 722	7 784	6 204	26 414	3 839	1 796	3265	458	458	6 879	241
NÄL Trollhättan**	14 886	155	1 720	2 550	8 515	5 390	33 970	4 700	1 500	4630	420	510	9 880	170
Umeå	12 074	538	3 177	3 595	11 795	4 430	32 886	4 380	1 710	4082	459	614	9 102	114
Uppsala	17 682	723	4 977	2 331	14 374	7 403	31 379	5 441	3 074	5250	691	553	8 736	605
Visby	3 457	4	2 514	570	2 578	NP	6 786	1 087	746	1183	330	110	2 157	108
Västerås	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Växjö	6 404	77	2 211	2018	6 300	4 700	19 950	3 810	1 387	3 100	336	440	4944	192
Örebro	15 013	256	8 611	1 648	14 669	6 189	31 439	5 040	2 556	5 865	1 125	562	7 785	563
Östersund	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Total	381 697	10 452	136 460	95718	351 743	430 516	972 189	163 282	71 499	152 351	21 066	20 857	249 920	8 573

* Included is data from the Kristianstad laboratory which closed in May 2009.
** Former Uddevalla laboratory.
MRB = multiresistant bacteria
SSYC = Salmonella, Shigella, Yersinia and Campylobacter spp.

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 2009 is not available. Therefore, data from 2008 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.

Information about the incidence of mastoiditis and pneumonia is obtained from the register of inpatient diseases held by the National Board of Health and Welfare.

Data on antibiotic consumption in Swedish ICUs were obtained from Apotekens Service AB and expressed as defined daily doses (DDD) per 1000 occupied bed day (DDD1000). We used the annually updated DDD calculated by the WHO Collaborating Centre for Drug Statistics Methodology as the average maintenance dose per day in adults for the main indication of the drug. Data were analysed using the non-parametric test for trend across ordered groups and Spearman's rank correlation using STATA/SE 9.2(StataCorp LP, College Station, TX, USA) and SPSS version 11.5 (SPSS Inc., Chicago, IL, USA). Statistical significance was assumed if $P < 0.05$.

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/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/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 ad Welfare. Administrative data within hospital care include, among others, date of admission, date of discharge and length of stay. Since data for 2007 is not available until August denominator data from 2006 and sales

data from 2007 are used in some figures in this report. The number of admissions and patient-days in Swedish medical care 1997-2006 is shown in Appendix 2, Table App 2.3. The Swedish Association of Local Authorities and Regions keeps a searchable database at the web, http://www.skl.se/artikel.asp?A=3768&C=1801.

Appendix 4. Antibiotic susceptibility testing

The **agar dilution method** is the reference method in Swedish susceptibility testing to which other methods are compared. Clinical microbiology in Sweden has 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 SRGA-M. It is used as the routine method for susceptibility testing, and as a screening method which in some instances needs to be followed up by methods for gene detection (e.g. MRSA, VRE) and in other instances by MIC-determination using broth- or agar-dilution or with Etest (betalactam resistance in pneumococci, chromosomally mediated betalactam resistance in Haemophilus influenzae), and still in others by methods for enzyme detection (beta-lactamase detection in *Haemophilus influenzae*, *Neisseria gonorrhoeae and* others).

Phenotypic methods (disk diffusion or MIC) are performed on a basic medium for AST, ISA (IsoSensitest Agar) from Oxoid Ltd, UK. For this medium and the corresponding antibiotic paper disks, interpretive criteria for SIR-categorization are provided by the SRGA-M. The criteria are regularly updated and available through the web-site www.srga.org .

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 (every day, once a week) 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.srga.org) External quality control is often done by participation in UK-NEQAS and/or other international programs, whereas quality assurance is one of the features of the Swedish "100-strains 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 Infectious 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 carriage) with different antibiotic resistant pathogens are included in the list of notifiable diseases. *Streptococcus pneumoniae* with Penicillin G MIC > 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. 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, VRA and PNSP strains are sent to SMI for epidemiological typing using pulsed-field gel electrophoresis (PFGE). For MRSA from 1 July 2006 spa-typing replaced PFGE as the primary typing method.

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

The feed back of notification data is done monthly on SMI nternet homepage (http://www.smittskyddsinstitutet.se) and yearly in "Communicable Diseases in Sweden – the Yearly Report of the Department of Epidemiology" 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 29 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 are standardized through the combined work of the SRGA-M (Swedish Reference Group of Antibiotics – subcommittee on Methodology) 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 number 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 a web-based software (ResNet) will receive the 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 maps 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. The Resnet software also has the feature of displaying aggregated, quantitative data of invasive isolates which form the Swedish part of the EARSS network (see below).

EARSS

EARSS, funded by DG SANCO of the European Commission, is an international network of national surveillance systems, collecting comparable and validated antimicrobial susceptibility data for public health action. EARSS performs on-going surveillance of antimicrobial susceptibility 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.

Participation in EARSS was initially intended for member states of the European Union, also including Norway and Iceland, but in year 2000 six countries in eastern Europe were

included, and by 2003 28 countries provide susceptibility data regularly. Information about EARSS, as well as a database yielding information about the susceptibility results for each country, year and pathogen, is available through a web-site (www.earss.rivm.nl). During 2009 a transition of EARSS from RIVM in the Netherlands to ECDC in Stockholm is prepared and will be effective by 1st January 2010.

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

Although not perfect, the EARSS network of networks form a solid base for surveillance of resistance and is constantly extended and improved.

The participation from twentyone laboratories in Sweden is coordinated through the SMI, where electronic data collection, validation and verification of specific resistance mechanisms is performed. Sweden, because of its well organised network of clinical laboratories and high quality of routine susceptibility testing, is so far the largest contributor of national data to EARSS.

Surveillance of invasive isolates additional to EARSS data

Data on invasive isolates on all positive blood cultures were obtained from eleven laboratories that are using the same laboratory information system (ADBakt). Their total catchment population is 3.7 millions, thus representing more than 40% of the Swedish population. From these laboratories data for the pathogens specified by the EARSS network are retrieved, but also data on all other bacterial pathogens consecutively isolated from blood cultures. In the SWEDRES 2007-2009 data for Streptococcus pyogenes, Streptococcus agalactiae and Haemophilus influenzae are presented.

Sentinel surveillance

Susceptibility testing of gastrointestinal pathogens such as *Salmonella*, *Shigella*, *Campylobacter jejuni/coli* 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.

Appendix 6. Recent publications (2007-2009)

3. Use of antibiotics

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