SWEDRES 2003

A Report on Swedish Antibiotic Utilisation and Resistance in Human Medicine

STRAMA
The Swedish Strategic Programme for the Rational Use of Antimicrobial Agents

SMITTSKYDDSINSTITUTET
Swedish Institute for Infectious Disease Control

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

STRAMA
The Swedish Strategic Programme for the Rational Use of Antimicrobial Agents

STRAMA – The Swedish Strategic Programme for the Rational use of Antimicrobial Agents, was founded in 1995 and is supported by the Swedish Government since year 2000. A national steering committee with members from all relevant authorities and organisations collaborates with regional expert groups in every county.

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1. Preface

WELCOME to the second Swedish report combining results from the monitoring of antimicrobial resistance and antimicrobial usage in both human and veterinary medicine: SWEDRES and SVARM. It is today generally accepted that all use of antimicrobials in different sectors contributes to the development of resistance. This joint report will facilitate comparisons of resistance levels and incidence of use in the two areas. In Sweden human and veterinary medicine have collaborated and communicated over a number of years, not least within the Swedish Strategic Programme for The Rational Use of Antimicrobial Agents and Surveillance of Resistance (STRAMA). Based on this experience, we are convinced that collaboration and joint efforts between human and veterinary medicine are essential in order to counteract the threat that antimicrobial resistance poses to both human and animal health.

Data in this report indicate that the Swedish strategies in human and veterinary medicine have been successful in containing resistance. The general concept is to use antimicrobials only when needed, on prescription by a professional only, and that the choice of treatment is based on relevant information. Notwithstanding, some of the presented results in both veterinary and human fields are causes for concern. Examples on unfavourable development of resistance indicate that the antimicrobial arsenal available is becoming more and more limited. Further efforts must be made to prevent infectious diseases both in human and in veterinary medicine by other means.

Our hope is that this report will serve as a basis for policy recommendations and intervention strategies, and that it will increase our understanding of the dynamics of resistance. The ultimate goal is to preserve the effectiveness of available antimicrobials for man and animals.

2.1. Summary

SINCE SEVERAL YEARS there hase been a close collaboration in Sweden between human and veterinary medicine regarding anitbiotic resistance. The ultimate goal is to preserve the possibility for effective treatment of bacterial infections in humans and animals.

This second joint report SWEDRES/SVARM (available on www.sva.se) shows that, in both fields, the situation in Sweden is more favourable than in many other parts of the world. However, in both human and veterinary medicine there are trends that cause concern.

Use of antibiotics

In 2003 the total antibiotic sale (out-patient and hospital care) was 16.3 DDD/1000 inhabitants per day (DDD/1000/day) and in out-patient care 14.7 DDD/1000/day (13.0 excl methenamine). There has been a small reduction in the use of antibiotics in Sweden the last years. The total antibiotic sale was reduced by 0.5 DDD/1000/day between 2000 and 2003. The most notable change was the decreasing use of antibiotics against respiratory tract infections. The use of penicillin V, which is the most commonly prescribed antibiotic substance in Sweden, has decreased from 4.6 DDD/1000/day in out-patient care 2000, to 4.1 DDD/1000/day 2003. The sales numbers for other respiratory tract antibiotics; macrolides, tetracyclines and cephalosporins, were decreasing as well. This is probably caused by a reduced tendency for patients in Sweden to seek medical care for common colds.

A favourable trend was seen concerning treatment against urinary tract infections where the use of fluoroquinolones continued to decrease among women and the use of nitrofurantoin, on the other hand, increased. The worrying increase in the use of fluoroquinolones among older men seemed to have halted, although the total consumption of fluoroquinolones was still high compared to the other Nordic countries.

In the last years there has been an increase in the use of beta-lactamase resistant penicillins. One reason for this increase could probably be the ongoing epidemic of impetigo contagiosa, caused by *S. aureus* resistant to fucidic acid. Data show a seasonal increase in the use of beta-lactamase resistant penicillins among children.

Lincosamides is another group with increasing use where further analysis is needed.

Use of antifungals

The use of antifungals for systemic use against nail infections increased markedly during the first quarter of 2002 and has since then been continuously high. This was probably the result of a widespread marketing programme directed towards the general public, even though these drugs needs to be prescribed by a doctor. Whether the increased use of these drugs has influenced resistance against antifungals needs to be investigated.

Within hospital care the use of the new substances, voriconazole and caspofungin, continued to increase. The sales numbers of antifungals for systemic use (J02A) increased with 36% (0.015 DDD/1000/day) from 2000 to 2003.

Antibiotic resistance

From an international viewpoint Sweden has a comparatively low rate of infections caused by *Streptococcus pneumoniae* with reduced susceptibility to penicillin. Since 1996, infections and carriage due to *S. pneumoniae* with reduced susceptibility to penicillin (MIC ≥ 0.5 mg/L, PRP) have been notifiable by law. The number of PRP notifications in 2003 was stable compared to the previous year. A vast majority of the cases were detected by nasopharyngeal cultures. The highest incidence was seen in pre-school children, with a distinct seasonality (most cases in late autumn to early spring). Since 1996, there has been a decreasing trend in incidence, but this has been paralleled by a decreasing trend in numbers of cultures. In voluntary reports from the laboratories, a significant increasing trend was noted for resistance to other antibiotics (erythromycin, tetracycline and trimethoprim-sulfonamide), with resistance levels now twice as high as in the mid 1990s.

Also for methicillin resistant *Staphylococcus aureus* (MRSA), the Swedish incidence figures are comparatively low. A large outbreak in Göteborg in western Sweden in the late 1990s was curbed, but an increasing incidence in the Stockholm county reflects an ongoing outbreak since 2000. However, MRSA is a national problem with patients reported from all counties. Previously mainly being an imported disease, MRSA is now a domestic problem, with more than 75% of the cases infected in Sweden. Community-acquired MRSA is an increasing problem, and in almost half of the reported domestic cases in 2003 the infection was acquired outside hospitals and nursing homes. Almost all Swedish isolates since 2000 have been genetically typed with pulsed field gel electrophoresis (PFGE). The three most common types were identical or similar to the international clones UK E 15, DK E 97-1 and Berlin IV. In 2003, 0.8% of the invasive *S. aureus* isolates in the country have been MRSA.

Enterococcus faecium and *faecalis* with resistance to vancomycin (VRE) have also been notifiable since 2000. In 2003, the number of reported cases doubled to 45 from previous figures between 18 and 20 cases per year. The main part of this increase was due to hospital outbreaks in two counties, leading to extensive contact tracing. 2.2% of 231 invasive isolates of *E.faecium*, and 0 of 593 invasive isolates of *E. faecalis* were resistant to vancomycin in 2003. The corresponding figures for ampicillin resistance in 2003 was 76% and 0%, respectively.

Streptococcus pyogenes is one of the most important respiratory tract pathogens. Data from 10 years of surveillance of resistance indicated that tetracycline resistance, although still significant (13% in 2003), might show a trend of decreasing prevalence. Macrolide and lincosamide resistance (as exemplified by erythromycin and clindamycin) are still below 2% and 1%, respectively.

Escherichia coli, mainly derived from urinary tract infections, has been tested for commonly prescribed oral antibiotics for treatment of UTI. Resistance rates for ampicillin and trimethoprim showed a slow but steady increase during the years 1996-2003, reaching 24% and 15% in 2003, respectively. Ampicillin resistance among blood isolates of *E. coli*, was slightly higher (28.5%), but still lower than in most other European countries. Resistance to modern cephalosporins, by production of extended spectrum betalactamases (ESBL), or by other resistance mechanisms, was still below 1%, as was resistance to aminoglycosides. Resistance to fluoroquinolones (FQ) was screened for by using nalidixic acid on urinary isolates and by confirmation with ciprofloxacin on blood isolates. The frequencies of nalidixic acid resistance (FQ I+R) and ciprofloxacin I+R were almost the same, 8.1% and 8.3%, respectively.

In 2003, *Pseudomonas aeruginosa* was included in the surveillance programme. Average resistance rates to ciprofloxacin of 14% and to carbapenems of 5% were of greatest concern.

Resistance rates in *Neisseria gonorrhoeae*, derived from a subset of isolates from notified cases, were alarmingly high for fluoroquinolones (ciprofloxacin), the drug of choice for treatment, but also for penicillins and tetracycline.

In *Mycobacterium tuberculosis*, resistance to isoniazid was most common (7.4%). Few multidrug resistant isolates were found among Swedish patients.

National and regional projects

Infections in day care centers (DCC) are common and create large costs for the society. Many of these infections lead to antibiotic treatment. A large national survey was performed at 338 randomly selected Swedish day-care centres to identify factors that may be of importance for spread of infections in this settings. In 35% of the DCCs recommendations from the National Board of Health and Welfare were used. Routines for when children should stay at home and for handwashing of children existed in more than 90% of the DCCs. Routines for handwashing for the personell was lacking in 48% and hygienic routines for diaper changing was lacking in 22%. The results of this survey will be compared with the rate of infections in the children.

As part of an EU-funded project, Sweden participated in a study on self-medication with antibiotics. The objective was to assess the prevalence of self-medication and self-reported use of prescribed antibiotics, as well as storage of antibiotics in homes. 1 000 randomly selected subjects were asked to give information. The response rate was 70%. Use of antibiotics during the last year was reported by 17%. Four per cent stated that they at present had at least one antibiotic at home. In all cases except three, the antibiotic was reported to be obtained with a doctors prescription. In those three cases the antibiotics were leftovers from previous treatment or given by a friend or relative.

Weekly antibiotic use in outpatients were studied in comparison with verified influenza cases over five seasons. A co-incidental relationship between the peaks of influenza activity and antibiotic use was found, especially for older age groups. However, there were no obvious differences in the total amounts dispensed over the years that could be related to influenza activity.

Antibiotic use in hospitals was studied in a large point prevalence study comprising 54 hospitals and more than 13 500 admitted patients. Antibiotic treatment was evaluated in relation to the diagnosis and indication. 31% of the admitted patients were treated with antimicrobials. The distribution of therapy reasons were; community acquired infections in 52,4%, hospital acquired infections in 28,2% and prophylaxis in 19,4%. The study describes overuse of cephalosporins in community acquired pneumonia, fluoroquinolones in urinary tract infections and too long duration of prophylaxis.

A study has also been conducted to describe the treatment of infectious diseases in elderly in nursing homes. During three months, the nurses at 60 participating nursing homes in Sweden registered each infection that led to a consultation with a physician. 78% of the registered infections were treated with antibiotics, most commonly with quiniolones (22% of treatments) and trimethoprim (16%). Infections in the urinary tract, skin and soft tissue and respiratory tract were responsible for 55%, 16% and 14% respectively.

2.2. Sammanfattning

Användning av antibiotika

År 2003 var den sammanlagda försäljningen av antibiotika (öppenvård och slutenvård) 16.3 definierade dygnsdoser/1000 invånare och dag (DDD/1000/dag) och enbart i öppenvård 14.7 DDD/1000/dag (13.0 exkl methenamin). Försäljningen av antibiotika i Sverige har minskat de senaste åren, även om nedgången är ganska liten. Den totala försäljningen var 0.5 DDD/1000/dag lägre år 2003 jämfört med 2000. Den mest märkbara minskningen är bland antibiotika som används vid luftvägsinfektioner. Användningen av penicillin V, som är det mest förskrivna medlet i Sverige, sjönk från 4.6 DDD/1000/dag år 2000 till 4.1 DDD/1000/dag 2003. Försäljningssiffrorna för andra luftvägsantibiotika; makrolider, tetracykliner och cefalosporiner, minskar också. Den här minskningen beror troligtvis på att man, i mindre utsträckning, söker läkarvård vid vanliga förkylningar.

Beträffande behandling av urinvägsinfektioner bland kvinnor ses en fördelaktig trend där användningen av kinoloner bland kvinnor fortsätter att minska och användningen av nitrofurantoin i stället ökar. Trenden med ökande användning av kinoloner bland äldre män verkar ha avstannat, även om användningen av kinoloner fortfarande är hög jämfört med övriga nordiska länder.

Användningen av penicilliner resistenta mot betalaktamas har ökat de senaste åren. En möjlig anledning till ökningen är den pågående epidemin med impetigo contagiosa, orsakad av *S. aureus* resistenta mot fucidinsyra. Försäljningssiffrorna visar en säsongsbunden ökning av betalaktamas-resistenta penicilliner bland barn upp till 19 år.

Linkosamider är en annan grupp antibiotika som ökar och där vidare undersökningar krävs för att finna möjliga orsaker till detta.

Användning av antimykotika

Användningen av antimykotika för systemiskt bruk mot nagelsvamp ökade märkbart under det första kvartalet 2002 och ligger kvar på den nivån. Detta är troligen en följd av en landsomfattande reklamkampanj riktad till allmänheten, trots att dessa medel måste förskrivas på recept. I vilken grad den ökade användningen av dessa medel påverkar resistensen mot antimykotika är oklart och kräver vidare utredning.

Inom slutenvården fortsätter användningen av de nya substanserna, vorikonazol och caspofungin, att öka. Användningen av antimykotika för systemiskt bruk (J02A) ökade med 36% (0.015 DDD/1000/day) från år 2000 till 2003.

Antibiotikaresistens

Ur internationell synvinkel har Sverige en låg andel infektioner orsakade av *Streptococcus pneumoniae* med nedsatt känslighet för penicillin. Sedan 1996 är infektioner och bärarskap av *S. pneumoniae* med nedsatt känslighet mot penicillin (MIC = ≥0.5 mg/L, PRP) anmälningspliktiga enligt lag. Antalet anmälningar av PRP 2003 var stabila jämfört med 2002. En övervägande del av dessa fall upptäcktes vid nasofarynxodling. Den högsta förekomsten sågs bland gruppen förskolebarn och med tydlig årstidsvariation (de flesta fallen under sen höst till tidig vår). Sedan 1996 har en sjunkande trend noterats i antal fall parallellt med färre antal tagna odlingar. I laboratoriernas frivilliga rapportering noterades en signifikant ökning av resistens mot andra antibiotika (erytromycin, tetracyklin och trimetoprim-sulfa), med resistensnivåer dubbelt så höga som i mitten av 90-talet.

Antal fall av meticillinresistenta *Staphylococcus aureus* (MRSA) i Sverige är också jämförbart få. Ett stort utbrott i slutet av 90-talet i Göteborg i västra Sverige har bromsats, men sedan 2000 tyder en ökning i antal fall i Stockholms län på ett pågående utbrott. Dock är MRSA ett nationellt problem med rapporterade fall från alla län. Efter att tidigare enbart varit en importerad smitta är MRSA nu ett inhemskt problem där mer än 75% av fallen infekterats i Sverige. Samhällsförvärvad förekomst av MRSA ökar och i nästan hälften av de inhemskt rapporterade fallen var infektionen förvärvad utanför sjukhus eller äldreboende. Nästan alla svenska isolat sedan 2000 har typats med pulsfältsgelelektrofores (PFGE) för genetisk information. De tre vanligaste typerna var identiska eller liknande de internationellt beskrivna typerna UK E15, DK E 97-1 och Berlin IV. År 2003 var 0,8% av landets invasiva *S. aureus* isolat MRSA.

Enterococcus faecium och *faecalis*, resistenta mot vankomycin, är anmälningspliktiga sedan 2000. 2003 fördubblades antalet rapporterade fall till 45 från att tidigare ha utgjort 18 till 20 fall per år. Den huvudsakliga delen av denna ökning härrörde från sjukhusutbrott i två län vilka ledde till en omfattande kontaktspårning. 2.2% av 231 invasiva isolat av *E. faecium* och 0 av 593 invasiva isolat av *E. faecalis* var resistenta mot vankomycin 2003. Motsvarande siffra för ampicillin resistens var 76% respektive 0%.

Streptococcus pyogenes är en av de viktigaste luftvägspatogenerna. Data från 10 års övervakning visar att tetracyklinresistensen fortfarande är omfattande (13% år 2003) även om en tendens till minskning kan ses. Makrolid- och linkosamidresistensen är fortfarande låg, 2 respektive 1%.

Escherichia coli, i huvudsak härrörande från urinvägsinfektioner, har testats för de vanligast förskrivna orala medlen vid behandling av urinvägsinfektioner. Resistensnivåerna för ampicillin och trimetoprim visar en långsam men stadig ökning under åren 1996-2003, och nådde 2003 24 respektive 15%. Ampicillin-resistens hos *E. coli* bland invasiva blodisolat var något högre (28,5%) men fortfarande lägre än i de flesta andra europeiska länder. Resistens mot nya cefalosporiner, orsakad av betalaktamasproduktion (ESBL) eller andra mekanismer, var fortfarande under 1% vilket också gällde för resistens mot

aminoglykosider. Resistens mot fluorokinoloner testades med nalidixinsyra på urinisolat och med ciprofloxacin på blodisolat. Frekvensen resistens mot nalidixinsyra (R) respektive ciprofloxacin (I+R) var ungefär densamma; 8.1 och 8,3%.

2003 inkluderades *Pseudomonas aeruginosa* i övervakningsprogrammet. De genomsnittliga värdena 14% ciprofloxacinresistens och 5% karbapenemresistens var mest anmärkningsvärda.

Resistenssiffror för *Neisseria gonorrhoeae* är baserade endast på en del av de stammar som anmälts enligt Smittskyddslagen. Resistens mot ciprofloxacin, som är förstahandsval vid behandling, var alarmerande hög, liksom också penicillin- och tetracyklinresistens.

För *Mycobacterium tuberculosis* var resistens mot isoniazid vanligast (7.4%). Ett fåtal multiresistenta isolat har hittats bland svenska patienter.

Nationella och regionala projekt

Infektioner på daghem är vanliga och orsakar stora kostnader för samhället. Många av dessa infektioner resulterar också i antibiotikabehandling. En nationell studie genomfördes på 338 slumpvis utvalda daghem i Sverige för att identifiera vilka faktorer som påverkar smittspridning i denna miljö. 35% av daghemmen använde riktlinjer utgivna av Socialstyrelsen. Rutiner för när barnen ska vara hemma, när handtvätt ska ske fanns på fler än 90% av daghemmen. Rutiner för handtvätt hos personalen saknades i 48% och hygienrutiner för blöjbyte saknades i 22%. Resultatet av denna studie kommer att jämföras med antalet infektioner hos barnen.

Sverige har deltagit i en EU-studie kring självmedicinering med antibiotika. Målet med studien var att bedöma förekomsten av självmedicinering med antibiotika och tillgången till antibiotika i hemmet. 1 000 slumpvis utvalda personer tillfrågades. Svarsfrekvensen var 70%. 17% rapporterade användning av antibiotika det senaste året. 4% uppgav att de för tillfället hade minst ett antibiotikum hemma. I alla fall utom tre var medlet erhållet via läkarordination. Dessa tre uppgav att medlet var överbliven från tidigare behandling eller tillhandahållits av vän eller släkting.

Veckovis antibiotikaförbrukning inom öppenvård har studerats i jämförelse med verifierade influensafall över fem säsonger. Ett tidsmässigt samband mellan influensatopp och antibiotikaanvändning kunde ses, särskilt i de äldre åldersgrupperna. Över åren var det emellertid ingen skillnad i den totala antibiotikaförskrivningen som kunde relateras till influensaaktiviteten.

Antibiotikaanvändning inom slutenvård studerades i en stor punktprevalensstudie på 54 sjukhus och mer än 13 500 patienter. Antibiotikabehandlingen bedömdes i förhållande till diagnos och indikation. 31% av de intagna patienterna var behandlade med antibiotika. Fördelningen av terapiorsaker var: samhällsförvärvade infektioner 52,4%, sjukhusförvärvade infektioner 28,2% och profylax 19,4%. Studien vittnar om överanvändning av cefalosporiner vid samhällsförvärvad pneumoni, fluourokinoloner vid urinvägsinfektioner och för lång profylaxbehandling.

En studie har utförts för att kartlägga behandlingen av infektioner hos äldre på sjukhem. Under 3 månader har sköterskor vid 60 äldreboenden registrerat alla infektioner som lett till en läkarkonsultation. 78% av de registrerade infektionerna blev behandlade med antibiotika, oftast med fluourokinoloner (22%) och trimetoprim (16%). Av alla infektioner var 55% urinvägsinfektioner, 16% hud- och mjukdelar och 14% luftvägar.

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3. Use of antimicrobials

3.1. Use of antibiotics

Background

In 2003 a new system for retrieving data of drug sales came into use in Sweden. This new database includes data from 2000 (see Appendix 3) which complicates long-term analysis. This report includes data for the period 2000-2003. For historical comparison we refer to Swedres 2001 and 2002.

Who prescribes antibiotics in Sweden?

A few years ago a coding system was introduced in Sweden to make it possible to derive a redeemed prescription to a certain health care centre, ward or even doctor. The reason was mainly to follow the costs but the system can also be used to follow, for instance, the prescriptions of antibiotics. According to data received from the National board of health and welfare more than 90% of the prescriptions were coded in 14 out of 21 counties. With data from these counties it is possible to calculate to which extent general practitioners, other specialists (mainly out-patient care in hospitals) and dentists prescribes antibiotics. General practitioners accounts for approximately 60% of the antibiotic prescriptions, other specialists almost 30% and dentists 5%. The total antibiotic sale in Sweden 2000-2003, out-patient and hospital care, was 16.8, 16.8, 16.4 and 16.3 DDD/1000 inhabitants per day (DDD/1000/day) respectively. Below, the use of antibiotics is presented as out-patient care and hospital care separately.

Out-patient care

In 2000 the WHO classified methenamine as an antibacterial. Since the substance is of no interest regarding resistance the amount prescribed will be separated from the total antibiotic consumption in this report. There has been a small reduction in the use of antibiotics in out-patient care the last years. The antibiotic sale 2000-2003, excluding methenamine, was 13.7, 13.8, 13.3 and 13.0 DDD/1000/day respectively (Figure 3.1).

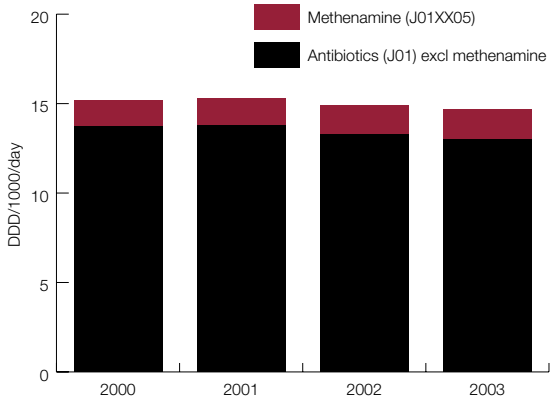

Figure 3.1. Antibiotics, out-patient care in Sweden (J01), DDD/1000/day, 2000-2003.

The most notable change is the decreasing use of antibiotics against respiratory tract infections. The use of beta-lactamase sensitive penicillins, tetracyclines, macrolides and cephalosporins, has decreased although to a different extent. This development is probably caused by a reduced tendency for patients to seek medical care for common colds. The largest decrease was seen for beta-lactamase sensitive penicillins when expressed in total amounts. The greatest relative reduction (%) was seen for macrolides and cephalosporins. The increase of beta-lactamase resistant penicillins that was noted in 2002 continued in 2003 and will be further analysed below. The use of lincosamides (clindamycin) and nitrofurantoin also increased (Figures 3.2 and 3.3).

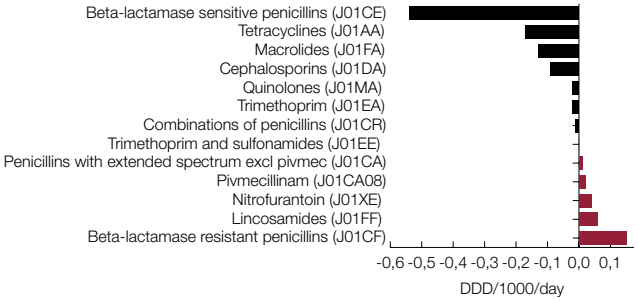

Figure 3.2. Out-patient care, changes in consumption 2003 compared to 2000, DDD/1000/day

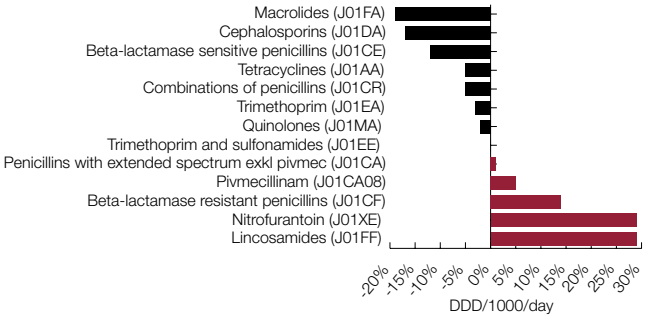

Figure 3.3. Out-patient care, percent change in consumption 2003 compared to 2000.

In Table 3.1 and 3.2 figures for different groups of antibiotics, age groups and sex are presented and some comments follow below. According to Table 3.1 the use of tetracyclines is highest (DDD) for women in the age group 20-59 years. When dividing data in smaller age groups it turns out that women 20-24 years old accounts for the highest use with 4.8 DDD/1000/day 2003. Among men the age group 15-19 has the highest comsumption, 6.2 DDD/1000/day. This most probably reflects the treatment of acne vulgaris.

The highest prescription rate of penicillins with extended spectrum is seen for women >80 years. This is mostly due to the prescription of pivmecillinam (J01CA08), against urinary

tract infections, that was 2.8 DDD/1000/day for women >80 years old 2003.

Beta-lactamase sensitive penicillins includes penicillin V and penicillin G. Penicillin V is the most prescribed substance in Sweden and represents about 30% of all agents sold in out-patient care (31% 2000, reduced to 28% 2003). There has been a reduction in all age groups, but most notable for patients <60. Most prescriptions are given to children 0-6 years old.

The number of prescriptions for combinations of penicillins (amoxicillin with clavulanic acid) decreases in the age group 0-6 years. There is also a small reduction in number of prescriptions for cephalosporins, except for women in the youngest ages. The number of prescriptions of trimethoprim decreases slightly among women >80 years and is probably replaced by nitrofurantoin which increases in the same age group during the period.

As for the other agents against respiratory tract infections, the sales number for macrolides decreases. There is a slight change which is most notable among number of prescriptions for the younger age groups, both girls and boys.

The use of lincosamides increases, most notable among the elderly. The reason for this could be the treatments of leg ulcers but needs further analysis.

In Swedres 2002 a decrease in the use of fluoroquinolones among women was described as well as an increase among older men. There is still an ongoing decreasing trend among women and the increase among older men seem to have halted, although the total consumption of fluoroquinolones is still high compared to the other Nordic countries.

Table 3.1. Antibiotics, out-patient care, different groups of antibiotics and different age-groups, women and men, 2000-2003 DDD/1000/day.

	Women DDD/1000/day				Men DDD/1000/day			
Age-group (years)	2000	2001	2002	2003	2000	2001	2002	2003
Tetracyclines (J01AA)								
0-6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7-19	2.2	2.0	2.0	2.1	2.3	2.2	2.2	2.4
20-59	4.3	4.2	4.0	4.0	2.9	2.9	2.7	2.7
60-79	4.0	3.9	3.8	3.9	3.9	3.8	3.6	3.7
80-	2.8	2.6	2.6	2.6	3.9	3.7	3.5	3.5
All ages	3.5	3.4	3.3	3.3	2.7	2.7	2.6	2.6
Penicillins with extended spectrum (J01CA)								
0-6	1.4	1.4	1.3	1.2	1.5	1.5	1.5	1.4
7-19	0.6	0.7	0.7	0.7	0.3	0.4	0.4	0.3
20-59	1.4	1.4	1.4	1.4	0.6	0.6	0.6	0.5
60-79	2.3	2.3	2.4	2.5	1.4	1.5	1.5	1.5
80-	3.8	4.0	4.1	4.1	2.6	2.7	2.7	2.7
All ages	1.6	1.6	1.6	1.6	0.8	0.9	0.8	0.8
Beta-lactamase sensitive penicillins (J01CE)								
0-6	4.3	4.2	3.8	3.5	4.8	4.8	4.4	4.0
7-19	4.4	4.6	4.1	3.7	3.7	4.1	3.6	3.2
20-59	5.8	5.8	5.4	5.0	4.2	4.1	3.8	3.6
60-79	4.3	4.1	4.1	4.3	3.9	3.7	3.8	3.9
80-	3.5	3.4	3.3	3.2	4.1	3.9	3.7	3.7
All ages	5.0	5.0	4.7	4.5	4.1	4.1	3.8	3.6
Beta-lactamase resistant penicillins (J01CF)								
0-6	0.2	0.2	0.3	0.4	0.2	0.2	0.4	0.4
7-19	0.5	0.5	0.6	0.7	0.6	0.6	0.8	0.8
20-59	0.7	0.7	0.8	0.8	0.9	0.9	1.0	1.0
60-79	1.6	1.7	1.7	1.7	2.1	2.2	2.3	2.3
80-	4.1	4.4	4.5	4.4	4.5	4.8	5.0	4.9
All ages	1.0	1.1	1.2	1.1	1.1	1.2	1.2	1.3
Combinations of penicillins (J01CR)								
0-6	0.8	0.7	0.7	0.7	1.0	0.9	0.9	0.9
7-19	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
20-59	0.2	0.2	0.2	0.2	0.1	0.1	0.1	0.1
60-79	0.1	0.1	0.2	0.2	0.1	0.1	0.2	0.2
80-	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
All ages	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2

Cephalosporins (J01DA)								
0-6	0.6	0.5	0.6	0.6	0.6	0.6	0.6	0.6
7-19	0.4	0.4	0.4	0.4	0.3	0.3	0.3	0.3
20-59	0.5	0.5	0.4	0.4	0.3	0.3	0.3	0.2
60-79	0.6	0.5	0.5	0.5	0.6	0.5	0.5	0.5
80-	0.9	0.9	0.8	0.8	1.1	1.0	1.0	0.9
All ages	0.5	0.5	0.5	0.5	0.4	0.4	0.4	0.3
Trimethoprim (J01EA)								
0-6	0.2	0.2	0.2	0.2	0.1	0.1	0.1	0.1
7-19	0.4	0.4	0.4	0.4	0.0	0.0	0.0	0.0
20-59	0.7	0.7	0.7	0.7	0.1	0.1	0.1	0.1
60-79	1.5	1.4	1.4	1.4	0.5	0.5	0.5	0.5
80-	3.4	3.3	3.2	3.1	1.8	1.8	1.7	1.7
All ages	0.9	0.9	0.9	0.9	0.2	0.2	0.2	0.2
Trimethoprim and sulfonamides (J01EE)								
0-6	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.1
7-19	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
20-59	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
60-79	0.2	0.2	0.2	0.2	0.4	0.4	0.4	0.4
80-	0.2	0.2	0.2	0.2	0.5	0.5	0.5	0.5
All ages	0.1	0.1	0.1	0.1	0.2	0.2	0.2	0.2
Macrolides (J01FA)								
0-6	0.9	1.0	0.9	0.7	1.0	1.1	1.0	0.8
7-19	0.9	1.0	0.8	0.7	0.9	0.9	0.7	0.6
20-59	0.9	0.9	0.8	0.8	0.5	0.5	0.4	0.4
60-79	0.6	0.6	0.6	0.5	0.5	0.4	0.4	0.4
80-	0.4	0.4	0.4	0.3	0.4	0.4	0.4	0.3
All ages	0.8	0.8	0.7	0.7	0.6	0.6	0.5	0.5
Lincosamides (J01FF)								
0-6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7-19	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
20-59	0.2	0.2	0.2	0.3	0.2	0.2	0.2	0.2
60-79	0.3	0.3	0.4	0.4	0.4	0.5	0.5	0.6
80-	0.5	0.6	0.6	0.6	0.6	0.7	0.7	0.8
All ages	0.2	0.2	0.2	0.3	0.2	0.2	0.2	0.3
Fluoroquinolones (J01MA)								
0-6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7-19	0.2	0.2	0.2	0.2	0.1	0.1	0.1	0.1
20-59	0.8	0.8	0.8	0.8	0.8	0.9	0.8	0.9
60-79	1.8	1.7	1.6	1.6	2.4	2.5	2.5	2.6
80-	3.2	3.0	2.8	2.6	4.7	4.8	4.7	4.6
All ages	1.0	1.0	0.9	0.9	1.0	1.1	1.1	1.1
Nitrofurantoin (J01XE)								
0-6	0.1	0.1	0.1	0.1	0.0	0.0	0.0	0.0
7-19	0.2	0.2	0.2	0.2	0.0	0.0	0.0	0.0
20-59	0.2	0.3	0.3	0.3	0.0	0.0	0.0	0.0
60-79	0.3	0.3	0.3	0.4	0.1	0.1	0.1	0.1
80-	0.5	0.5	0.6	0.7	0.3	0.3	0.4	0.4
All ages	0.2	0.3	0.3	0.3	0.0	0.0	0.0	0.0
All agents (J01 excl methenamine)								
0-6	8.7	8.6	8.2	7.5	9.5	9.5	9.0	8.4
7-19	10.1	10.4	9.9	9.4	8.5	9.0	8.6	8.2
20-59	15.9	15.9	15.2	14.6	10.6	10.6	10.1	9.9
60-79	17.5	17.3	17.1	17.5	16.5	16.4	16.4	16.7
80-	23.5	23.5	23.2	22.8	24.8	24.9	24.5	24.2
All ages	15.2	15.2	14.7	14.4	11.6	11.7	11.3	11.1

Table 3.2. Antibiotics, out-patient care, different groups of antibiotics and different age-groups, women and men, 2000-2003, prescriptions/1000/inh/day.

	Women prescriptions/1000/year				Men prescriptions/1000/year			
Age group (years)	2000	2001	2002	2003	2000	2001	2002	2003
				Tetracyclines (J01AA)				
0-6	0	0	0	0	0	0	0	0
7-19	27	25	24	25	25	25	23	25
20-59	91	91	82	78	57	58	52	50
60-79	104	101	97	99	91	87	82	82
80-	79	74	71	72	103	98	91	90
All ages	75	75	69	67	54	54	50	49
				Penicillins with extended spectrum (J01CA)				
0-6	94	94	93	85	100	101	100	96
7-19	27	31	29	27	13	15	14	12
20-59	48	51	51	50	15	16	15	14
60-79	83	87	90	93	43	43	44	45
80-	160	168	172	171	86	89	86	84
All ages	62	65	65	65	29	30	29	28
				Beta-lactamase sensitive penicillins (J01CE)				
0-6	387	380	353	322	429	427	393	364
7-19	195	206	180	161	168	181	158	138
20-59	154	152	140	131	106	105	97	90
60-79	107	103	102	106	95	90	90	92
80-	99	97	90	85	112	111	100	97
All ages	166	165	151	142	141	141	129	120
				Beta-lactamase resistant penicillins (J01CF)				
0-6	18	23	34	37	20	25	37	39
7-19	22	25	32	33	26	29	37	38
20-59	26	28	30	30	30	32	33	34
60-79	47	48	50	50	56	59	62	62
80-	121	129	130	128	123	132	134	133
All ages	35	37	41	41	36	39	43	43
				Combinations of penicillins (J01CR)				
0-6	66	56	53	48	80	71	67	62
7-19	8	9	8	6	8	9	8	7
20-59	5	5	4	4	3	3	3	3
60-79	3	3	3	3	3	3	3	3
80-	2	3	2	2	3	5	4	3
All ages	10	9	8	7	10	9	9	8
				Cephalosporins (J01DA)				
0-6	50	51	53	55	55	54	54	55
7-19	26	27	27	27	20	22	22	22
20-59	27	26	24	23	15	14	14	13
60-79	28	26	26	26	27	25	24	24
80-	50	49	46	45	57	53	51	48
All ages	30	29	29	28	23	22	21	21
				Trimethoprim (J01EA)				
0-6	22	22	22	23	8	8	8	8
7-19	25	25	25	25	1	2	1	2
20-59	39	39	39	38	3	3	3	3
60-79	75	74	73	73	21	20	20	20
80-	193	192	187	182	89	86	84	83
All ages	52	52	51	51	9	9	9	9

Trimethoprim and sulfonamides (J01EE)								
0-6	27	25	23	23	20	19	18	17
7-19	6	6	6	5	4	4	3	3
20-59	3	3	3	3	3	3	3	3
60-79	5	4	5	5	9	9	10	10
80-	7	8	7	7	18	18	19	18
All ages	6	6	5	5	6	6	6	6
Macrolides (J01FA)								
0-6	44	47	41	34	48	52	45	38
7-19	28	31	25	21	26	28	23	18
20-59	28	29	26	23	14	15	13	12
60-79	19	19	18	17	13	13	12	11
80-	13	12	11	10	12	12	11	9
All ages	27	28	25	22	19	20	17	15
Lincosamides (J01FF)								
0-6	4	4	5	5	4	4	6	6
7-19	6	7	7	8	5	6	6	6
20-59	11	12	13	14	8	9	9	10
60-79	14	16	17	20	14	16	18	21
80-	24	25	27	29	22	28	28	32
All ages	11	12	13	15	9	10	11	12
Fluoroquinolones (J01MA)								
0-6	1	1	1	1	1	1	1	1
7-19	11	11	10	9	3	3	3	3
20-59	48	47	44	40	28	29	29	30
60-79	98	93	88	83	98	99	100	102
80-	200	185	169	152	231	231	222	212
All ages	57	55	51	48	40	41	41	42
Nitrofurantoin (J01XE)								
0-6	11	12	11	11	3	3	3	3
7-19	8	8	8	8	1	1	1	1
20-59	9	10	12	13	0	0	0	0
60-79	9	10	12	14	3	3	4	4
80-	19	24	29	33	12	12	15	15
All ages	10	11	12	14	2	2	2	2
All agents (J01 excl methenamine)								
0-6	724	715	690	643	770	767	733	690
7-19	391	414	384	357	300	325	301	274
20-59	492	494	469	449	284	288	273	263
60-79	599	591	585	593	477	472	471	480
80-	979	974	947	922	875	881	851	829
All ages	544	546	524	505	378	383	367	354

In the last years there has been an increase in the use of beta-lactamase resistant penicillins. As seen in Figure 3.4 this increase occurred in almost all Swedish counties, expressed as DDD/1000/day. These figures can be interpreted as an increase in use of dose. Since the number DDDs/prescription did not increase, a change in dose seems unlikely (Figure 3.5).

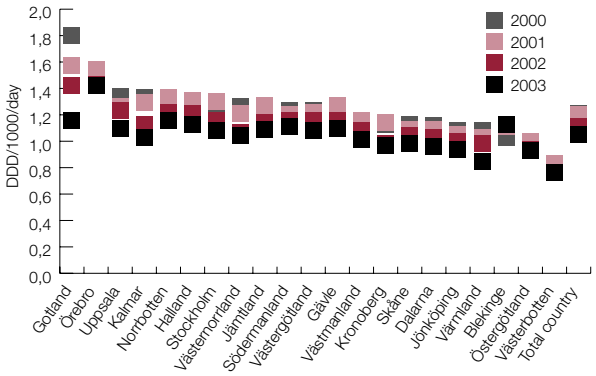

Figure 3.4. Swedish counties, beta-lactamase resistant penicillins (J01CF), DDD/1000/day, 2000-2003. The counties are sorted after the highest use 2003. Data is standardized to minimize differences in age and sex in the population.

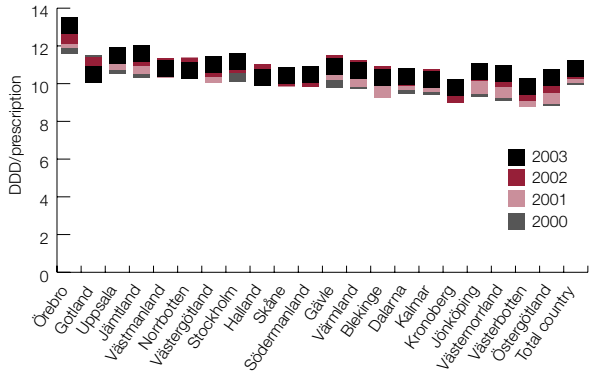

Figure 3.5. Swedish counties, beta-lactamase resistant penicillins (J01CF), DDD/prescription, 2000-2003. The counties are sorted after the highest use 2003.

One reason for this increase could probably be the ongoing epidemic of impetigo contagiosa caused by *S. aureus* resistant to fusidic acid. There is an obvious increase in the age groups 0-4, 5-9 and 10-14 years, with a peak in August each year, when impetigo can be expected to increase since the children start day care centres and school again after the summer (Figure 3.6).

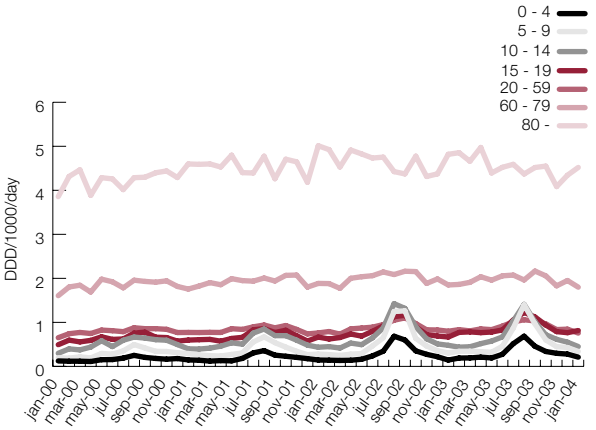

Figure 3.6. Beta-lactamase resistant penicillins (J01CF), out-patient care, per month 2000-2003, different age groups.

Among antibiotics used for urinary tract infections nitrofurantoin represents the greatest difference between 2000 and 2003, an increase of 29%, and the relative proportion between pivmecillinam, nitrofurantoin and trimethoprim was slightly affected by this (Figure 3.7 and 3.8). Note that the total amount of DDD for these substances against urinary tract infections is about six times larger for women than for men.

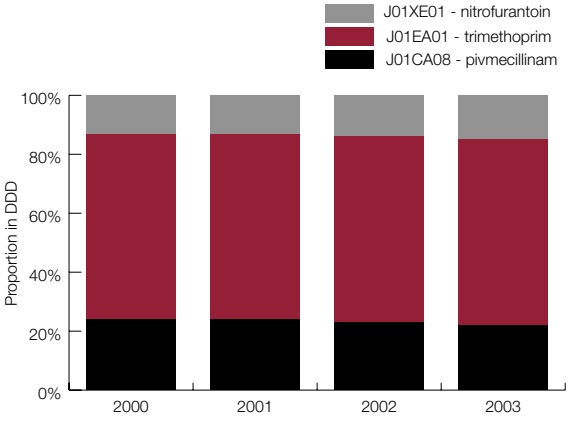

Figure 3.7. Proportion of pivmecillinam, nitrofurantoin and trimethoprim, DDD, men in out patient care, 2000-2003 Sweden.

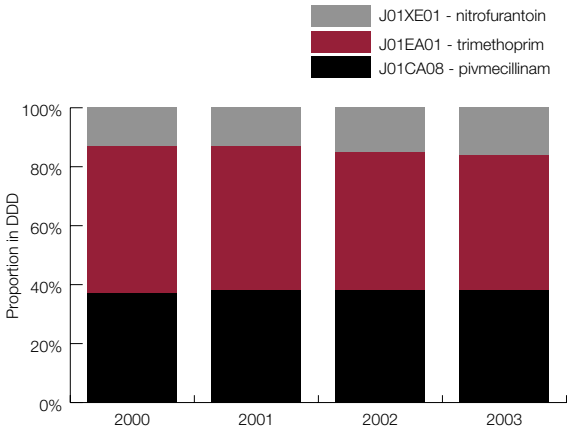

Figure 3.8. Proportion of pivmecillinam, nitrofurantoin and trimethoprim, DDD, women in out-patient care, 2000-2003 Sweden.

Hospital care

The antibiotic consumption (J01 excl methenamine) in hospital care has been constant during the period 2000-2003; 1.3 DDD/1000/day. However, slight changes in use are seen for different groups of antibiotics and penicillins with extended spectrum accounts for the greatest increase, followed by beta-lactamase resistant pencillins (Figure 3.9).

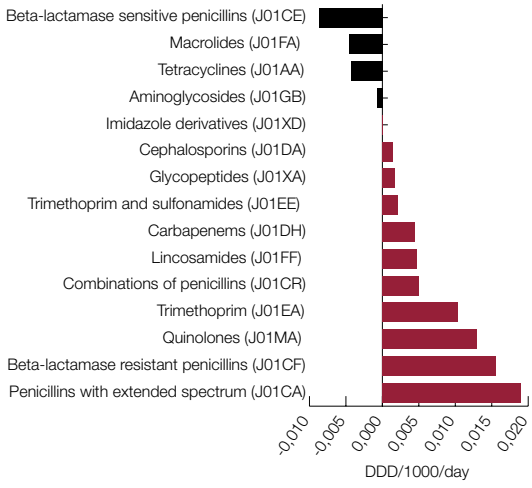

Figure 3.9. Antibiotics (J01) hospital care, changes, DDD/1000/day, 2003 compared to 2000.

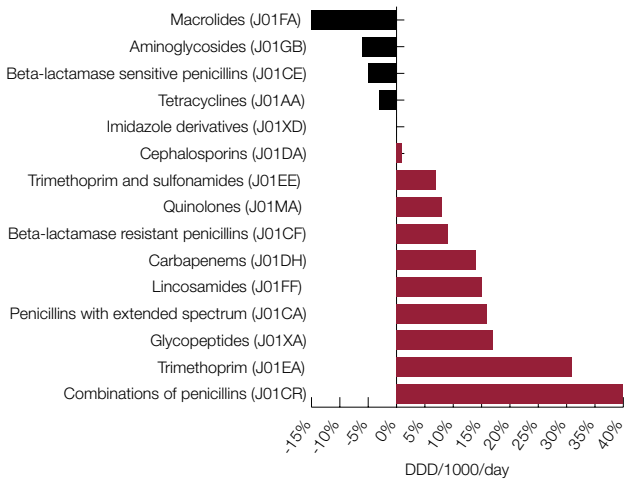

Figure 3.10. Antibiotics (J01) hospital care, percent changes, DDD/1000/day, 2003 compared to 2000.

Linezolid was introduced on the Swedish market in 2001 and in 2003 the use of it was 0.0007 DDD/1000/day, almost as much as for teicoplanin (0.0011) (Figure 3.11). The increase of the substances for treating MRSA, vancomycin, teicoplanin and linezolid, is shown in Figure 3.11.

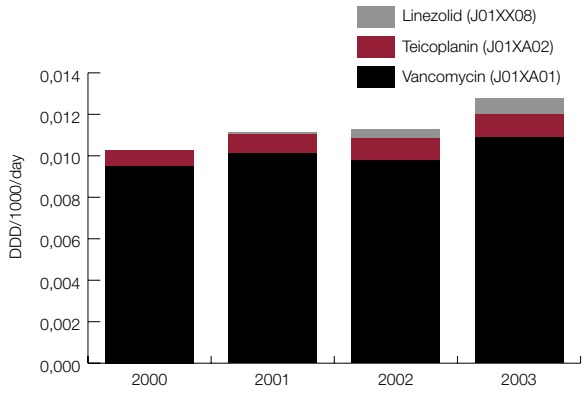

Figure 3.11. Vancomycin, teicoplanin and linezolid, DDD/1000/day in hospital care, 2000-2003.

ESAC

Sweden participates in the European Surveillance of Antimicrobial Consumption (ESAC) project, an international network granted by the European Commission. Sales statistic data have been collected for 31 countries retrospectively from 1997 to 2001 and after that prospectively. The ESAC project aims to develop a data collection system allowing to produce comprehensive national data on volume of antibiotic consumption in ambulatory and in hospital care. There is a wide variation in the prescription patterns between different European countries as can be seen in Figure 3.12 where valid out-patient data from 21 countries for 2001 are presented.

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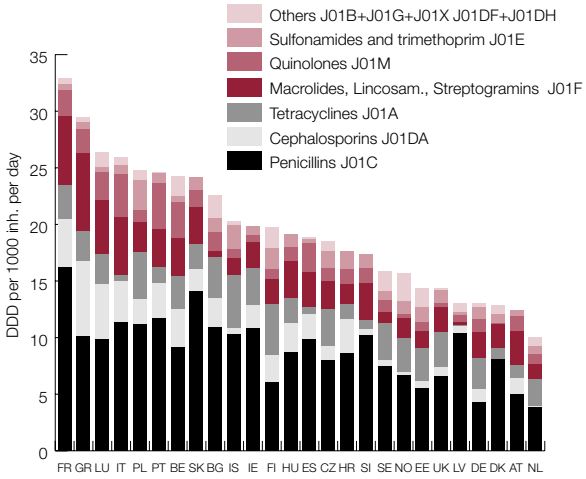

Figure 3.12. Total out-patient antibiotic use in 26 European countries 2001.

3.2. Use of antifungals

Out-patient care

Antifungals for topical use (D01A)

In 2003 almost 170 packages/1000 inhabitants of antifungals for topical use were sold in Sweden. Over the counter sales (OTC) accounted for about 50%. According to data from prescriptions antifungals for topical use are given to a larger extent to the elderly and in 55% to women. It is worth noticing that the sold number of packages of amorolfin, nail polish against fungal nail infections, increased during the beginning of 2002 in accordance with terbinafin as mentioned below.

Antifungals for systemic use (D01B)

The sales statistics show a dramatic increase of antifungals for systemic use (terbinafin) during the beginning of 2002. The data for the years 2000-2003 are 0.36, 0.39, 0.66 and 0.63 DDD/1000/day respectively. The number of prescriptions is increasing as well and the ratio DDD/prescription remain the same during the whole period. When looking closer at the data it turns out that there are two specific brands that cause the sharp raise. Probably this is the result of a widespread marketing programme concerning fungal nail infections.

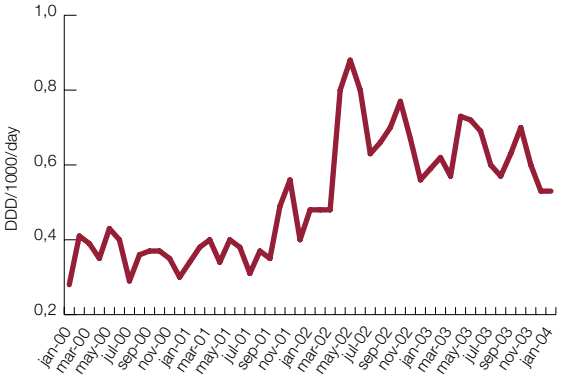

Figure 3.13. Antifungals for systemic use (D01B) out-patient care.

Antifungals for gynaecological use (G01AF)

There has been no increase in the number of packages of antifungals for gynaecological use in the last four years. The sales numbers, prescription and OTC, show about 50 packages/1000 inhabitants and the amount sold as OTC is stable near 90%. Econazole and klotrimazole are the dominating substances.

Antifungals for systemic use (J02A)

The use of antifungals for systemic use has been stable during the last four years. About two thirds of the use are prescribed to women and the dominating substances are fluconazole, itraconazole and ketoconazole.

Hospital care

Antifungals for systemic use (D01B)

In the same way as in out-patient care the use of terbinafin whitin hospital care increases dramatically during 2002 and remains on this (higher) level.

Antifungals for systemic use (J02A)

The total use of antifungals for systemic use has increased by 35% from 2000 to 2003 within hospital care. The new substances voriconazole and caspofungin, continue to increase with little expense of other substances. The use of flucytosine has been on a low level the last few years and has now decreased to almost zero. A slight decrease is seen for amphotericin B and itraconazole (Figure 3.14.).

Gunilla Skoog

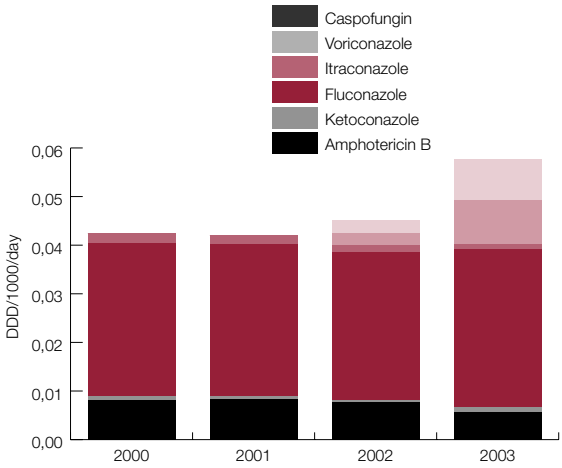

Figure 3.14. Antifungals for systemic use (J02), hospital care, 2000-2003, DDD/1000/day.

4. Antimicrobial resistance

In Sweden, routine susceptibility testing of clinical isolates is performed using standardized methods (Appendix 4). According to the national programme for surveillance of resistance which has been in place for three years (Appendix 5), well-characterised data on many bacterial pathogens are now available.

Streptococcus pneumoniae

Background

From an international perspective, Sweden still has a comparatively low rate of infections caused by *S. pneumoniae* with reduced susceptibility to penicillin, MIC> 0.12 mg/L (henceforth designated PNSP). Since 1996, infections and carriage due to *S. pneumoniae* with reduced susceptibility to penicillin, MIC ≥ 0.5 mg/L (henceforth designated PRP) has been notifiable according to the Communicable Disease Act.

Notifications according to the Communicable Disease Act Surveillance

The number of notified PRP cases in 2003 was relatively stable compared to the year of 2002. A vast majority of the cases were detected by nasopharyngeal culture. All but a few isolates had MICs of penicillin below 2 mg/L (categorized as I), and the few isolates with MICs above 2 mg/L (R) generally were from cases infected abroad.

Case-finding intensity has varied between counties, both due to contact tracing routines and culturing propensity. This makes it difficult to compare incidence between counties. County figures below are expressed as PRP proportion, i.e. the proportion of PRP out of all pneumococci to partly adjust for the differences in culturing propensity (Figure 4.1.).

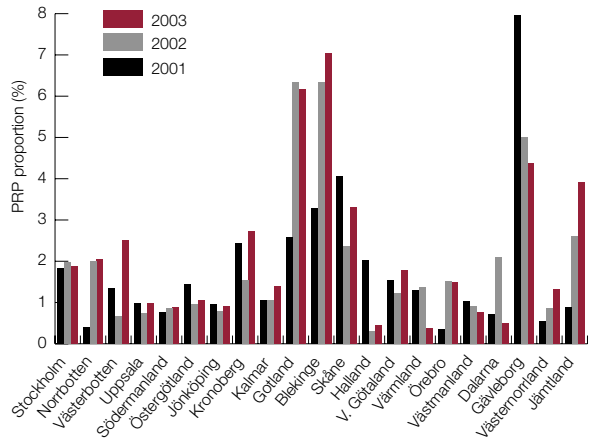

Figure 4.1. PRP proportion 2001, 2002, 2003.

As in previous years the highest incidince of PRP was found among children 0-6 years of age. Most cases were reported between late autumn and early spring, with the exception of the oldest age group (> 65 years) for which the number of notifications showed no clear seasonal pattern.

The number of notified cases of PRP has been decreasing since 1996. During the same period a parallel decrease in the number of performed nasopharyngeal cultures indicates a decrease in diagnostic intensity. For a more detailed analysis of the long-term national trends, see Swedres 2002.

Since 1998 most PNSP isolates were sent from clinical microbiological laboratories to the Swedish Institute for Infectious Disease Control (SMI) for further analysis. Approximately 90% of the isolates were recovered from nasopharyngeal cultures, mainly from children. More than half of these isolates were also resistant to trimethoprim/sulfametoxazole and often belonged to serotype 9V. Approximately 40% of the PNSP isolates were resistant to at least two more classes of antibiotics and therefore by definition multiresistant. The most commonly found serotypes were, in descending order, serotype/groups 9, 14, 19, 23, 6, 35 and 15, with a predominance for type 9 during several years and in year 2003 also for type 14.

Annual Resistance Surveillance and Quality Control (RSQC) programme

Pneumococci have been one of the targets for the annual Resistance Surveillance and Quality Control (RSQC) programme since 1994. In these studies, approximately 3000 consecutive clinical isolates of *S. pneumoniae*. i.e. 100 isolates from each of all clinical microbiology laboratories, have been tested for susceptibility to penicillin (by means of oxacillin 1 µg screen disk test), erythromycin, tetracycline and the combination of sulfonamide and trimethoprim, using the disk diffusion method. The national overview of these studies is given in Figure 4.2. A trend of increasing resistance is seen among all four groups of antibiotics.

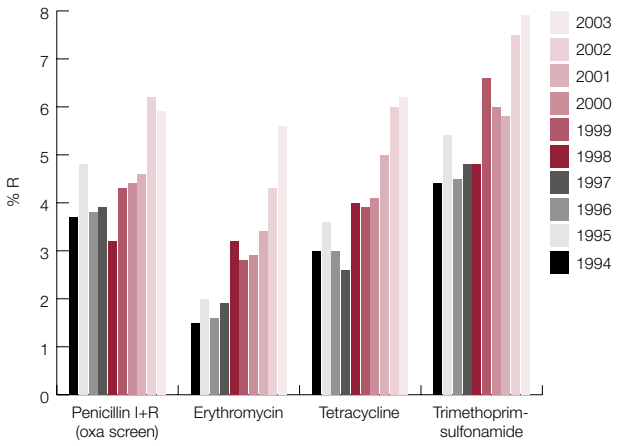

Figure 4.2. Overall national resistance rates (resistant isolates in percent of all pneumococcal isolates) for four different antibiotics 1994–2003 (data from the annual RSQC programme, approximately 3000 isolates per year).

Data from the EARSS network

Twentyone of the Swedish clinical microbiology laboratories, covering approximately 75% of the population, are reporting susceptibility data on invasive isolates of *S. pneumoniae* to EARSS (European Antimicrobial Resistance Surveillance System), enabling comparisons with other European countries (Figure 4.3).

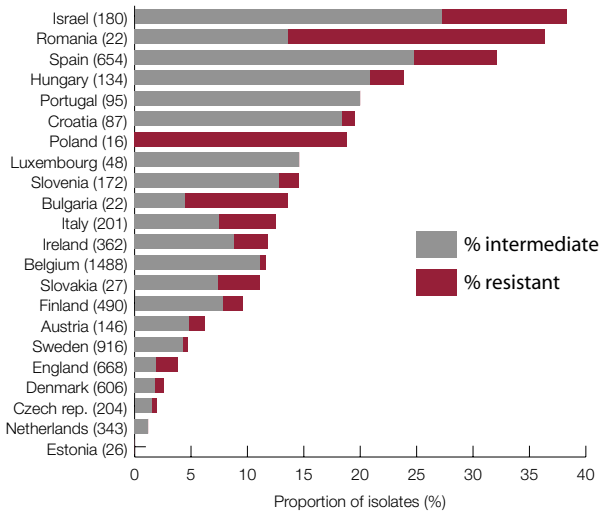

Figure 4.3. Frequencies of reduced susceptibility to penicillin among invasive isolates of *Streptococcus pneumoniae* in Europe 2003. Data from EARSS (www.earss.rivm.nl 2004-04-26)

The Swedish data on susceptibility to penicillin and erythromycin is given in Table 4.1. Overall levels of resistance have been lower in invasive isolates than in the nasopharyngeal isolates from the RSQC programme. This could partly be explained by a lower proportion of samples from children among the invasive isolates. It should be noted that MIC breakpoints for EARSS reporting (penicillin G MIC > 0.12 mg/L - PNSP) and notification by the Communicable Disease Act (MIC ≥ 0.5 mg/L - PRP) differ, and the figures from the different reporting systems are therefore not comparable.

Table 4.1. Invasive isolates of *Streptococcus pneumoniae* reported to EARSS.

	Penicillin			
Year	S%	I%	R%	Total
1999	98.5	1.4	0.1	**805**
2000	98.0	2.0	0.0	**803**
2001	97.2	2.3	0.5	**788**
2002	97.5	2.4	0.1	**783**
2003	95.3	4.3	0.4	**920**
	Erythromycin			
Year	S%	I%	R%	Total
1999	94.2	2.2	3.6	**535**
2000	96.7	0.5	2.8	**643**
2001	95.4	0.2	4.4	**653**
2002	94.7	0.1	5.2	**700**
2003	95.4	0.1	4.5	**759**

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

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Staphylococcus aureus

Background

Compared to many other European countries, the prevalence of MRSA in Sweden is still low. Policies for screening high-risk patients for multiresistant bacteria and continuous surveillance have been of importance in order to prevent spread of the organism. The decision to include both infection and colonisation with MRSA in the Communicable Disease Act in the year 2000 was due to an increasing national alertness, responding to the situation seen in many other European countries, where MRSA now represents an increasing proportion of staphylococcal infections in hospital settings, totally exceeding 50%.

Notifications of MRSA according to the Communicable Disease Act

The duration of MRSA carriage can be long, which might complicate the statistics when reporting systems change. A case that was reported through the voluntary reporting system before or during 1999, would be considered as a new case if the person provided a new culture positive for MRSA from the year 2000, even though that person was already known by the local Communicable Disease Officers. This situation was relevant especially for the Västra Götaland province, which had experienced a local outbreak of MRSA in the late 1990s, and screened many carriers from this outbreak in 2000. The notable decrease in reported cases from the Västra Götaland region is likely to in part be explained by such an over reporting in 2000 and in part by a true decrease in incidence.

The other most notable change in MRSA incidence during this period is the increasing incidence in the Stockholm region reflecting an ongoing MRSA epidemic. The Stockholm region, with a fifth of the total Swedish population, contributed more than two fifths of the reported MRSA cases in Sweden in 2002 (Table 4.2.).

Table 4.2. MRSA notified in 2000-2003 by county according to the Communicable Disease Act.

	2000		2001		2002		2003	
County	Number	Incidence/ 100 000 inh	Number	Incidence/ 100 000 inh	Number	Incidence/ 100 000 inh	Number	Incidence/ 100 000 inh
Stockholm	96	5.2	166	9.0	205	11.1	228	12.3
Uppsala	19	6.4	17	5.7	10	3.3	12	4.0
Södermanland	2	0.7	1	0.3	4	1.5	2	0.7
Östergötland	2	0.4	7	1.6	7	1.6	14	3.3
Jönköping	7	2.1	5	1.5	5	1.5	24	7.3
Kronoberg	1	0.5	0	0	4	2.2	5	2.8
Kalmar	3	1.2	2	0.8	5	2.1	6	2.5
Gotland	1	1.7	10	17.4	3	5.2	2	3.4
Blekinge	7	4.6	1	0.6	3	1.9	2	1.3
Skåne	22	1.9	75	6.6	68	5.9	104	9.1
Halland	10	3.6	25	9.0	13	4.6	13	4.6
Västra Götaland	110	7.3	54	3.6	48	3.1	63	4.1
Värmland	9	3.2	7	2.5	5	1.8	11	4.0
Örebro	8	2.9	6	2.1	16	5.8	8	2.9
Västmanland	3	1.1	8	3.1	7	2.7	11	4.2
Dalarna	0	0	4	1.4	1	0.3	2	0.7
Gävleborg	2	0.7	1	0.3	12	4.3	5	1.8
Västernorrland	14	5.6	12	4.8	7	2.8	10	4.0
Jämtland	0	0	0	0	2	1.5	5	3.8
Västerbotten	3	1.1	18	7.0	10	3.9	13	5.0
Norrbotten	3	1.1	5	1.9	6	2.3	9	3.5
Total	**322**	**3.6**	**424**	**4.7**	**441**	**4.9**	**549**	**6.1**

During 2003 a total of 549 cases were reported. The MRSA incidence was highest among the elderly (Figure 4.4.).

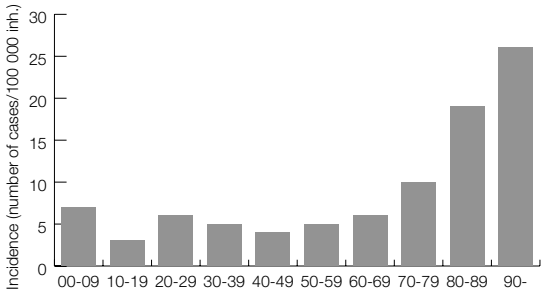

Figure 4.4. Age adjusted incidence of MRSA (n=549 cases).

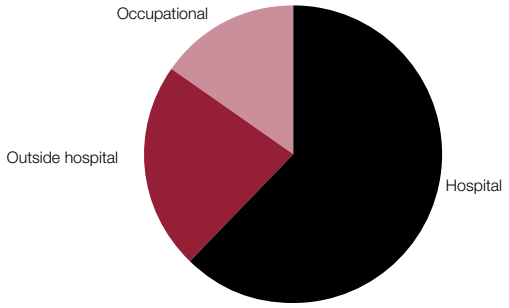

Figure 4.5. Reported mode of domestic health care related acquisition.

Of the reported cases 55% were considered to be infected with MRSA. Of the cases with a reported country of acquisition 76% were regarded as having acquired MRSA in Sweden. More than half of the imported cases had acquired MRSA in health care settings abroad. For the 306 domestic cases health care facilities were the most common place of MRSA acquisition (53%).

Of health care related acquisition 62% were reported to have taken place in in-patient care in hospital settings and 15% were occupational (Figure 4.5.). Many of the MRSA-cases in the older age group had frequent contacts with both in-patient and out-patient health care services as well as nursing homes. Thus, it was difficult to determine where the patient initially acquired MRSA. The multiple contacts with health care services for many of these patients pose a great challenge in information exchange between health care providers.

Typing of MRSA

A DNA-based method was used for typing of most MRSA isolates since the year 2000 (pulsed field gel electrophoresis; PFGE). PFGE patterns were included in a database and compared with international reference strains (epidemic MRSA from European countries, the Harmony project) (Table 4.3). Awaiting international consensus on nomenclature, names were adopted from the Harmony project for patterns identical to one of the reference strains (e.g. UK E15). Other patterns, when found in isolates from at least two patients, were given Swedish designations including the year of isolation (e.g. SE97-3). These patterns could be either related or unrelated to a reference strain.

Table 4.3. PFGE patterns of MRSA isolated in Sweden 2000-2003.

	No. of isolates with identical or related patterns (% of total)			
PFGE pattern	2000	2001	2002	2003
UK E15	20 (13)	66 (17.6)	111 (25.2)	125 (22.8)
DK E97-1	17 (11)	47 (12.5)	75 (17)	73 (13.3)
Berlin IV	7 (4.5)	50 (13.3)	13 (2.9)	62 (11.3)
Bel EC-3a	5 (3.2)	22 (5.9)	30 (6.8)	47 (8.6)
UK E16	8 (5.2)	31 (8.3)	40 (9.1)	31 (5.6)
Fra B	4 (2.6)	19 (5.1)	14 (3.2)	28 (5.1)
Fra A	33 (21.4)	31 (8.3)	28 (6.3)	20 (3.6)
UK E1	14 (9.1)	21 (5.6)	36 (8.2)	19 (3.5)
UK E3	3 (1.9)	9 (2.4)	11 (2.5)	16 (2.9)
S German II	3 (1.9)	6 (1.6)	8 (1.8)	7 (1.3)
Unrelated SE-patterns	38 (24.7)	73 (19.5)	75 (17)	100 (18.2)
Total	**154**	**375**	**441**	**549**

Annual Resistance Surveillance and Quality Control (RSQC) programme

Staphylococcus aureus from wound infections were included in the annual RSQC programme since 2001 (Appendix 5). Twenty-nine laboratories delivered data on consecutive isolates using the disk diffusion method for oxacillin, clindamycin, fusidic acid, aminoglycoside (gentamicin, netilmicin or tobramycin) and vancomycin. Resistance rates, compared to corresponding data for invasive isolates (as reported to EARSS), are presented in Table 4.4.

Table 4.4. Resistance rates for *Staphylococcus aureus* in 2001-2003 (RSQC-data compared to EARSS-data for Sweden)

		Oxa-cillin	Clinda-mycin	Fusidic acid	Amino-glyco-side	Vanco-mycin
2001 RSQC wound isolates	Total (n)	3466	3458	3209	2817	2910
	R (%)	0.1	2.1	7.1	0.4	0
2001 EARSS (Sweden). invasive isolates	Total (n)	1632	1588	586	1575	1395
	R (%)	0.9	1.2	2.5	0.3	0
2002 RSQC wound isolates	Total (n)	4291	3778	3812	2755	2841
	R (%)	0.2	1.9	9.5	0.2	0
2002 EARSS (Sweden). invasive isolates	Total (n)	1842	1826	797	1711	1653
	R (%)	0.7	1.8	2.9	0.5	0
2003 RSQC wound isolates	Total (n)	2929	3578	3700	3257	3061
	R (%)	0.5	1.8	8.4	0.6	0
2003 EARSS (Sweden). invasive isolates	Total (n)	1861	1860	886	1828	1804
	R (%)	0.8	1.9	10.5	0.8	0

The observations from year 2001 and 2002 of high rates of fusidic acid resistance in wound infections were verified also in 2003. One fusidic acid resistant clone (MIC of fusidic acid 4 m/L) was shown to cause impetigo in young children in 2002. The constant high resistance rate in 2003 implies the continuing presence of this clone.

Data from the EARSS network

Twenty-one of the Swedish laboratories (covering approximately 75% of the population) are reporting susceptibility data on invasive isolates of *S. aureus* to EARSS (Appendix 5). On average 0.75% of the invasive *S. aureus* isolates were MRSA (identified by the oxacillin screen disk test and confirmed by the detection of the mecA gene). Swedish data from the last five years indicate a low rate of MRSA among invasive isolates (Table 4.5.). Comparative data for Europe are given in Figure 4.6.

Table 4.5. *Staphylococcus aureus* susceptibility results (number of strains and percentage) using the oxacillin disk diffusion method according to SRGA in Sweden. Data reported from SMI to EARSS .

Year	S	I	R	Total
1999	1307 (99%)	0	13 (1.0%)	1320
2000	1469 (99.4%)	0	9 (0.6%)	1478
2001	1618 (99.1%)	0	14 (0.9%)	1632
2002	1830 (99.4%)	0	12 (0.6%)	1842
2003	1647 (98.9%)	0	18 (1.1%)	1665

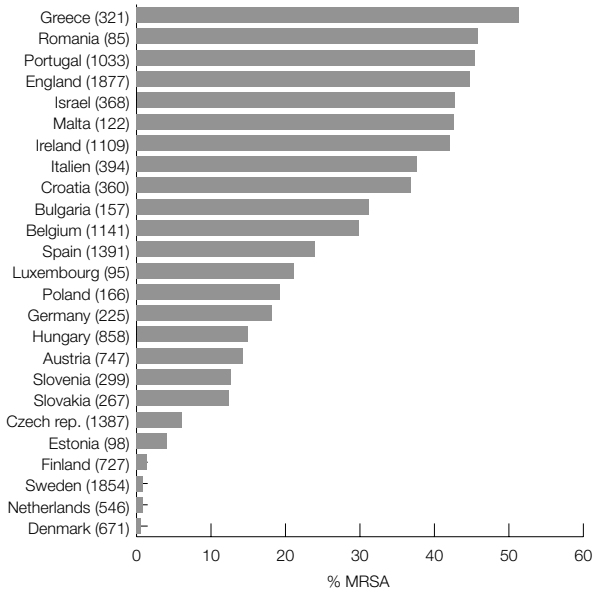

Figure 4.6. MRSA in Europe 2003, invasive isolates. Data from EARSS (www.earss.rivm.nl 2004-04-26).

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Enterococcus faecium and *faecalis*

Background

Enterococci, and specifically VRE, have become important causes of nosocomial outbreaks in many parts of the world, usually involving high-risk populations such as immunosuppressed and intensive care patients. Like MRSA, VRE were made notifiable pathogens according to the Communicable Disease Act in the year 2000. Surveillance of this pathogen was previously done through the voluntary laboratory reporting system.

Notifications of VRE according to the Communicable Disease Act and the Voluntary Laboratory Report System

Between 2000 and 2002, the number of annually reported cases varied between 18 and 20 cases. In 2003 however, this number more than doubled to 45 reported cases. The main part of this increase was due to two hospital outbreaks in Örebro County and Skåne Region (Malmö), respectively, leading to extensive contact tracing (Figure 4.7.). Previously one such outbreak took place in Västerbotten County (Umeå) in the year 2000. Stockholm is the only county that each year in the period has had eight or more cases.

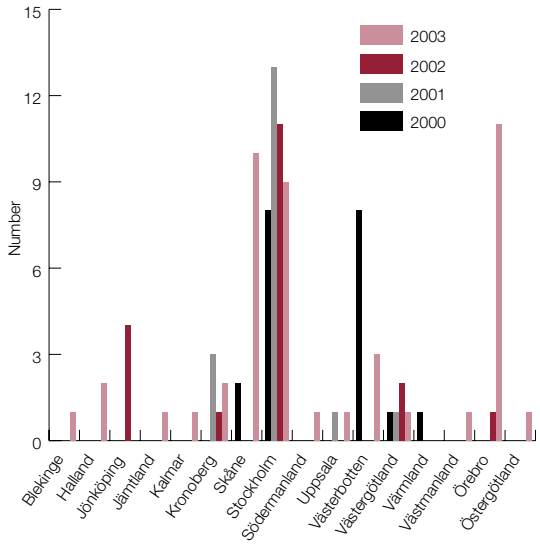

Figure 4.7. Reported VRE cases by county 2000–2003 (counties not in the graph did not report any case).

Carriage/infection with VRE is increasingly common with older age, except for the oldest age group (Figure 4.8.).

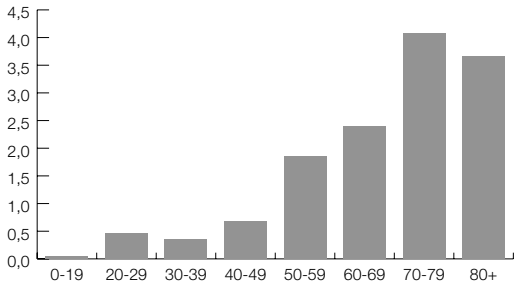

Figure 4.8. Reported VRE cases 2000–2003; age adjusted incidence.

Data from the EARSS network

Since the year 2001, *Enterococcus faecalis* and *Enterococcus faecium* were included in the EARSS network (Appendix 5). The main focus has been on vancomycin resistance, but also on high-level resistance to aminoglycoside antibiotics. This latter property may be of major clinical concern since it makes combination therapy using penicillin and aminoglycoside of no use. From Sweden 21 laboratories (covering approximately 75% of the population) contributed with quality assured routine disk diffusion data (Table 4.6). Alarming was that five vancomycin resistant isolates of *Enterococcus faecium* were found among the blood isolates.

Table 4.6. Susceptibility of invasive isolates of *Enterococcus faecalis* and *Enterococcus faecium* to three antibiotic groups in Sweden 2001-2003. Data from EARSS.

		Ampicillin	Amiono-glycosides (gentamicin or tobramycin)	Vancomycin
2001 *Enterococcus faecalis*, invasive isolates	R (%)	0	13	0
	Total (n)	479	212	396
2002 *Enterococcus faecalis*, invasive isolates	R (%)	0	15	0
	Total (n)	453	368	368
2003 *Enterococcus faecalis*, invasive isolates	R (%)	0	17.5	0
	Total (n)	612	448	593
2001 *Enterococcus faecium*, invasive isolates	R (%)	71	9	0
	Total (n)	196	102	172
2002 *Enterococcus faecium*, invasive isolates	R (%)	72	5.6	0
	Total (n)	167	88	148
2003 *Enterococcus faecium*, invasive isolates	R (%)	76.3	11.2	2.2
	Total (n)	241	170	231

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Streptococcus pyogenes

Annual Resistance Surveillance and Quality Control (RSQC) programme

Being one of the most important respiratory tract pathogens, *Streptococcus pyogenes* has been one of the regular pathogens of the national surveillance program since 1994. The antibiotics chosen for surveillance are those which are considered as treatment options and for which resistance mechanisms have been described. Penicillin is still the drug of choice, and remarkably enough resistance to penicillin or other betalactams has never been described in clinical isolates. Resistance to macrolides (represented by erythromycin), clindamycin and tetracyclines occur more or less frequently.

Resistance to erythromycin and clindamycin are in some cases mechanistically related (altered target, so called MLS-resistance) but in others unrelated (efflux mechanism) and affecting only erythromycin.

Summarized data for the years 1994-2002 are presented in Figure 4.9. For more detailed information, please visit http://www4.smittskyddsinstitutet.se/ResNet/index.jsp where data on county level can be found.

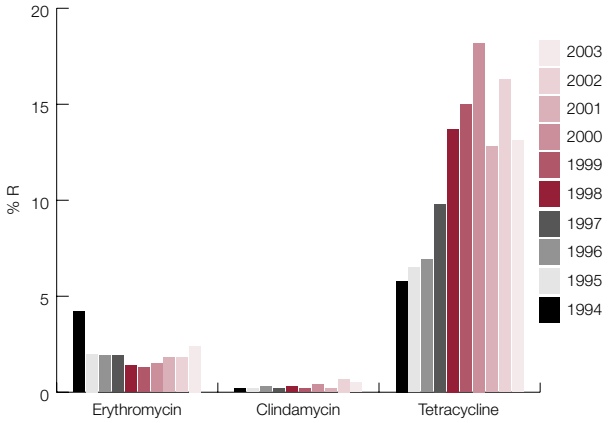

Figure 4.9. Resistance rates (resistant isolates in percent of all *Streptococus pyogenes* isolates) for three different antibiotics 1994-2003.

Data on invasive isolates were available from 2002, since during almost 9 months in 2002 all invasive isolates of Group A streptococci were sent to SMI for further characterization. The frequencies of resistance were 3% to erythromycin, <1% to clindamycin, 39% to tetracycline and none to penicillin. The most common T-type among the tetracycline resistant isolates was T3.13.B3264.

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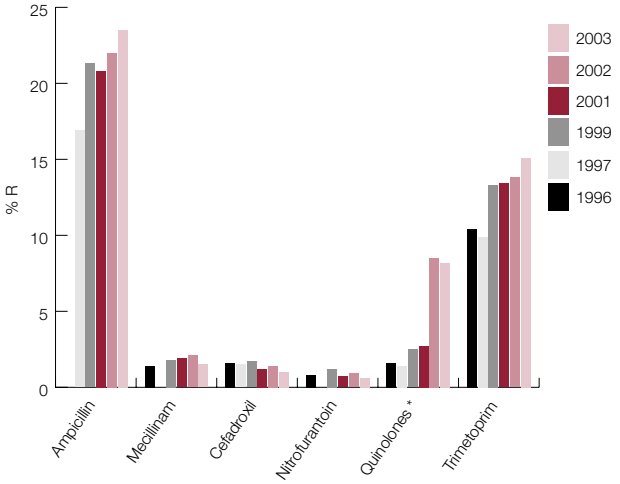
Haemophilus influenzae

There are no data in the RSQC programme on *Haemophilus influenzae* for 2003. The most recent data are given in Swedres 2001.

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 UTI were tested each year. The average resistance rates to ampicillin have shown a steady increase every year from 17 to 24%. The same was true for trimethoprim where resistance rates varied between 8 and 15%. Fluoroquinolone resistance (represented by norfloxacin) was below 5% but slightly increasing year by year, requiring special attention. In 2002, it was proposed by SRGA-M to use nalidixic acid instead of norfloxacin to screen for resistance to fluoroquinolones. It was anticipated that the screening result R would include all isolates that deviated from the wild-type population of *E. coli* with respect to fluoroquinolone susceptibility. This was shown to be true when analysing data from 6 laboratories who delivered data for both nalidixic acid and norfloxacin, and when adjusted breakpoints close to the wildtype populations were applied for norfloxacin (data not shown). In 2002 and 2003 all but five of the Swedish laboratories used nalidixic acid, and enough data for comparison were thereby obtained. No increase in resistance to fluoroquinolones was seen in this period (Figure 4.10).



Figur 4.10.Resistance rates (resistant isolates in percent of all *Escherichia coli* isolates) for six different antibiotics 1996-2003.
*** Between 1996-2001 fluoroquinolone resistance was detected with Norfloxacin, from 2002 with Nalidixic acid.**

Data from the EARSS network

Escherichia coli derived from invasive infections (blood isolates) have been part of the European Antimicrobial Resistance Surveillance System (EARSS) since the year 2001. Focus for the surveillance activities has been on resistance to betalactam antibiotics, especially occurrence of strains producing betalactamases with so called extended spectrum (ESBL), resistance to aminoglycosides and to fluoroquinolones.

Twentyone Swedish laboratories have taken part in this surveillance and have delivered data on more than 2500 blood isolates in 2003. Results are presented in Table 4.7. together with data from the RSQC programme on urine isolates from 2001-2003. Ampicillin resistance, caused by production of plasmid-mediated betalactamase (TEM-type most common) was equally high in the two sets of isolates, yet these figures are low compared to most other countries in Europe. The level of resistance to third generation cephalosporins among blood isolates was only 0.4%, and in most of those resistance was contributed to the presence of ESBL. Aminoglycoside resistance in *Escherichia coli* is extremely rare in Sweden. Resistance to fluoroquinolones is increasing every year, and taking into account both resistant (R) and indeterminant/intermediate (I) isolates, the rates are almost the same in blood as in urine isolates. Data from other European countries 2003 are presented in Figure 4.11. (data from EARSS).

Table.4.7. *E. coli* from UTI and blood in Sweden 2001-2002.

		Ampicillin	Cefotaxime (3rd gen cef)	Amino-glycosides*	Fluoro-quinolone
2001 RSQC, urine isolates	R (%)	20.8	Nt	Nt	2.8 (nor)
	Total (n)	3803	Nt	Nt	3814
2001 EARSS (Sweden), Invasive isolates	R (%)	26.5	0.5	1.0	3.7R/1.8I (cip)
	Total (n)	1513	2627	1241	2273
2002 RSQC, urine isolates	R (%)	22	Nt	Nt	8.5 (nal)
	Total (n)	5906	Nt	Nt	4253
2002 EARSS (Sweden), Invasive isolates	R (%)	24.9	0.5	0.6	5.1R/2.0I (cip)
	Total (n)	1753	3062	1585	2414
2003 RSQC. urine isolates	R (%)	23.5	Nt	Nt	8.2 (nal)
	Total (n)	4488	Nt	Nt	3971
2003 EARSS (Sweden), Invasive isolates	R (%)	28.5	0.4	1.0	6.6R/1.7I (cip)
	Total (n)	1953	3300	2819	3120

* gentamicin. tobramycin.

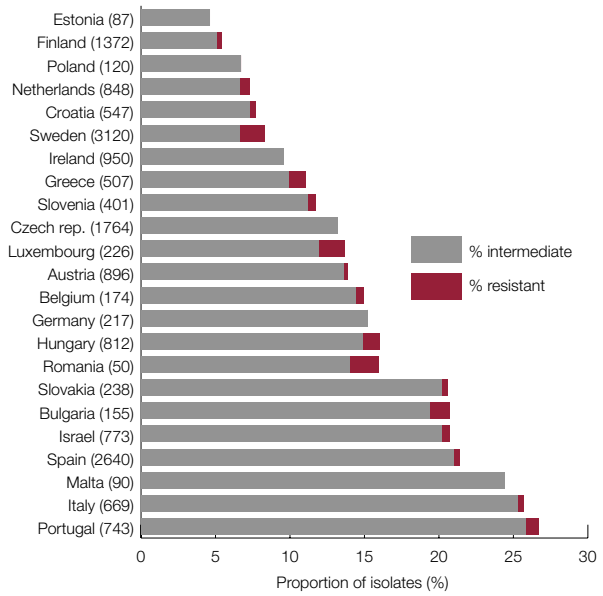


Figure 4.11. Resistance rates (% R and I) to fluoroquinolones in *Escherichia coli* in Europe 2003. Data from EARSS (www.earss.rivm.nl 2004-04-26)

Gunnar Kahlmeter, Barbro Olsson Liljequist

Klebsiella pneumoniae

There are no data in the RSQC programme on *Klebsiella pneumoniae* for 2003. Sporadic cases of both *Klebsiella pneumoniae* and *Klebsiella oxytoca* are found, which exhibit high-level resistance to third generation cephalosporins, often caused by ESBL. The most recent data are given in Swedres 2001.

Enterobacter species

There are no data in the RSQC programme on Enterobacter species for 2003. The most recent data are given in Swedres 2001.

Helicobacter pylori

Annual Resistance Surveillance and Quality Control (RSQC) programme

Helicobacter pylori derived from gastric biopsies have been monitored locally at a few laboratories in Sweden. In vitro resistance against metronidazole has been reported in 10-40% of Scandinavian strains. Resistance to clarithromycin is less common (3-7%) and not increasing and has not reached over 10% at any laboratory. Resistance to tetracycline is less than 1% and resistance to amoxicillin has only been described in a few strains and only outside Scandinavia. Resistance-figures from strains isolated in southwest of Sweden are presented. The population is about 300 000 and between 100-600 new Helicobacter strains are isolated yearly.

Table 4.8. *Helicobacter pylori* University Hospital MAS. Sweden 1994-2003,%R (- = not tested).

Year	Total number	Clarithro-mycin	Metro-nidazole	Tetra-cycline	Amoxi-cillin
1994	536	1.0	29.0	0.2	0
1995	588	2.9	32.1	0.1	0
1996	381	3.9	35.2	-	0
1997	331	7.7	39.8	-	0
1998	116	6.7	34.3	-	0
1999	149	6.1	33.1	-	0
2000	216	7.8	30.5	-	0
2001	188	8.8	40.2	-	0
2002	124	9	44.1	-	0
2003	112	7.2	42.6	-	0

Mats Walder

Salmonella and Shigella spp.

Annual Resistance Surveillance and Quality Control (RSQC) programme

Salmonella spp. and *Shigella* spp. derived from faecal cultures have not been included in the annual RSQC program 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 sensitivity patterns reflect their geographical origin. Too few strains are included in the Swedish survey to obtain a conclusive result.

Mats Walder

Campylobacter spp.

Annual Resistance Surveillance and Quality Control (RSQC) programme

Campylobacter spp. derived from patients with diarrhoea has not until 2001 been included in the annual RSQC programme but has been monitored locally at a few laboratories. About 50% of *Campylobacter* strains are imported cases. Since resistance to fluoroquinolones is a major concern worldwide it is interesting to notice a small decline in fluoroquinolone resistance among *Campylobacter* isolates. This is despite the fact that many laboratories perform resistance screening with nalidixic acid since 2001, which was expected to increase resistance figures with 25-30%. The overall fluoroquinolone resistance for *Campylobacter* spp. isolated in Sweden was approximately 30% (Table 4.9.).

Table 4.9. *Campylobacter jejuni/coli*, University Hospital MAS, Sweden 1991-2003, %R

		Percentage of resistant strains (R%)		
Year	Nalidixic acid	Ciprofloxacin	Tetracycline	Erythromycin
1991	-	16	27	4
1992	-	17	30	2
1993	-	24	28	5
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	24	0

Mats Walder

Pseudomonas aeruginosa

Annual Resistance Surveillance and Quality Control (RSQC) programme

Pseudomonas aeruginosa was included the first year of the RSQC programme (1994) using the disc diffusion (DD) method. Those data are compared with two sentinel studies from 1984 and 1994, respectively, in which isolates were collected and tested at SMI from 8 and 4 laboratories, respectively (total of 200 isolates in each collection), MICs were determined by agar dilution method.

In 2003 *Pseudomonas aeruginosa* again was included in the RSQC programme. Laboratories were asked to collect and test 50 isolates of *Pseudomonas aeruginosa* from wound infections and 50 isolates (or as many as possible, not less than 30) from respiratory tract infections. Data from all these collections are shown in Figure 4.12.

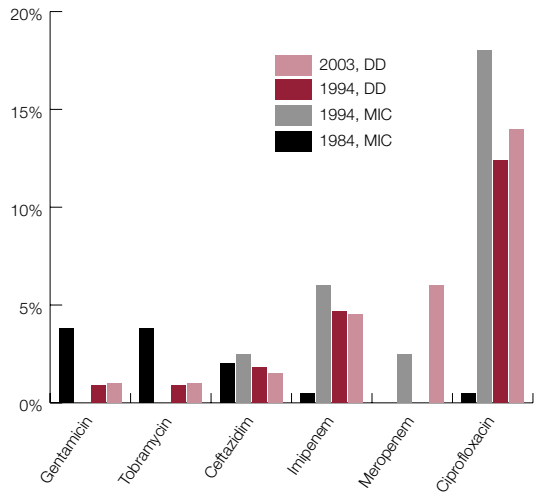


Figure 4.12. Resistance rates (resistant isolates in percent of all *Pseudomonas aeruginosa* isolates)

Gunnar Kahlmeter, Barbro Olsson Liljequist

Neisseria gonorrhoeae

Notifications according to the Communicable Disease Act

Gonorrhoea is a notifiable disease, and 596 clinical cases of the disease were reported in 2003. Clinical isolates were analysed at the Swedish Reference Laboratory for Pathogenic Neisseria, Department of Clinical Microbiology, Örebro University Hospital.

In 2003, isolates from 130 patients were sent to the reference laboratory, representing 22% of the notified cases. Isolates from the counties containing the largest cities in Sweden were underrepresented in this material. Susceptibility testing was performed according to standardized methodology using Etest for determination of MIC for ampicillin, cefixime, ceftriaxone, azithromycin, ciprofloxacin and spectinomycin. Production of ß-lactamase was examined by using Nitrocefin discs. Results for 2003 are compared with those from 1998, and 2000-2002 in Table 4.10.

Table 4.10. Antibiotic resistance rates (%) and ß-lactamase production of *Neisseria gonorrhoeae* in 1998 and 2000-2003 (data from the Swedish Reference Laboratory).

	1998 (n=348)	2000 (n=131)	2001 (n=141)	2002 (n=120)	2003 (n=130)
ß-lactamase pos.	24	37	37	39	22
Penicillin G	32	42	38	48	-
Ampicillin	24	37	37	39	22
Cefuroxime	0	2	0	4	-
Cefixime	-	-	-	0	0
Ceftriaxone	0	-	-	0	0
Azithromycin	0	-	-	0	<1
Tetracycline	32	52	56	54	-
Ciprofloxacin	10	28	43	48	52
Spectinomycin	0	0	0	0	0

(- = not analysed)

Hans Fredlund, Magnus Unemo

Neisseria meningitidis

Notifications according to the Communicable Disease Act

Invasive meningococcal disease is a notifiable disease. 56 clinical cases of the disease were reported in 2003. A total of 41 clinical isolates from blood or cerebrospinal fluid were analysed at the Swedish Reference Laboratory for pathogenic Neisseria, Department of Clinical Microbiology, Örebro University Hospital.

Susceptibility testing was performed according to standardized methodology using Etest on Müller Hinton II agar medium with 5% horse serum for determination of MIC for bensylpenicillin (pcG), phenoxymethylpenicillin (pcV), cefotaxime, ciprofloxacin, chloramphenicol and rifampicin.

None of the isolates produced beta-lactamase. Eight isolates (20%) had reduced susceptibility to pcG (MIC>0.064 mg/L). The MIC for pcV is normally 5-10 times higher and seven isolates had MIC ≥0.5 mg/L. All the strains had cefotaxime - MIC ≤0.008 and ciprofloxacin - MIC ≤0.008. Chloramphenicol - MIC varied between 0.5 and 4 and rifampicin was not higher than 0.25 mg/L. The MIC breakpoints of the SIR-system (S ≤ / R > as determined by SRGA) are the following: pcG 0.25 / 1, pcV 1 / 1, cefotaxime 0.06 / 1, ciprofloxacin 0.03 / 0.25, chloramphenicol 2 / 8 and rifampicin 1 / 1.

Per Olcén

Mycobacterium tuberculosis

During 2003 resistance against at least one of the five drugs (isoniazid, rifampicin, ethambutol, pyrazinamide or streptomycin) was reported in 41 patients i.e. 11.7% of the 350 patients with culture confirmed *M. tuberculosis* or *M. africanum*. The total number of patients with resistant TB was about the same as in previous years (Figure 4.13.). Resistant TB was reported in 4.5% of the Swedish born patients and 14.1% of those foreign borns. Among 27 patients with a previous history of TB after 1949, when tuberculosis drugs became available, there were 4 patients with resistant TB (14.8%).

Resistance to isoniazid was most common, reported in 7.4% of the patients, followed by streptomycin 5.1%, rifampicin 3.1% and resistance to pyrazinamid in 3.1% (Table 4.11.). Single resistance to rifampicin was reported in 2. An increased number of patients with multidrugresistant TB was reported in total nine patients (2.6%) (Figure 4.14.). Two of them developed MDR TB during treatment for isoniazid resistant TB and one patient who was previously treated for MDR TB several times during the period 1994-1999, relapsed with the same resistant strain.

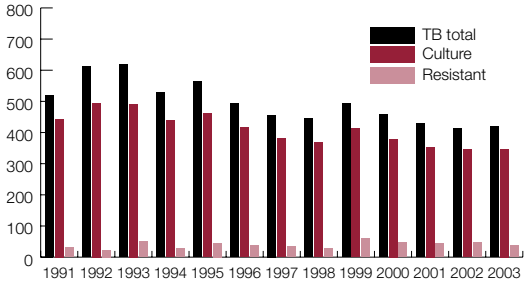


Figure 4.13. Tuberculosis in Sweden 1991-2003. Number of cases confirmed by culture and number of whom with reported drug resistance.

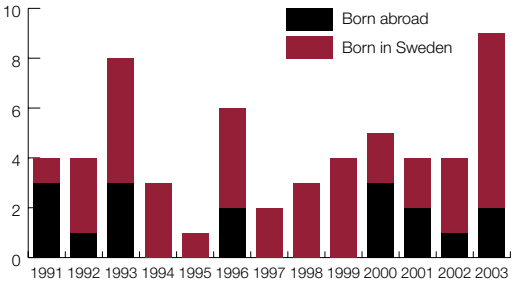


Figure 4.14. Annual number of cases with MDR-TB related to national origin.

Table 4.11. Drug resistant tuberculosis in Sweden. Resistance among initial isolates of *Mycobacterium tuberculosis* of *africanum* to at least one of the five drugs: isoniazid, rifampicin, ethambutol, pyrazinamid or streptomycin.

Year of diagnosis	2001	2002	2003
Culture confirmed *M. tuberculosis* of *M. africanum* (N=)	354	346	350
Any resistance total	12.5	13.6	11.7
Resistance to one drug only	5.9	8.4	6.3
Resistance to two or more drugs	6.5	5.2	5.4
Isoniazid	8.8	9.8	7.4
Rifampicin	1.7	1.2	3.1
Ethambutol	0.8	0.3	1.7
Pyrazinamid	1.7	1.2	3.1
Streptomycin	6.8	7.2	5.1
Isoniazid + rifampicin (MDR)	1.1	1.2	2.6

Victoria Romanus

5. National and regional projects

5.1. Survey of Activities at the County Level

Aim

A prerequisite for a successful work to minimize the emergence of antibiotic resistance is recognition of the problem and activities at the local level. In 2003 a nationwide survey was conducted to get an overview of the local organization, its resources and barriers in the Swedish counties.

Method

All twenty-one county councils have been visited by a specialist in infectious diseases and a pharmacist. Both of them have participated in meetings with all twenty-four regional STRAMA groups. Furthermore interviewed were held with the heads of the following units; communicable disease control, infectious diseases, microbiological laboratories and infection control sections. In addition, they interviewed all directors of county councils, county council primary care units, and drug committees. In connection to this all pharmacists working in a STRAMA group was formed into a network.

The proposal for a "National Action Plan Against Antibiotic Resistance" has been used as the basis of discussions and interviews. The intention was to review the following factors, stated in the action plan, that are regarded the most significant in prevention of resistance development:

- resources and methods of resistance surveillance
- surveillance of antibiotic use
- prevention of infectious diseases
- improved diagnostic methods
- improved antibiotic therapy
- education and information

Preliminary results

Already at this point it is clear that this inventory will help to bring forward good examples of well-functioning local networks for prevention of resistance development. Concurrently it will point out obvious shortcomings in health and medical care preventing efficient STRAMA work:

- lack of resources for infection control: in eight of the counties the accessibility for doctors within the hygiene sector is only ten hours or less per week.
- lack of single rooms with private WC and shower facilities; in more than half of the Swedish county councils, less than 20 percent of the in-patients have access to such rooms.
- acute wards with shortages of beds with isolation care facilities; 90 percent of the county councils are reported to have such shortages.
- lack of competence in the area of medical care and infection control within nursing homes; half of the Swedish municipalities lack in hygiene competence at their nursing homes.
- lack of infectious disease specialists at certain hospitals; in six counties there are hospitals lacking such competence.
- resource related obstacles for continuous training of health care workers within the area of infectious diseases and antibiotic use
- in only seven of the twenty-one counties an automatic annual report on antibacterial resistance within the region is fed back to physicians.

The result of the inventory will also be returned to all local STRAMA groups and will constitute a basis on which to set a program for educational training days throughout 2004 and ahead.

Seth-Olof Bergquist

5.2. Studies on antibiotic use in out-patient care

1. A Study of Hygienic Routines and Infections in Child Day Care

Aim

The primary aim of the study was to survey factors of potential importance for spread of infections in child day-care e.g. hand washing, diaper changing, length of outdoor staying and food hygiene. The second aim was to study how the staff handle infections and how information of infections are mediated to the child day-care centre (DCC). The study will be the basis for further interventions in DCC.

Method

During three weeks in the autumn 2003 a national survey at Swedish DCCs was performed. The DCCs were chosen at random and each DCC was visited by a study-nurse who interviewed the staff using a structured questionnaire.

Results

338 DCCs participated. There were totally 14 172 children and 2 735 personnel in the DCCs. Almost 40% of the children were younger than three years old. 86% of the children stayed at the DCCs more than 15 hours a week. The DCC had between one and eight departments and 75% of the DCCs had 3 or less departments. 84% were public managed. The DCCs were on average open 55 hours a week. On average there were 16 children in each department and 5 children/child care personnel. Data adjusted to be representative for the whole country showed that 35% had the recom-

mendations from the National Board of Health and Welfare about infections in child day care. For 55% of these, the recommendations had changed the routines at the DCC.

The policies for hygiene routines are shown in Table 1 and the attitudes for the DCC in Table 2.

Table 1. Hygiene routines at the Child Day Care Centres

Do you have routines for:	N=	Written routines %	Routines but not written %	No routines %	Do not know %
When children should stay at home?	338	53.1	43.2	3.7	0
Hand washing for the children?	338	10.2	82.0	7.7	0.1
Hand washing for the personnel?	338	0.9	50.7	47.6	0.8
Diaper changing?	333	3.0	74.4	22.2	0.4
For food hygiene control?	330	51.0	16.9	16.4	15.7

Table 2. Attitudes at the Child Day Care Centres

How is the attitude to:	N =	Very permittive %	Rather permittive %	Neither permittive nor rigorous %	Rather rigorous %	Very rigorous %
Children being at the child day care centre with fever, runny nose and cough?	338	6.5	28.9	22.4	36.2	6.0
Children being at the child day care centre with diarrhoea?	338	2.3	17.5	24.8	43.7	11.7

Patricia Geli, Katarina Hedin

2. Self-Medication with Antibiotics in a Swedish General Population

Aim

To investigate the issue of self-medication with antibiotics among the general public of Europe, the University of Groningen, the Netherlands, initiated a study in 19 European countries. The objective of the study was to assess the prevalence of self-medication and self-reported use of prescribed antibiotics, as well as storage of antibiotics in homes, sources for obtaining antibiotics, reasons for self-medication and types of antibiotics used. The long-term aim of the project is to achieve an overview of antibiotic consumption including self medication in order to plan future interventions.

Method

A self-administered postal questionnaire was distributed to 1000 randomly selected subjects in four municipalities in Västmanland county, Sweden. The study population consisted of adults, aged 18 and above, who, when appropriate, were also asked to give information about their children less than 16 years of age. The participants were asked a series of standardized questions regarding their use of antibiotics during the last 12 months, how these were obtained, if they had any antibiotics at home and if they would consider using antibiotics without consulting a physician.

Results

The response rate totalled 70% after two reminders. Use of antibiotics during the last year was reported by 17% of the respondents. Four per cent stated that they at present had at least one antibiotic at home. In both cases penicillin V was the most frequently mentioned antibiotic. The antibiotics were in all cases, except three, reported to have been obtained with a prescription. In those three cases the antibiotics were leftovers from previous treatment or given by a friend or relative. Eleven per cent said that they would consider self-medicating with antibiotics if possible. The most common reason stated for using antibiotics, as well as a reason for possible self-medication, was cystitis. From the findings in this report, it is concluded that persons from the study area in general only use antibiotics after consultation with a doctor.

Emma Svensson, Cecilia Stålsby Lundborg

3. Weekly Antibiotic Prescribing and Influenza Activity in Sweden; A Study throughout Five Influenza Seasons

Influenza is caused by a virus and can therefore not be cured with antibiotics. However, the disease often leads to bacterial complications that require treatment. Influenza may also be confused with bacterial respiratory infections, leading to unnecessary prescription of antibiotics.

This study is the first that examines influenza activity and antibiotic prescribing on a weekly basis for a whole country. The study includes the total dispensing of antibiotics used for respiratory tract infections, for all ages, in relation to verified influenza cases throughout 5 influenza seasons, 1997-2002. The peak of influenza activity occurred during the winter. In 4 out of the 5 monitored seasons it occurred in February-March. The dispensing of the selected antibiotics was rela-

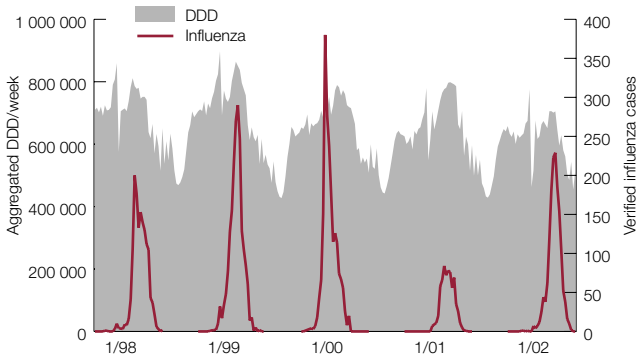


Figure 5.1. Antibiotic dispensing presented as the aggregated amount of defined daily doses of the selected antibiotics for each calendar week, and the number of laboratory verified influenza cases, from calendar week No. 40, 1997 through calendar week No. 22, 2002, in Sweden.

tively stable throughout the years under study. Narrow-spectrum penicillins were commonly used which is in accordance with national and local guidelines.

For all the included years a fluctuation in antibiotic dispensing over the year with 2 peaks during the wintertime was noted. The figure presents the variability in antibiotic dispensing for the 5 seasons, in relation to the number of verified influenza cases. There were no obvious differences in the total amount of antibiotics dispensed over the years that could be related to influenza activity, but a coincidental relationship between the peaks of diagnosed influenza cases and the peaks of antibiotic utilization was indicated, especially for older age groups.

Frida Ganestam, Cecilia Stålsby Lundborg

5.3. Studies on antibiotic use in hospital care

1. The STRAMA Point Prevalence Study 2003 on Hospital Antibiotic Use

Aim

Although some hospitals in Sweden have carried out local studies on the indication for hospital antibiotic prescriptions, no nationwide data are available. The objective of this study was to introduce a system for frequent assessment of the use of antimicrobial agents against bacteria and fungi, in relation to diagnosis in hospital wards.

Method

A case record form was developed which included demographic data as well as the amounts and indications for antimicrobial agents against bacteria and fungi. Data were collected at the hospital ward level through personal visits and separated for treatment of infection vs prophylaxis and community vs hospital acquired infections. 19 pre-defined diagnosis groups were used. Data were reported to STRAMA using a web-based reporting system. The study was performed during a two-week period in November 2003.

Results

The method was successfully introduced resulting in one of the largest surveys in Europe of antimicrobial use in hospital. 19 out of the 21 Swedish counties participated. Data was reported from 54 hospitals and included over 13 500 admitted patients. 31% of the admitted patients were treated with antimicrobials. The distribution of therapy reasons were; community acquired infections in 52,4%, hospital acquired infections in 28,2% and prophylaxis in 19,4%. The total amount of antimicrobials for adults was 40 DDD/100 admitted patients and the most commonly used antimicrobials were cephalosporins (8.5 DDD/100 admitted patients), beta-lactamase resistant penicillins (7.6), fluoroquinolones (4.7) and penicillins with extended spectrum (3.4).

Among the pre-defined diagnosis groups the most reported in adults were pneumonia 16%, skin and soft tissue infections 13%, cystitis 12%, bone and joint infections 11%, pyelonephritis 8% and infections in the lower gastrointestinal tract 7%.

The study describes sub-optimal prescription patterns for certain diagnoses. Analysis reveal over-use of cephalosporins particularly in community acquired pneumonia and of fluoroquinolones in urinary tract infections. The duration of perioperative prophylaxis was too long, 47% of all given prophylaxis were administered for more than one day.

Mats Erntell

2. Swedish Antibiotic Nursing home Trial (SANT)

Aim

The aim of this study is to describe the treatment of infectious diseases in elderly in nursing homes and evaluate the effect of an intervention package aiming at improving the treatment with antibiotics in nursing homes.

Method

Seven nursing homes in the county of Norrbotten participated in a pilot study. Baseline data, about diagnosis and prescribing pattern, were collected and the intervention was conducted. The intervention consisted of two group discussions of about 1.5 h each with nurses and physicians. The participants received the results from the diagnosis-prescribing study done earlier and were asked to read it before the group sessions. The participating peers were considered to have the necessary knowledge, but there were two facilitators for discussion: one pharmacist and one physician. During the first session the pharmacist showed the results from the diagnosis/prescribing study and initiated discussions around specific problem areas such as the trimethoprim resistance in the county and the use of fluoroquinolones for cystitis (a non-recommended treatment in Sweden). The physician also introduced the hygiene aspects and all participants received a small brochure concerning this area. During the second session the physician informed about pneumonia, UTI and skin- and soft tissue infections in elderly and the pharmacist and the physician informed together with the participants about the recommended treatment for these infections. At the end of the discussion all participants received a short written guideline for antibiotic prescribing in elderly.

In mid-September the diagnosis-prescribing survey in the main study started. The nurses at 60 participating nursing homes in Sweden registered each infection that led to a consultation with a physician during three months. The nurses and the physicians at the nursing homes was also asked to fill in a knowledge and attitudes questionnaire. It included questions on management of infectious disease, antibiotics and also fictitious cases on infections. A nursing home questionnaire with questions concerning e.g. human resources, care burden and availability of physicians, has also been filled in by the nurses. The analysis of these baseline data is in its initial stage.

Results

A selection of some of the preliminary results:

- A total of 737 forms were returned. Expected number was 770, based on the number of residents at the nursing homes and general frequency of infections.
- The average age was 86 years, (range between 48 and 101 and median 86 years).
- Infections in the urinary tract dominated (55% of treatments). Skin and soft tissue infections were responsible for 16%, respiratory infections for 14% and other infections for 15%.
- 78% of the registered infections were treated with antibiotics.
- Fluoroquinolone treatment dominated (22%) followed by trimethoprim 16%. Pivmecillinam was prescribed in 14% of the cases and flucloxacillin in 12%.

Eva Olsson, Cecilia Stålsby Lundborg

Appendix 1 – Abbreviations

AST	Antibiotic susceptibility testing
ATC	The Anatomical Therapeutic Chemical classification system
CCDC	Centre of Communicable Disease Control
DCC	Day care-centre
DDD	Defined daily dose
DST	Drug susceptibility testing
EARSS	European Antimicrobial Resistance Surveillance System
ESAC	European Surveillance of Antimicrobial Consumption
ICU	Intensive care unit
MDR	Multidrug resistance
MIC	Minimal Inhibitory concentration
MRSA	Methicillin resistant *Staphylococcus aureus*
PFGE	Pulsed field gel electrophoresis
PNSP	Penicillin non-susceptible pneumococci. MIC ≥ 0.12 mg/L
PRP	Penicillin non-susceptible pneumococci. MIC ≥ 0.5 mg/L
RSQC	Resistance Surveillance and Quality Programme
SMI	Swedish Institute for Infectious Disease Control
SRGA-M	The Swedish Reference Group of Antibiotics- subcommittee on Methodology
STRAMA	Swedish Strategic Programme for the Rational use of Antimicrobial Agents and Surveillence of 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 31 December 2003.

	Age (years)					
County	**0 - 6**	**7 - 19**	**20 - 59**	**60 - 79**	**> 80**	**Total**
Blekinge	10 141	24 162	76 400	30 323	8 863	149 889
Dalarna	17 894	48 095	139 659	53 756	17 116	276 520
Gotland	3 730	10 300	29 618	10 660	3 227	57 535
Gävleborg	18 014	45 957	141 503	54 806	16 586	276 866
Halland	21 477	50 309	143 868	50 607	15 061	281 322
Jämtland	8 211	21 526	65 077	24 674	8 157	127 645
Jönköping	24 495	59 143	166 984	58 909	19 128	328 659
Kalmar	15 003	40 338	117 558	47 037	14 950	234 886
Kronoberg	12 423	29 964	91 878	32 813	10 370	177 448
Norrbotten	16 752	42 285	131 322	50 416	12 099	252 874
Skåne	84 112	188 961	611 875	205 053	62 696	1 152 697
Stockholm	153 463	293 247	1 055 735	275 570	82 857	1 860 872
Södermanland	18 488	45 282	132 873	49 340	14 397	260 380
Uppsala	22 777	51 738	167 143	45 449	13 388	300 495
Värmland	18 022	45 232	139 404	54 476	16 429	273 563
Västerbotten	17 602	43 917	135 561	46 296	12 580	255 956
Västernorrland	16 276	39 540	123 673	50 201	14 415	244 105
Västmanland	18 208	44 600	134 238	49 007	14 081	260 134
Västra Götaland	111 483	254 084	810 172	258 807	80 446	1 514 992
Örebro	19 594	45 930	142 384	49 724	16 303	273 935
Östergötland	29 263	70 252	219 127	73 466	22 789	414 897
All counties	657 428	1 494 862	4 776 052	1 571 390	475 938	8 975 670

Table App 2.2. Population of Sweden 1998-2003 (December 2003)

	1998	**1999**	**2000**	**2001**	**2002**	**2003**
Population (x1000)	8 851	8 861	8 882	8 908	8 940	8 976

Table App 2.3. Denominator data from the microbiological laboratories.

	Catchment area and population	Number of analyses 2003*								Number of positive cultures 2003*			
Laboratory	Catchment area	Catchment population (x1000)	Blood (pair of bottles)	Cerebro-spinal fluid (CSF)	Nasopharynx	Throath	General culture	Screen MRB	Faeces SSYC	*Staphylococcus aureus*	Streptococcus pneumoniae	*Streptococcus pyogenes*	E coli
Borås	SW Götaland	273	10132	163	4262	5572	6142	650	6334	4096	776	1018	7221
Eskilstuna	Södermanland	257	6117	151	5046	5715	8261	824	4777	3474	897	795	6386
Falun	Dalarna	278	8745	150	1813	1821	7659	650	3921	3449	395	690	6303
Gävle	Gävleborg	277	6704	179	2450	1314	5525	684	3857	3077	479	407	5678
Göteborg	V Götaland	700	23870	928	3595	4292	16293	7930	15267	6925	862	1120	15806
Halmstad	Halland	280	6193	126	3121	3464	7964	12506	5540	2760	659	594	6142
HS, Stockholm	Stockholm	900	21247	530	14742	6529	27605	13507	10705	9991	2469	2062	16926
Jönköping	Jönköping county	330	8560	130	186	4415	11938	1350	5318	4440	548	1130	7980
Kalmar	Kalmar county	235	6217	148	3820	3128	6403	1740	5840	3676	719	700	7182
Karlskrona	Blekinge	152	3600	76	1095	2138	4988	1243	3623	1835	284	448	3661
Karlstad	Värmland	273	10839	181	762	2446	10065	3457	4130	4723	265	701	6377
Kristianstad	Skåne	203	6820	134	5260	5218	11161	3177	6761	4887	983	800	7769
KS, Stockholm*	Stockholm	900	21709	2214	29662		36100	10000	13989	11850	3739		19195
Linköping	Östergötland	412	12283	594	4666	3269	15465	1749	7099				
Lund	Skåne	520	16278	1151	9188	7295	20354	8683	13276	8996	2236	1882	17192
Malmö		510	13765	280	4593	7464	14343	7466	10549	6465	1487	1926	13238
Medilab	Stockholm		NA	NA	9649	4752	5489	1680	7262	3205	964	864	7317
St Göran*	Stockholm + national		3530	136	5887		9421	1272	7467	3155	895		15260
Skövde	Skaraborg	260	8861	146	1910	2123	8495	1359	4970	3381	535	654	8897
Sunderby (Luleå)	Norrbotten	260	7149	132	2971	3839	7428	288	3489	2997	340	534	6545
Sundsvall	Västernorrland	245	7849	95	3287	2371	8717	3179	4471	3588	687	617	7851
Uddevalla	V Götaland	280	11555	128	1822	3299	7334	1204	5316	3720	398	698	9772
Umeå*	Västerbotten	255	6920	580	1710		8717	2300	4850	2968	301		6613
Uppsala*	Uppland	300	11510	763	4314		14379	2326	6558	3945	821		6464
Visby	Gotland	215	2671		3606	1541	2774	0	1229	1348	525	375	2123
Västerås	Västmanland	260	7421	183	2418	2498	8178	624	4407	3344	526	522	6864
Växjö	Kronoberg	190	3560	54	1500	2100	4900	620	3800	1500	256	392	3600
Örebro	Örebro county	274	11631	234	6972	1668	12114	1514	4452	5378	1133	549	6739
Östersund*	Jämtland	128	4185	277	2241		5557	893	2002	2674	459		4959

* Data only available from 2002

Appendix 3 – Surveillance of antibiotic consumption

The ATC classification system and defined daily doses (DDD)

Since 1988 the Anatomical Therapeutic Chemical (ATC) classification, 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 Apoteket AB are upgraded yearly according to the recommendations made by the WHO Collaborating Centre for Drug Statistics methodology in Oslo, Norway.

The sales of medicines 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 read with caution.

Swedish national statistics on drug utilisation

Since 1974 the National Corporation of Swedish Pharmacies (Apoteket AB) regularly produces sales statistics on medicines, for the country as a whole and for individual counties. The sales are registered as number of DDD, cash value and number of packages.

Out-patient care data includes information on the sales of medicines 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) is also included in the survey.

Recorded data include 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 and packages.

Hospital care data includes medicines 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. Since 2003 Apoteket AB has a new statistical system; Xplain. Through this system data since 2000 are available. Data from previous years are no longer automatically accessable but can be obtained after specific request.

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 suseptibility 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* (indeterminate; in previous nomenclature 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 (betalactamase detection in *Haemophilus influenzae*, *Neisseria gonorrhoeae* and others).

Phenotypic methods (disk diffusion or MIC) are performed on one of two basic media for AST, PDM Antibiotic Sensitivity Medium from Biodisk, Sweden, and ISA (IsoSensitest Agar) from Oxoid Ltd, UK. For these two media and their corresponding antibiotic paper disks, interpretive criteria for SIR-categorization are provided by the SRGA-M. They are regularly updated and available through the website 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 or 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 surveys".

Appendix 5 – National surveillance of antibiotic resistance

Surveillance of pathogens regulated in the Communicable Disease Act

Statutory notifications of certain communicable diseases are regulated in the Communicable Disease Act (SFS 1988:1472). With the exception of certain sexually transmitted infection (STI), 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 and to the Swedish Institute for Infectious Disease Control (SMI). Some diseases, mainly gastrointestinal infections, should also be notified to the municipal environmental health office. 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 four different antibiotic resistant pathogens are included in the list of notifiable diseases. Penicillin-resistant *Streptococcus pneumoniae* with Penicillin G MIC ≥ 0.5 mg/L (PRP) have been notifiable since 1996. Methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus faecalis* and *Enterococcus faecium* (VRE) have been notifiable since 2000.

The notifications are entered into the national computerized surveillance system, SmiNet. 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 requested to supplement the information. As an important complement to the notifications, the MRSA and PRP strains are sent to the SMI for epidemiological typing, using pulsed-field gel electrophoresis (PFGE) and other molecular epidemiological methods.

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

The feed back of notification data is done monthly on the SMI Internet 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.

Voluntary laboratory reporting

A system for individual, anonymised case reporting of certain very rare (or not yet identified) pathogen-resistance combinations is under construction. The pathogens are so selected that each finding should trigger some action (either confirmation testing or infection control measures). To make the system exhaustive, the identification and reporting of these pathogens from the local laboratory computer systems to the SmiNet must be automated.

Swedish combined surveillance and QC program (RSQC surveys) further developed into ResNet 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 microbiological 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 29 laboratories (see also Appendix 4).

Each year the laboratories are asked to collect quantitative data (zone diameters) for defined antibiotics in 100 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. On one or several occasions *Escherichia coli*, *Enterococcus faecalis*/*E. faecium*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Klebsiella* and *Enterobacter* have been part of these surveys. The number of antibiotics tested for each pathogen has varied between 4 and 6.

Laboratory specific zone diameter distributions were compared with SRGA-M reference distributions. The median, the width and the shape of the distributions were used for methodological discussions with the laboratories. Provided the individual distributions fitted the reference distributions, the SRGA recommended breakpoints were used to calculate the resistance frequencies of clinical isolates from the laboratories. In a few selected cases adjusted breakpoints based on the deviation of individual distributions were used.

Development of ResNet

Originally data were sent on paper (1994-1997) to be entered in spreadsheet (Excel)-format at the reference laboratory. Between 1998 and 2001 the laboratories have sent their

data in Excel-format for a central semi-automatic work-up with "on-paper" feedback in the mail and in yearly workshops on AST methodology and resistance development.

From 2002 a web-based newly developed 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). Recently the software has been updated to display also the 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.

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 website (www.earss.rivm.nl).

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 been carried out by EARSS in cooperation with UK-NEQAS and the EARSS Advisory Board in 2000, 2001, 2002 and 2003. 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 seems to form a solid base for surveillance of resistance, yet could and should be 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.

Sentinel surveillance

Susceptibility testing of gastrointestinal pathogens such as *Salmonella, Shigella, Campylobacter jejuni/coli* and *Helicocobacter 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) 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 dispaying in ResNet.

Appendix 6 – Recent publications

Use of antibiotics

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