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PUBLIC HEALTH AGENCY OF SWEDEN

Swedish work on containment of antibiotic resistance

Tools, methods and experiences

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Preface

Resistant bacteria pose a threat to the global health. Collaboration and exchange of experiences between countries are vital for the work to counteract the increasing resistance development. Sweden is a small country with a relatively low consumption of antibiotics and favourable resistance conditions in an international perspective. Sweden initiated long-term, structured measures early on, characterised by work on both local and national levels with the collaboration of many disciplines and sectors both nationally and locally, which is further described in the report. There is also a long tradition of working for rational use of antibiotics and reduced spread of infections within veterinary medicine, animal husbandry and agriculture. From an international perspective the level of antibiotic use and the prevalence of resistant bacteria in animals in Sweden is low. This report focuses, however, on human medicine.

This report has been produced within a collaboration project with the Indian National Center for Disease Control (NCDC) as a part of Sweden's and India's work for rational antibiotic consumption and improved surveillance of antibiotic resistance and is financed by Sida. The Governments of India and Sweden signed an agreement of cooperation in 2009 in the field of healthcare and public health which points out antibiotic resistance as an area for collaborate efforts. Within this agreement there is an ongoing collaboration between NCDC and the Public Health Agency of Sweden.

The ambition is that the report or chosen chapters and examples can be useful for other organisations and countries that want to develop or further strengthen their work on rational antibiotic use and resistance surveillance within human medicine. The report can be seen as a "tool-box" where present or previous Swedish tools and experiences can be adapted to different countries levels of progress in the area.

The Public Health Agency of Sweden

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Main editors and authors of the report are Karin Carlin, analyst, and Sonja Löfmark, PhD, microbiologist, from the Public Health Agency of Sweden and Lars Blad, Deputy Medical Officer for Communicable Disease Control in the county of Västernorrland, chair of the local Strama group and member of the Strama advisory council. The four interviews with the experts were done by Natasha Brieger, who also contributed with English language and text editing.

The report is based on interviews with experts with experience of the work against antibiotic resistance and is also based on previous reports from the former national Strama, the Public Health Agency of Sweden – former Swedish Institute for Communicable Disease Control, and the National Board of Health and Welfare. Input from reference groups within the area have continuously been collected.

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Abbreviations

AOM	Acute otitis media
ATC	Anatomical therapeutic chemical classification system
BVC	Children's health centres
CASE	Software for statistical analyses
CDA	Communicable disease act
CDC	Center for Disease Control
CeHis	Center for eHealth in Sweden
CNS	Central nervous system
COPD	Chronic obstructive pulmonary disease
CPE	Carbapenemase producing enterobacteriaceae
CRE	Carbapenemase resistant enterobacteriaceae
CRP	C-reactive protein
CVC	Central vein catheter
DDD	Defined daily dose
DG-SANCO	Directorate general Health and consumers
EARSS/ EARS-Net	European resistance surveillance system/network
ECDC	European Centre for Disease Prevention and Control
EMA	European Medicines Agency
ESAC-Net	European surveillance of antibiotic consumption network
ESBL	Extended spectrum beta lactamases
$ESBL_A$	ESBL, plasmid mediated, inhibited by clavulanic acid (A=classical)
$ESBL_{carba}$	ESBL with activity against carbapenems
$ESBL_M$	ESBL, plasmid mediated, inhibited by clavulanic acid (M=miscellaneous)
ESCMID	European Society of Clinical Microbiology and infectious diseases
EU	European Union
EUCAST	European committee on antimicrobial susceptibility testing

GP	General Practitioner
ICD	International classification of diseases
ICU	Intensive care unit
IPSE	Improved Patient Safety in Europe
MIC	Minimal inhibitory concentration
MRB	Multi resistant bacteria
MRSA	Methicillin resistant Staphylococus aureus
NEPI	the Network for Pharmaceutical Epidemiology
NordicAST	Nordic Committee on Antimicrobial Susceptibility Testing.
OECD	The Organisation for Economic Co-operation and Development
OIE	World organisation for animal health
OTC	Over the counter
PcG	Penicillin G (Benzylpenicillin)
PcV	Penicillin V
PDD	Prescribed daily dose
PNSP/PRP	Penicillin non-susceptible (resistant) pneumococci
PPS	Point prevalence study
PRIS	Primary care record of infections in Sweden
PV-quality	Quality register for primary care
RAVE	Search engine used for Primary care Register of Infections in Sweden
ReAct	Action on antibiotic resistance, independent global network
ResNet	Webb application for Resistance surveillance and quality control programme
RIVM	The National Institute for Public Health and the Environment, the Netherlands
RTI	Respiratory tract infections
SAI	Healthcare Antibiotics and Infection Tracking System
SALAR	the Swedish Association of Local Authorities and Regions
SIR	Swedish Intensive Care Registry

SIR	Categorisation of infectious agents as Susceptible Intermediate or Resistant to particular antibiotics antibiotics
SMI	the Swedish Institute for Communicable Disease Control
SmiNet	Electronic notification of communicable diseases
SRGA	Swedish Reference Group for Antibiotics
Strama	Swedish strategic programme against antibiotic resistance
SWEDRES/ SVARM	A Report on Swedish Antibiotic Utilisation and Resistance in Human Medicine (SWEDRES) and Swedish Veterinary Antimicrobial Resistance Monitoring (SVARM)
UK-NEQAS	United Kingdom National External Quality
UTI	Urinary tract infections
VAP	Ventilator associated pneumonia
VRE	Vancomycin resistant enterococci
WHO	World Health Organisation

Summary

The antibiotic consumption in Sweden has decreased substantially since the mid-1990s. Sweden has a relatively low use of antibiotics per capita and favourable resistance conditions. Sweden was early to initiate long-term and structured measures, characterised by work on both national and local levels coordinated by the Strama network.

Factors that may explain the favourable situation in Sweden include regulated sales of antibiotics and high coverage of data on antibiotic sales. Within the Swedish healthcare there is a tradition of relatively frequent sampling and culturing of patients, which generates data for continuous resistance surveillance. Over all, the laboratory standard is high. Part of the strategy has been implementation of treatment recommendations for common infections in outpatient care resulting in a sustained decrease in antibiotic consumption. There are also directives for basal hygiene routines for all health care workers to reduce contact transmission. Sweden has a strong core of specialists in clinical microbiology and infectious diseases who play a key role in promoting rational use of antibiotics and have done so from an early stage.

National, local and cross-sectoral collaboration

The Swedish work is characterised by involvement on local and national levels, and there are platforms for exchange of information between the two levels. Political support and commitment for the work is strong and many stakeholders are involved. A national action plan was published in 2000 which has been important for the continuous work. Based on the action plan, the government submitted a proposition concerning a strategy for coordinated work towards the containment of antibiotic resistance and healthcare-related diseases, which was adopted by the parliament in March 2006. The action plan as well as the proposition have a cross-sectoral approach. As an extension of the strategy, a national intersectoral coordinating mechanism was established in 2012 for work on the containment of antibiotic resistance and healthcare-associated infections jointly run by the National Board of Health and Welfare and the Swedish Board of Agriculture. It involves cooperation between 20 authorities active within public health, animal health, food and the environment.

Joint international efforts are important. Sweden has several bilateral collaborations and is actively involved in global efforts to contain antibiotic resistance through cooperation with actors in other countries, the EU and the WHO.

Strama – the Swedish strategic programme against antibiotic resistance

Strama plays a central role on both a national and regional level and has brought about many initiatives, being a driving force on issues concerning antibiotic resistance. Strama was formed in the mid-1990s as a voluntary network of agencies and

organisations on a national level, tied together by a network of local Strama groups. The organisation as well as the financing of Strama has successively been more formalised. The overall aim from the start has been to work to safeguard the efficiency of antibiotic treatment.

There are local Strama groups in every county council, most often under the leadership of the county medical officer for communicable disease control. A prerequisite for effective preventive work is that different competencies work together to exchange experiences and with problem-solving. The composition of the Strama groups may vary, but they generally contain physicians from primary care as well as hospital specialties, pharmacists and clinical bacteriologists, in some groups dentists, and sometimes nurses. Cooperation with local pharmaceutical committee and infection control unit is also ongoing.

Swedish experience demonstrates that work for rational use should be carried out close to the prescriber. A key component in the work of the Strama groups is the regular meetings with the prescribers with feedback of resistance and prescription data analysis in relation to treatment recommendation. Within an increasing number of county councils, IT-systems are now being constructed so that feedback can be given on an individual level to enable every physician to compare their prescribing with that of their closest colleagues. The national guidelines form the basis of local guidelines and have an impact through the local engagement.

On a national level The Public Health Agency of Sweden works, with support from the Strama advisory council, for an interdisciplinary, locally approved model by ensuring involvement of all relevant stakeholders including national and local authorities and professional and non-profit organisations. Central activities include producing treatment recommendations and knowledge base documents, information, conducting studies, international monitoring, training of physicians, and advocacy.

Resistance monitoring with good geographic coverage

National and local monitoring forms the basis for developing treatment recommendations and following resistance development and implementing and measuring the effect of interventions. Resistance monitoring in Sweden is mainly done on a voluntary basis and has good geographic coverage based on an established collaboration between the Public Health agency and local laboratories. The majority of patients in Swedish hospitals are cultured prior to antibiotic treatment. Data generated from clinical cultures, along with data from screening and transmission tracing of antibiotic-resistant bacteria form the basis of the resistance surveillance. Epidemiological typing is carried out on all notifiable forms of resistance. Sweden is actively working for quality assured methodology and has since many years used the common breakpoints established by the European Committee on Antimicrobial Susceptibility Testing (EUCAST).

The Public Health Agency of Sweden is responsible for national monitoring and analysis of antibiotic resistance. Four different systems are used in Sweden for national coverage of resistance surveillance; Res-Net, EARS-Net, SMI-Net and Svebar. Svebar is a system to which all culture findings from the country's laboratories are automatically transferred on a daily basis. This allows for an early alert on findings of very serious antibiotics resistance.

Monitoring of antibiotic consumption includes all sales

The Swedish eHealth Agency maintains pharmaceutical sales statistics, delivered by all registered pharmacies. At the national level, the Public Health Agency of Sweden is responsible for the surveillance, analysis and feedback of statistics on antibiotic consumption in human medicine. The surveillance allows for continuous information with good coverage of the amount of antibiotics consumed in Sweden. There is a lack of adequate IT systems for diagnosis-linked prescribing data, needed for the information on why the antibiotics have been prescribed and to follow the adherence to the treatment recommendations. Several initiatives have been taken to set up registers and systems that automatically generate diagnosis-linked data in outpatient care as well as in inpatient care, such as the Anti-Infection Tool IT system for registering of antibiotic prescriptions and healthcare-associated infections.

Evidence based treatment recommendations give support to the prescriber

National recommendations set a standard for when antibiotics are indicated. They are important for reaching similar management in the country and to reduce overprescribing. The Medical Products Agency and the Public Health Agency of Sweden have published national recommendations for treatment of common infections in outpatient care. To gain the highest possible credibility and acceptance they are written in consensus with experts representing several medical specialties from both out-patient and hospital care. National care programmes for infections in inpatient care have been developed by the Swedish Society of Infectious Diseases, a nationwide group consisting mainly of infectious disease specialists.

Local organisations such as Strama groups and pharmaceutical committees are key actors for the dissemination and implementation of recommendations in healthcare settings. Based on national recommendations, local guidelines and memoranda adapted to local needs are produced.

Information for health care workers and the public

No sales of antibiotics is directly directed toward patients – only the prescribers can prescribe antibiotics in Sweden. Still, the patients' knowledge, attitudes and expectations affect the prescribers. Information targeting both health care workers, patients, the public and the media is therefore part of the strategic work. The Public Health

Agency of Sweden and local Strama groups have a continuous cooperation on communication efforts and strategies.

Brochures and apps for smartphones with summarised treatment recommendations, patient information, posters at health clinics, brochures for elderly and parents of younger children, education at children's health centres, school material, shorter films for the web and TV as well as a website "antibiotics or not" are examples of produced information material. The Strama groups also share their experiences at recurrent Strama Days and through the web portal Strama.se.

Statistics over antibiotic sales and – resistance provide central information and are produced and communicated both locally and nationally. The Public Health Agency of Sweden compiles and analyses national data together with the National Veterinary Institute in the SWEDRES/SVARM annual report and continuously on its website and in electronic newsletters. Strama groups publish local statistics on local websites, news letters and emails. The Public Health Agency of Sweden and the Strama groups often coordinate press releases on data from international, national and local surveillance to reach both national and local media. Sweden also participate in the yearly European antibiotic awareness day (18th of November), coordinated by the European Centre for Disease Control to draw attention to the importance of rational use in all Europe. ECDC also produces information material targeting different groups in conjunction with the day. Joint efforts on many levels are important in the communication of the work for containing antibiotic resistance.

Guidance for readers

The report is divided into six chapters dealing with different aspects of the Swedish work against antibiotic resistance. The chapters can be viewed separately for in-depth reading of specific areas, and some basic descriptions are therefore repeated in the different chapters.

Chapter 1 describes Sweden, Swedish healthcare and the organisation of the Swedish work against antibiotic resistance.

Chapter 2 describes the development and continuous work of Strama (the Swedish strategic programme against antibiotic resistance).

Chapter 3 and 4 deals with surveillance of antibiotic resistance and antibiotic use, respectively.

Chapter 5 brings up the work with national and local treatment recommendations.

The **final sections of chapter 3–5** give examples of local initiatives, based on interviews with chairmen of local Strama groups.

Chapter 6 focuses on communication. Many of the examples on information campaigns and strategies in chapter 6 are described in the other chapters but is here contexualised.

Four interviews with experts that have been influential in the Swedish work for containment of antibiotic resistance within human medicine are presented in the report. In the interviews the experts share their experiences on the work conducted and points to future needs and measures for improvement.

Appendix 1 and 2 provide a more detailed presentation of important and useful examples of studies conducted and information material produced, illustrating the Swedish work over the years. The appendixes can be downloaded from the Public Health Agency of Sweden's website

A brief background

Resistant bacteria pose a global threat which not only causes increased mortality and morbidity but also results in high healthcare costs. Collaboration and exchange of experiences between countries are vital since the resistance spreads across national borders: through travel, through the exchange of healthcare, through the transportation of food and animals, and through the environment. To secure a future with effective antibiotics we need sustainable solutions within all the sectors in which antibiotics are used. It is also important that the effect of antibiotics on bacteria in the external environment is limited, which is done by minimising discharges at all stages – from production all the way to sewage.

Nearly 70 years have passed since Alexander Fleming, Ernst Boris Chain and Howard Walter Florey received the Nobel Prize in Physiology or Medicine for their discovery of penicillin. Since then, antibiotics have saved millions of lives. Since then, at least one million tonnes of antibiotics have also been manufactured and used within human medicine, veterinary medicine, and agriculture and food production. All use of antibiotics increases resistance to antibiotics, and the extent of usage affects the rate at which resistance spreads.

Sweden has a long tradition of work to promote rational use of antibiotics and containment of antibiotic resistance and participates actively in the global efforts. The Swedish strategic work also focuses on intersectoral collaboration and includes human and veterinary medicine, agriculture, food production and environmental sectors. The extensive use of antibiotics, both adequate and inadequate, has led to a globally escalating resistance to antibiotics. At the same time, the development of antibiotics with new mechanisms of action has virtually come to a halt. The effective treatment options for bacterial infections that penicillin and subsequent antibiotic substances developed in the 1940s to the 1980s offered have been reduced, which has resulted in an increasing number of infections being difficult or impossible to treat. Reports of patients dying from resistant bacterial infections following transplants, cancer treatment and operations show that antibiotic resistance can also compromise advances in modern medicine. Every year, hundreds of millions of people are affected by healthcare-associated infections, according to WHO. The most common way of transmission in healthcare is through contaminated hands. Sweden has joined the WHO campaign Clean Care Is Safer Care and observes the WHO's annual hand hygiene day. The WHO has declared 5 May Global Hand Hygiene Day, aimed at improving hand hygiene in healthcare throughout the world.

One of the cornerstones of the WHO strategy for containment of antimicrobial resistance from 2001 is to address unnecessary and incorrect use of antibiotics in order to slow the spread of antibiotic resistance as far as possible. Resistance monitoring and measures to reduce the transmission and burden of infections are also areas of priority. The strategy underlines the need for research into the development of antibiotics with new mechanisms of action and the development of vaccines.

We currently lack knowledge about the extent of the resistance issues and the consequences thereof. There is however some knowledge about the "burden" of antibiotic resistance. The countries most affected are those with limited resources and those where access to data is the most limited. For example, 70 percent of the cases of sepsis in infants born in hospitals in Tanzania could not be treated effectively with the preparations recommended by the WHO, because of the development of resistance to these preparations (1). Within the EU, infections caused by a number of significant resistant bacteria are estimated to be responsible for at least 25,000 deaths every year. These infections lead to increased annual healthcare costs and losses of productivity amounting to at least EUR 1.5 billion in the EU (2). An extrapolation of results from a study in the USA shows that infections caused by resistant bacteria are estimated to cost the US healthcare system USD 20 billion every year. These infections result in an extra 8 million days being spent at hospitals (3). In another study from the American CDC it is estimated that MRSA (Methicillin-resistant Staphylococcus aureus) infections alone cause 19,000 deaths every year (4).

Cooperation between countries has led to success in the fight against communicable diseases such as smallpox, polio, tuberculosis and measles. Many important initiatives regarding the containment of antibiotic resistance have been taken by international associations and by the governments and experts in individual countries. Working together is the only way we can secure a future with effective antibiotics and we need to act now. As the WHO slogan clearly states: No action today, no cure tomorrow.

Chapter 1. An overview of Sweden and the Swedish work on containment of antibiotic resistance in human medicine

Sweden was one of the first countries to initiate long-term, structured measures to contain antibiotic resistance. The work has proved to be a success as Sweden, in a global context, has a relatively low use of antibiotics per capita and in total, and favourable resistance conditions. But the current situation is also influenced by other factors. This is why any work on containment of resistance must be seen in and adapted to its given context. The intention of this chapter is to provide an overview of Sweden, Swedish healthcare and of how the work on containment of antibiotic resistance has been organised.

The focus of this report is on the rational use of antibiotics and resistance monitoring. Strategic work on the containment of antibiotic resistance also includes efforts to reduce the transmission of infection and healthcare-associated infections. This chapter will thus conclude with a general description of Sweden's work in this important area.

Basic facts about Sweden and Swedish public health

Sweden forms part of the Scandinavian peninsula in northern Europe. Sweden is a democracy with a parliamentary form of government. There are three democratically elected levels. On a national level there is the Riksdag (the national parliament), which holds the legislative power. The party or parties that receive the most votes in the general election form the Government that, among other things, may propose new legislation. At a local and regional level there are 20 County Councils/regions and 290 municipalities. Sweden has also been a member of the European Union (EU) since 1995.

The country has 9.5 million inhabitants. The population density is low with an average of 23 inhabitants per square kilometre. However, around 85 percent live in urban areas. In 2011, approximately 15 percent of the population of Sweden had been born in another country. More than half of those born in another country came from Europe, mainly Finland (5).

The population has high life expectancy, almost 84 years for women and nearly 80 years for men (6). Maternal and infant mortality is very low. In 2010, maternal mortality was 4 per 100,000 live births and infant mortality was 2 (probability of dying between birth and 1 year per 1,000 live births) according to statistics from the WHO.

The overall goal of public health work in Sweden is to create social conditions that promote good health on equal terms for the entire population**.** A report from the Swedish National Institute of Public Health/the Public Health Agency of Sweden entitled "Health of the Swedish People – a Historical Perspective" maintains that the increased life expectancy and reduced premature mortality over the last centuries

can be attributed to "multiple policies specific to public health but also, and perhaps above all, to an improved standard of living as a result of general social and welfare policies" (7).

The most common causes of death in Sweden are cardiovascular diseases and tumours, while infection as a cause of death is very unusual (8). In the early 19th century infectious diseases caused more than 20 percent of all deaths. Since then, the proportion of deaths caused by infectious diseases has decreased (9). With the introduction of urban sanitation reforms, mortality caused by waterborne (and other) infectious diseases was drastically reduced in the last decades of the 19th century. The cities' water and sewage systems were expanded and waste management was improved (7). In the early 20th century, infectious diseases were responsible for 5 percent of mortality and in the 1940s for only 1 percent (9). An improved standard of living and greater knowledge of disease transmission were instrumental in reducing cases of tuberculosis, even before means of treatment were developed (7).

Other key steps towards improved public health in the 20th century were preventive measures such as child vaccination programmes and the introduction of maternal and child health centres (7).

Today, all children are offered free vaccination against 9 diseases: diphtheria, tetanus, whooping cough, polio, Haemophilus influenzae type b, pneumococci, measles, mumps and rubella. (Furthermore, vaccination against tuberculosis and hepatitis B is recommended for children with an increased risk of infection. Girls born 1999 or later are offered a vaccine against human papillomavirus, HPV). The level of coverage is very good. Over 98 percent of the children born in 2004 received all vaccines included in the Swedish child vaccination programme. Many of the diseases that are included in the child vaccination programme have almost been eradicated in Sweden (10). The National Board of Health and Welfare also recommends that elderly people and people who are at risk of severe illnesses are vaccinated against influenza and pneumococci.

Swedish healthcare

The aim of the Swedish healthcare system is good health and care on equal terms for the entire population. The care should be given with respect for the equal worth of all human beings and for the dignity of the individual. Those who are in greatest need of healthcare should be given priority of access to care (11).

Swedish healthcare performs well compared to other OECD countries as far as public health and clinical indicators for major disease areas are concerned, as has been documented in several reports (12).

Healthcare expenditure is largely funded by taxes (80 percent). To a large extent, healthcare is thus provided without any direct fees for patients. In 2009, 9.9 percent of Sweden's GDP was used to cover the cost of healthcare (12).

Responsibility for healthcare is shared between the State and the 20 County Councils/regions and 290 municipalities. The State is responsible for overall healthcare policies and funds part of the healthcare system through grants. The main financing of the healthcare system comes from the County Councils/regions through direct taxation at that level.

The County Councils and the municipalities are responsible for meeting the healthcare needs of their inhabitants. This includes work on the prevention of ill-health. They have extensive autonomy and freedom when it comes to deciding on the organisation of the healthcare. This enables County Councils and municipalities to adapt their activities to local conditions. The County Councils organise healthcare while an important responsibility of the municipalities is to organise care of the elderly and people with disabilities along with basic healthcare in certain care homes.

Primary healthcare is the cornerstone of healthcare run by County Councils and in this care, basic medical treatment, prevention and physical therapy are provided, mainly via local health centres. There are more than 1,100 health centres in the country. Approximately 60 percent of all antibiotics are prescribed in primary care, so general practitioners and nurses employed in primary care play a key role in work to promote the rational use of antibiotics.

Treatment requiring hospital care is provided at district, county and regional hospitals. Highly specialised care is provided in regional and university hospitals. Most health centres and the vast majority of hospitals are owned by the County Councils. Over the past few years, the number of health centres that are privately run has increased and currently constitutes approximately 40 percent of all health centres. Since 2010, County Councils have been obliged to introduce systems in primary care that enable patients to choose their own primary care physician (GP) and hospital for specialist care in accordance with the Act on System of Choice in the Public Sector. This allows inhabitants to choose which health centre they prefer to visit. Primary care providers may also establish private practices and receive public funds, provided that they meet the County Council's requirements.

The number of hospital beds in Sweden has decreased over the past few decades. Like many other countries, Sweden has since the 1990s increasingly moved towards providing care through outpatient services (12). A report from the OECD containing European health statistics shows that Sweden has 2.7 beds per 1,000 inhabitants. Of the 35 countries listed, only Turkey reports a lower number, with 2.5 beds per 1,000 inhabitants. The average is 5.3. Germany, Austria, Hungary and the Czech Republic have the highest number of beds per 1,000 inhabitants (8.3, 7.6, 7.2 and 7.0, respectively) (13).

Healthcare professionals

Healthcare professionals are obliged to carry out their duties in line with scientific evidence and proven experience according to Swedish law. National authorities and organisations draw up guidelines and treatment recommendations. On a local level,

pharmaceutical committees are responsible for issuing recommendations regarding the use of medication and they often cooperate with Strama groups on issues concerning antibiotic treatment (chapters 2 and 5).

Sweden has 3.8 physicians per 1,000 inhabitants, which is above the European average of 3.4 (13). In 2012, more than 20 percent of the 31,888 physicians were employed within the specialisation of general medicine/primary care. Compared with some other countries, nurses have a greater patient responsibility – administering injections and infusions and managing their own medical units for certain patient categories, especially in primary care, and providing comprehensive telephone advice services for patients. Requests for advice are common in the case of infection. Pharmacists also provide a great deal of information to patients and healthcare professionals.

Swedish work on containment of antibiotic resistance is characterised by local and national cooperation

There are currently many different actors in Sweden who are involved in work against antibiotic resistance and healthcare-associated infections. The work is characterised by involvement at both a local and national level with existing forums for exchange of information between the two levels.

Several structural aspects of Swedish healthcare may have played an important role in the development of this interaction. The country has a strong core of specialists in infectious diseases, with clinics in most of the hospitals at county level or above. This has led to better availability of staff knowledgeable about minimising the transmission of disease and isolating patients compared with many other countries. Infectious disease specialists have also been key in controlling antibiotic use with focus on narrow-spectrum use and have done so from an early stage. Working in increasingly consultative roles in hospitals, the specialists have had a major influence, particularly on the use of antibiotics in hospital care.

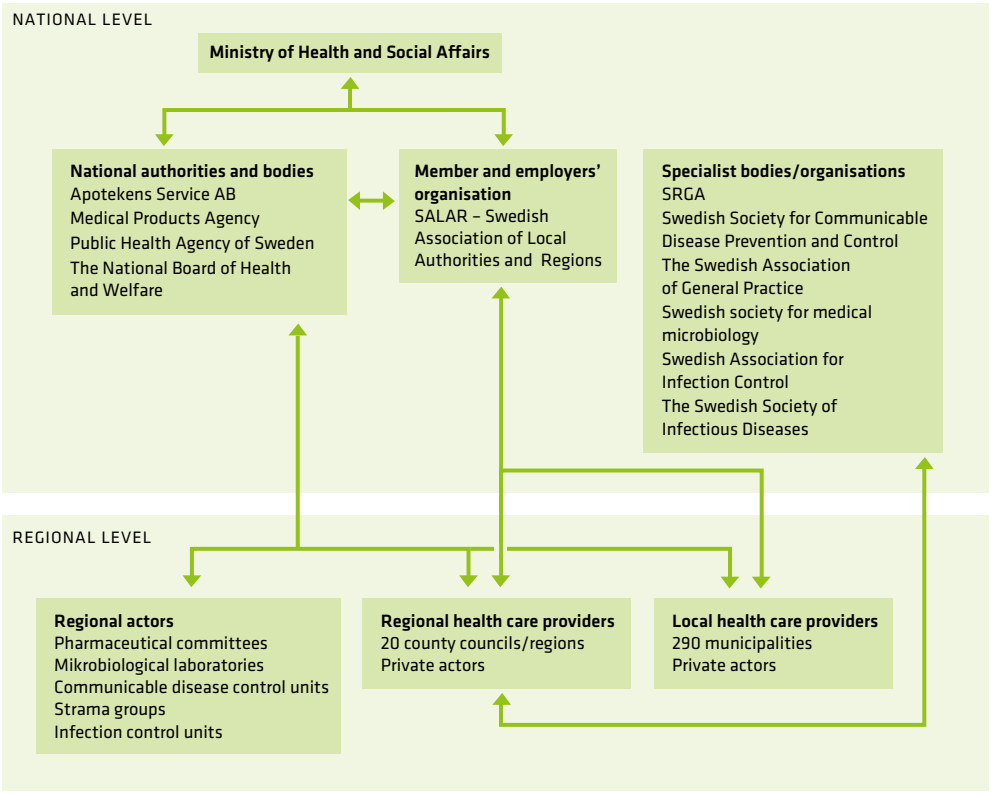
A system of County Medical Officers for communicable disease control was established in 1989 according to the Communicable Diseases Act (CDA). Every county is required to have such an Officer, responsible for communicable disease prevention and control both within and outside healthcare, in the specific geographic area. The County Medical Officer for communicable disease control is most often an infectious disease specialist, has public authority status, and also liaises with other parts of the healthcare system, not least with physicians in primary care. As a group, they have been able to influence the use of antibiotics and have also assumed great responsibility for the rational use of antibiotics. Many of them also joined the Strama network early on by taking on the chairmanship of the local Strama group (see below).

Both the infectious disease clinics and the units for communicable disease control have close links with the clinical microbiological laboratories, as well as with the infection control units in all larger hospitals. They bring important elements to the work; resistance data is brought from the laboratories and can be used to regulate the

local use of antibiotics, while infection control plays a key role in limiting the transmission of resistant bacteria in healthcare.

In the mid-1990s, Sweden was one of the first countries where a strategic cooperation on the containment of antibiotic resistance was initiated with the Swedish strategic programme against antibiotic resistance (Strama) (chapter 2). This was formed as a network of authorities and organisations on a national level that tied in with the network of local Strama groups that rapidly followed in the County Councils. The local groups are designed as multi-professional teams with representatives from general medicine as well as from inpatient care among other areas.

Figure 1.1 Stakeholders involved in the Swedish work on containment of antibiotic resistance and healthcare-associated infections.



On a national level, the Ministry of Health and Social Affairs is working to realise the objectives of the national health policies developed by the Swedish Parliament. A number of different authorities support the Ministry's activities. The main authorities that work on the containment of antibiotic resistance and healthcare-associated infections in human medicine are the National Board of Health and Welfare, the Public Health Agency of Sweden and the Medical Products Agency. On a national level, there are also a number of specialist associations such as the Swedish Association of Local Authorities and Regions (SALAR), which is an employer and interest organisation for the municipalities and County Councils. On a regional and local level, microbiological laboratories, communicable disease units, Strama groups, pharmaceutical committees and infection control units are involved. Every County Council has a County Medical Officer for communicable disease control who is responsible for planning and leading the local work for communicable disease prevention and control within the County Council/region.

Sweden's small population facilitates the creation of personal contacts and networks. Cooperation between Strama groups, pharmaceutical committees, microbiological laboratories and networks for prevention and control also promotes communication and the establishment of a nationally developed knowledge base for target groups in healthcare. Local and regional actors are in direct contact with the target groups in healthcare and can, at an early stage, identify the need for new information to be compiled on a national level. Local actors are also involved in drawing up local guidelines and procedures.

There has been strong political support and commitment for the work on containment of antibiotic resistance. When the problems became evident in the 1990s and the Strama network was formed, the National Board of Health and Welfare was commissioned by the Government to draw up a proposal for a Swedish action plan for the containment of antibiotic resistance. The subsequent SPAR plan was developed in 2000 in cooperation with relevant authorities, Strama and other organisations. The existing knowledge base regarding the issue of resistance was examined and measures were proposed aimed at containing antibiotic resistance in both the short and the long term. The plan involved active efforts in human and veterinary medicine and food production and highlighted the need for documentation in order to evaluate the significance of the external environment as a reservoir for antibiotic resistance. The plan emphasised the importance of adequate monitoring of resistance and the use of antibiotics. It also underlined the significance of a rational use of antibiotics as well as the importance of limiting the need for antibiotics by reducing the incidence and transmission of infections. Further, it emphasised the importance of cross-sectoral work on the containment of resistance. The overall goal of the action plan was to safeguard the efficiency of antibiotic treatment for humans and animals (14).

Based on the action plan, the Government submitted a proposition concerning a strategy for coordinated work towards the containment of antibiotic resistance and healthcare-associated diseases, which was adopted by the Riksdag in March 2006 (15). The proposition has a cross-sectoral approach and includes initiatives within human and veterinary medicine, the non-medical use of antibiotics within the agriculture and food sectors, and initiatives to prevent environmental effects stemming from the use of antibiotics.

As an extension of the strategy, a national coordinating mechanism was established in 2012 for work on the containment of antibiotic resistance and healthcare-associated infections. This is in line with the EU Council's recommendation (16) which calls upon the EU's member states to establish an *Intersectoral Coordinating Mechanism*. It is jointly run by the National Board of Health and Welfare and the Swedish Board of Agriculture and includes 20 Governmental agencies. One of the aims is to facilitate the exchange of information and bring about successful cross-sectoral work between authorities, interest organisations and professional organisations active within public health, animal health, food and environmental sectors..

In 2010 the Government launched a four-year patient safety initiative as the result of an agreement with the Swedish Association of Local Authorities and Regions. The initiative identifies the rational use of antibiotics and healthcare-associated infections as central patient safety issues. During 2011–2014, the Government is allocating SEK 400 million a year to County Councils as a stimulus, provided that they meet certain basic requirements and implement measures to increase patient safety in healthcare. The requirements to be fulfilled in order to receive the additional funding include the establishment also formally of a local Strama group and the reduction of antibiotic prescription, with greater attention to treatment recommendations for common infections in outpatient care (chapter 4). A stimulus is also allocated to those County Councils that monitor compliance with basic procedures for infection control, including the hospital dress code.

International efforts

Sweden is actively involved in international efforts on antibiotic resistance through cooperation with actors in other countries, the EU and the WHO. By participating in international efforts, Sweden can keep track of and prepare more effectively for new variants of antibiotic resistance. Important lessons can also be learned from experiences of preventive measures in other countries. The export of Swedish expertise in this field has also been seen as a means of influencing the development of resistance in the international arena. For example, Sweden has drawn up bilateral agreements with India and China including initiatives concerned with the containment of antibiotic resistance in human medicine.

ReAct is a Swedish-based international network that has been working on the containment of antibiotic resistance in several countries for 10 years, including parts of Latin America. ReAct works for increased awareness of the problem posed by increased antibiotic resistance and to create an environment for cooperation and joint action on this issue. On its website (www.reactgroup.org), ReAct has gathered information material in a so called “Resource Centre”.

Sweden is also actively involved in the World Organisation for Animal Health (OIE) and in Codex work. From an international perspective, Sweden also has a low use of antibiotics and very favourable resistance conditions in animal husbandry (SWEDRES/SVARM 2012) (17). While many countries still use antibiotics as growth promoters in animal feed, this practice was banned in Sweden in 1986 and in the EU in 2006.

Monitoring of the use of antibiotics and antibiotic resistance

The sale of pharmaceuticals is regulated in Sweden. Antibiotics can only be obtained by prescription in outpatient care or by prescription by a physician in hospital. This means that there is no over the counter sale to patients without a prescription. Resistance conditions and the use of antibiotics are constantly monitored both nationally

and locally, with the development of increasingly sophisticated systems (chapter 3 and 4).

The Public Health Agency of Sweden is responsible for the national monitoring of antibiotic resistance and the use of antibiotics in human medicine. Since the 1970s, Swedish pharmacies have contributed statistics on the sale of antibiotics, which has provided valuable insight into the changes that occur over time. Sweden's statistics, as far as the sale of antibiotics is concerned, compare favourably when viewed in an international context.

National resistance monitoring is to a great extent dependent on voluntary reporting of resistance data by regional microbiological laboratories to The Public Health Agency of Sweden. In addition to this, certain cases of serious antibiotic resistance are notifiable according to the Communicable Diseases Act (chapter 3).

Prevention and control of disease transmission

The transmission of resistant bacteria also drives the development of resistance. This is why preventive efforts to reduce the transmission of disease and healthcare-associated infections are vital in the work to contain resistance. This matter will not be discussed at any length in other parts of this book; the following section will therefore give a brief overview of Sweden's work in this area.

In every Region/County Council there is a County Medical Officer for Communicable Disease Control, with public authority status, who with his/her unit is responsible for planning and leading the work against communicable diseases within the geographical area. The assignments, that are regulated according the CDA, include among other things to follow the presence of notifiable diseases and resistant bacteria, and follow up on the actions taken for containment of further spread. Most outbreaks of resistant bacteria in the health care setting are detected on a local level by notification according to the CDA to the County Medical Officer, and is dealt with by the unit for communicable disease control together with the local unit for infection control and the responsible health care provider.

Sweden has a long tradition of promoting disease prevention and control. In the 1960s, the first nurses and physicians specialised in disease prevention and control were employed in Swedish healthcare. Since the very start they have worked methodically to prevent healthcare-associated infections and have thus pioneered work on quality control. Among other things, this work has involved issuing recommendations on a national, regional and local level (18).

Many of the infectious agents that cause healthcare-associated infections are transmitted through contact, often via contaminated hands. Hand disinfection with an alcohol-based disinfectant has been recommended in Sweden since the 1980s. Bottles of hand disinfectant are today available to staff, patients and visitors in hospitals. Basic procedures for infection control are a key concept in the work on disease prevention

and control in Sweden. This includes all aspects of infection control that healthcare professionals are required to apply in order to avoid transmission via direct contact when caring for patients. All healthcare staff in Sweden must follow certain basic procedures in their work close to patients, as is outlined in an instruction issued by the National Board of Health and Welfare (19).This involves disinfecting hands with an alcohol-based hand disinfectant before and after patient contact. In order to carry out hand disinfection correctly, healthcare professionals must not wear wrist watches or rings. They must also wear short-sleeved uniforms.

Swedish healthcare professionals are generally well aware of the basic procedures for infection control, and surveys show that it is considered a priority. National point prevalence surveys, which have been carried out by the Swedish Association of Local Authorities and Regions twice a year since 2008, measure the incidence of health-care-associated infections in inpatient care, and since 2010 also the compliance with the procedures. These surveys show that approximately 10 percent of patients in inpatient care have a healthcare-associated infection, which is equal to the number often quoted in international literature. Compliance surveys show that healthcare professionals (physicians, nurses, assistant nurses) follow basic procedures for infection control to a large extent but that there is still room for improvement. The most problematic aspect of compliance is ensuring hand disinfection *before* patient contact. By contrast, healthcare staff are normally compliant in wearing short-sleeved uniforms.

The Health and Medical Services Act states that healthcare providers are responsible for ensuring that the quality of care is good and has a high standard of hygiene. Rules have been in place since 2006 to ensure that all healthcare providers have access to competence in infection control. This is why there are infection control units equipped with specialised physicians and nurses within every County Council. The work of the infection control units involves training healthcare professionals in how to prevent healthcare-associated infections, monitoring the incidence of healthcare-associated infections, management of outbreaks and drawing up local guidelines on disease prevention and control.

The field of work has been broadened to include outpatient care where an increasing number of patients are being cared for. Many issues are handled through interaction with other local actors such as microbiological laboratories, Strama groups, infectious disease clinics and communicable disease control units. In consultation with the communicable disease control unit, local guidelines are often developed for measures on infection control for screening and tracing the transmission of multi-resistant bacteria, and for treatment of patients with such infections, including policies for single rooms.

Many physicians and nurses specialised in infection control are members of the Swedish Association for Infection Control, which organises training, develops knowledge in the field of prevention and control, and pursues issues of infection control on a national level. Other national actors include the Swedish Association of Local Authorities and Regions, the Public Health Agency of Sweden, the National Board of Health and Welfare and the Swedish Work Environment Authority.

A group was formed in 2013 made up of the actors working with infection control in human medicine on a national level. The participating experts are to identify important and current issues in the field of infection control, keep the group up to date on planned activities and suggest and coordinate joint action when needed.

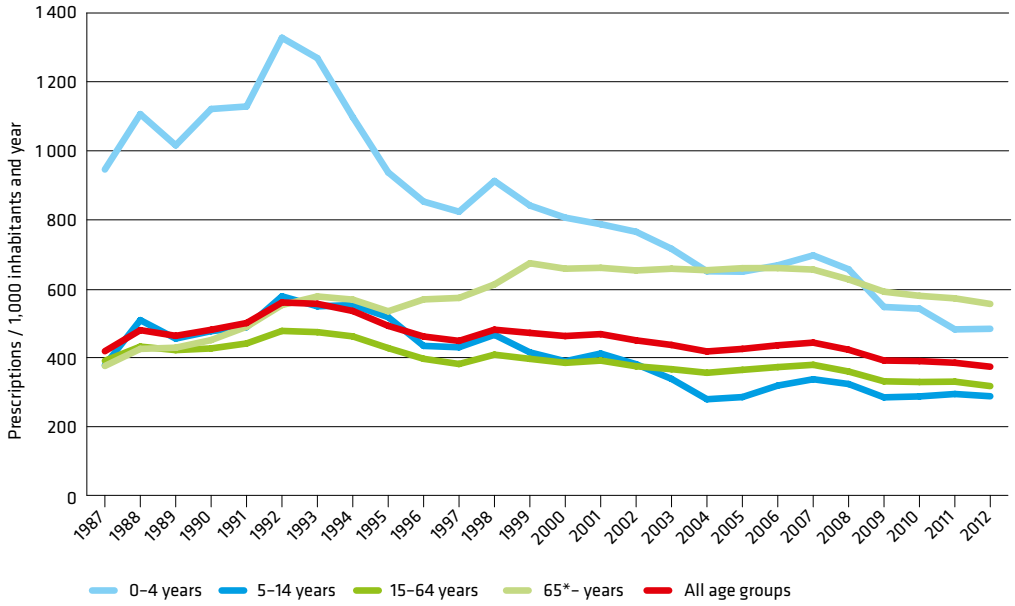
Chapter 2. Strama work

This chapter will describe Sweden's successful work on containment of antibiotic resistance, with a focus on the rational use of antibiotics in human medicine. In a description of the Swedish efforts in this field, the Swedish strategic programme against antibiotic resistance, known as Strama, plays a central role. This does not mean that Strama is the only, or the largest, party involved in this work. On the contrary, Strama has often had the role of stimulating, coordinating and cooperating with a number of other important parties. Whilst the use of antibiotics has been one of many areas of interest to other actors, authorities and organisations, the *sole* aim and task of Strama is to work to safeguard the efficiency of antibiotic treatment for bacterial infections. As a result, Strama has brought about many of the initiatives and has been the driving force on issues concerning antibiotic resistance. The local Strama groups also play an important role in implementation of recommendations and routines in the healthcare setting.

Strama was formed in the mid-1990s as a voluntary network consisting of two levels, a national level and a regional level, with local Strama groups. Initially, the national level was an independent organisation in which representatives from authorities and organisations made up a national working group. Since 2010, this group has been incorporated into the Public Health Agency of Sweden.

As mentioned, the two decades following Strama's foundation coincide in time with a favourable development in Sweden's work for rational antibiotic use and containment of antibiotic resistance. This chapter will describe Strama's role in this context in greater detail.

Figure 2.1 Antibiotic consumption in Sweden over time. Source SWEDRES 2012.



A summary overview of how antibiotics have been prescribed in the country over time shows that the founding of Strama and its early, dynamic process of establishment coincide in time with a decrease in the total number of prescriptions; after an increase between 1987–1993, a significant decrease was noted between 1994 and 2012.

Figure 2.2a Sweden's levels of resistance are favourable compared to other European countries in respect of MRSA (percent MRSA of invasive isolates). EARSNet 2012.

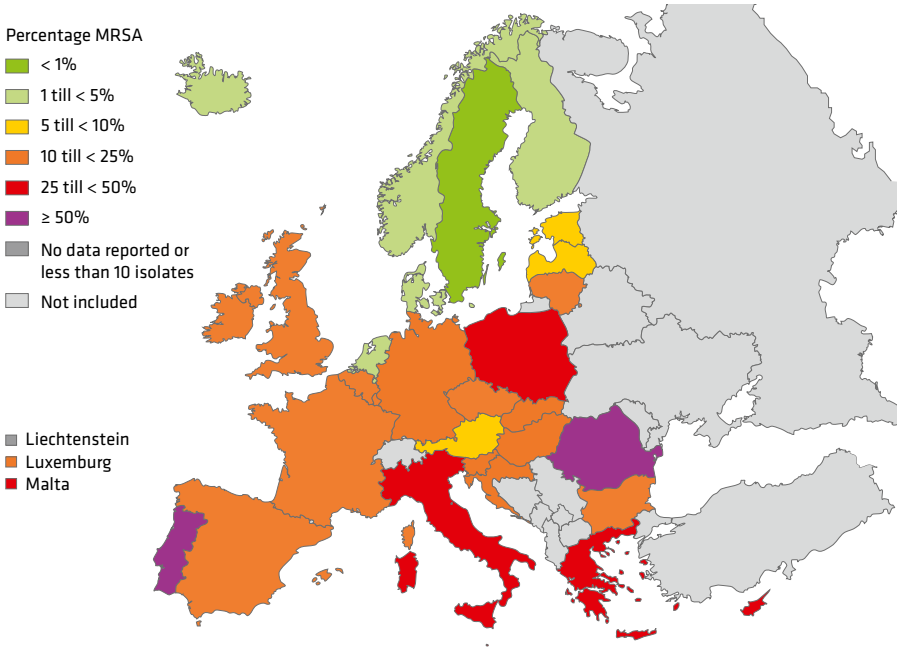
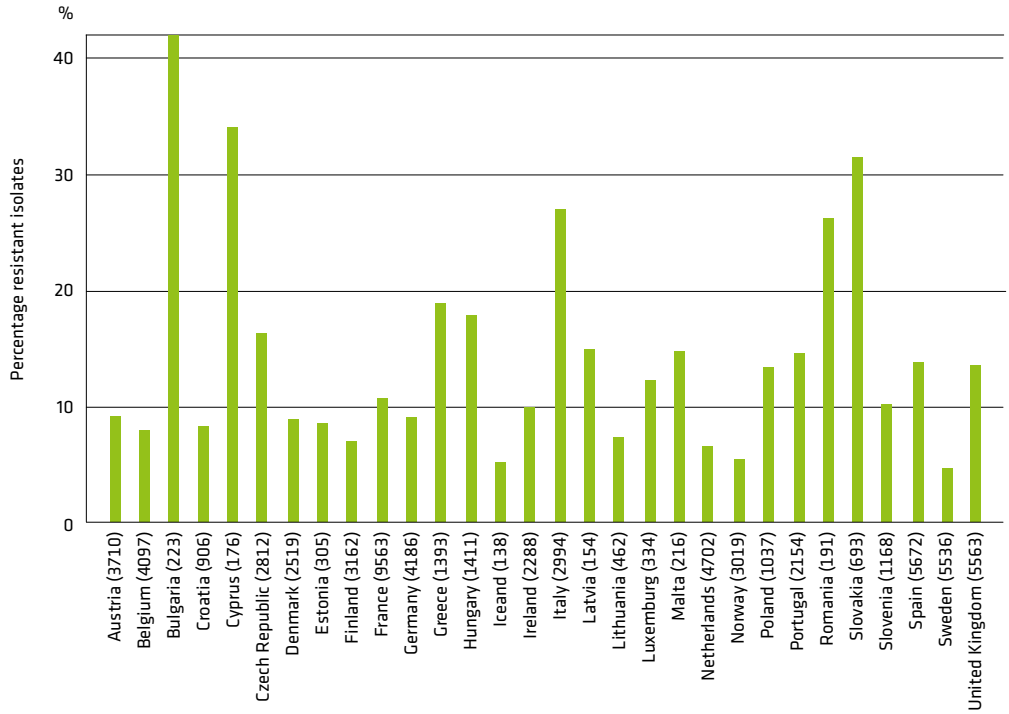


Figure 2.2b Sweden's levels of resistance are favourable compared to other European countries in respect of resistance to third generation cephalosporins and ESBL in *E. coli*. Ears-Net 2012. (Number of isolates in brackets after the country name).



Sweden's levels of resistance are also favourable from an international perspective. It is difficult to give a simple and concise account of reality considering the multitude of combinations of bacteria and antibiotics – the existence of MRSA, ESBL, quinolone resistance in *E. coli*, aminoglycoside resistance in Pseudomonas, to mention only a few of importance. As examples, two of the more well-known resistance forms, MRSA and ESBL, with data from ECDC are described below.

The development of the organisation and work of Strama

The foundation of Strama was triggered by a rapid increase in resistance to penicillin among pneumococci in southern Sweden in the early 1990s (20). The existence of strong, independent specialist bodies in the fields of infectious disease and general medicine may have contributed to the early and coordinated response to this phenomenon. It soon became evident that a coordinated national strategy was needed to deal with the problem. An expert meeting was convened in 1995 at the initiative of the Swedish Society of Medicine's expert group on antibiotic issues (SRGA, see below), which saw the participation of many authorities and organisations working in different ways with antibiotic resistance (see the fact box below). The meeting resulted in an agreement between the various parties to form the informal Strama network (the Swedish strategic programme against antibiotic resistance), led by a chairman.

The different parties that agreed to form the informal Strama network were:

- The Swedish Society of Medicine's expert group on antibiotic issues
- The Swedish Institute for Communicable Disease Control
- The Swedish Society for Communicable Disease Prevention and Control
- The Medical Products Agency
- The National Board of Health and Welfare
- Apoteksbolaget AB
- NEPI – Nätverk för Läkemedelsepidemiologi (the Network for Pharmaceutical Epidemiology)
- The National Veterinary Institute
- Representatives of pharmaceutical committees

The broad representation of authorities and expert bodies helped to establish a firm basis and a wide perspective in terms of how Strama's strategic work would be organised. In parallel with this, local Strama groups were formed in different parts of the country, usually under the direction of the County Medical Officer for communicable disease control. By 1996, such groups had already been formed in nearly all of the 21 counties. Representatives from the Strama groups joined the national managing body of Strama, thereby securing important organisational links between the national and local levels (21).

In terms of finances, activities were initially conducted both nationally and locally without any specific funding – experts' participation being paid for by their authority or the organisation they represented. The contributions of the NEPI foundation were also vital.

In 2000, the first action plan on the containment of antibiotic resistance was presented; the Government had commissioned the National Board of Health and Welfare to produce this, in close cooperation with Strama (chapter 1). It contained a number of goals and priorities for the work on containment of antibiotic resistance and laid the foundation for further work in Sweden. The plan highlighted the need to improve resistance monitoring and monitoring of the use of antibiotics. One of the early and

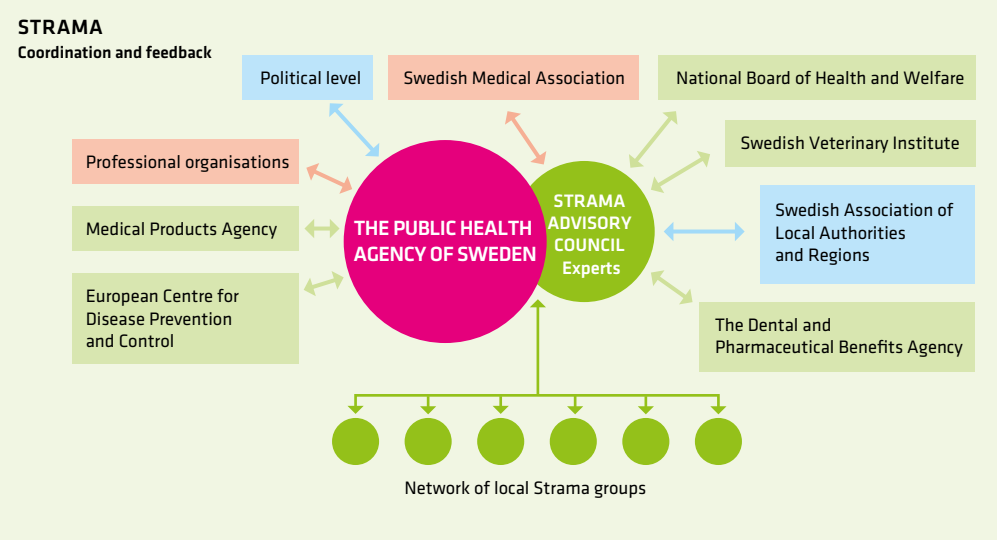
important realisations was that the measures proposed in the plan had to include implementation within the healthcare system throughout the country. The locally formed Strama groups played an essential role in this work.

In 2000, national Strama began receiving funding from the Government and in 2006 it was also given a Government commission stating that "Strama is an interactive body aimed at promoting the cross-sectoral coordination of issues that relate to safeguarding the efficiency of antibiotic treatment for bacterial infections in humans and animals, and to initiate measures that primarily concern human health" (22, 23) . Since 2010, the work done by national Strama has been incorporated into that of the Public Health Agency of Sweden (formerly the Swedish Institute for Communicable Disease Control, SMI), and their previous managing body has been turned into a Strama council within this agency.

When the government commission for Strama was transferred to SMI, the local Strama groups organised themselves into the formal Strama network. The Strama network continually works to facilitate the lateral exchange of ideas and initiatives between the local groups and with this in mind manages the website www.Strama.se, which was set up back in 1998.

The patient safety plan promoted by the Government in cooperation with the Swedish Association of Local Authorities and Regions (SALAR) for 2010–2014 (chapter 1) also promotes the importance of the local Strama groups. As a result of the plan, Strama groups have now also been formed in the few County Councils which had none, and all the groups have been given formal assignments by the board of their County Council. For most of the groups, this has resulted in more clearly defined goals, and often a better organisational foundation and better finances.

Figure 2.3: Strama's relationship with several other actors.



The figure illustrates how Strama has worked, and is working together with many others for continuing effective antibiotics. Even though other actors have been larger, Strama has since the formation in 1995 often contributed with coordination and energy, by having the focus on this one only topic and by the structure of networks with close collaboration of national and regional/local levels.

Network and interaction – key elements in Strama work

Essential catchwords in Strama's work are interaction, network, multi-disciplinary work – and local implementation. There has always been interplay between the national level and the local groups, where questions from local groups, events and national and local meetings have presented ample opportunities for both vertical and horizontal exchanges. National "Strama Days" have provided an important arena for this interplay and networking, completely independent of the pharmaceutical industry and other commercial interests. They have been organised annually since 1997 to offer educational updates on antibiotic issues, to facilitate the exchange of experiences and establish policies and campaigns, often with significant media exposure. The Strama.se website contributes to the lateral exchange of local initiatives and presentations.

Since 2001, a newsletter (known as Strama-Nytt until 2011 and subsequently integrated into the Public Health Agency of Sweden's newsletter) has also been produced at the national level containing presentations of new data, summaries of current articles or other important reports

There is strong involvement at a local level, stimulated by direct contact with prescribers and patients, and at a national level, which provides a good overview of national and international tendencies and threats. Close contacts and interaction between the levels has brought a great deal of energy to the local implementation efforts, and vice versa, rendering the quote "Strama is a blowlamp".

An important realisation has been that it is not sufficient to produce data, knowledge and recommendations on a national level. They must also be implemented to be effective. The experience from the creation of local Strama groups and how they carry out their work may prove valuable to others who are initiating or strengthening their work on the containment of antibiotic resistance.

The national level

Since its foundation in 1995, national Strama organised broad strategic efforts where important components have been to:

- interact with other national actors
- create meeting places for all concerned actors, both national and regional
- monitor and analyse the development of resistance
- monitor and analyse the use of antibiotics
- issue treatment recommendations
- develop a knowledge base and training material
- monitor international developments
- carry out surveys regarding antibiotic prescription
- pursue international collaborations and projects
- communicate the issue of antibiotic resistance to healthcare professionals, the media, the general public and decision-makers

The interaction for which national Strama was initially responsible has since 2012 been formalised and further expanded through the establishment of an "Intersectoral Coordinating Mechanism" (in accordance with an EU Council recommendation). In Sweden this is managed by the National Board of Health and Welfare together with the Swedish Board of Agriculture and involves Governmental agencies active in human and veterinary medicine, the food and environment sectors, etc.

Both national and local levels of Strama are closely involved in the efforts mentioned above. A description of the structure and focus of the local Strama groups will therefore also be presented. An illustration will then follow of how the work is carried out at national and local level.

Local Strama groups

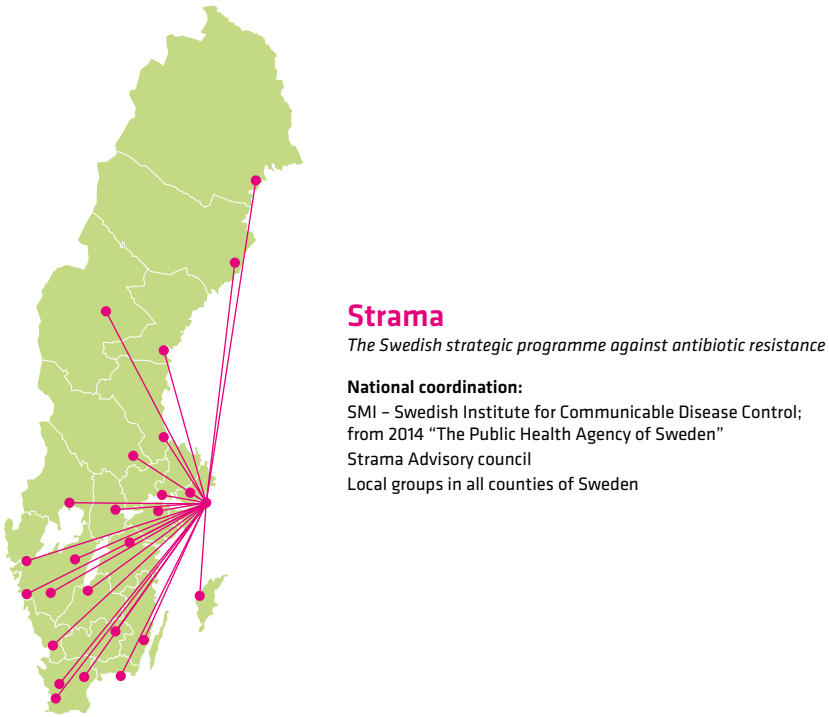
The local Strama groups may be organised in a variety of ways but work according to the same plan, drawn up in connection with their formation back in 1995–96. Since then, the overall goal has been to prevent the development of resistance through

a. the rational use of antibiotics, and

b. epidemiological measures (tracing transmission, imposing specific restrictions on MRSA carriers, single room policies etc).

Initially, the focus was on resistance in *S. pneumoniae*, *S. pyogenes*, *H. influenzae*, *S. aureus*, enterococci, urinary pathogens and other nosocomial pathogens. A number of interim goals were set for antibiotic prescription. These have gradually been revised and adapted to a changing reality, where the emergence of ESBL and later $ESBL_{CARBA}$ (CPE) has prompted powerful new measures.

Figure 2.4. The Strama network – local groups all over the country



The local Strama groups were formed in the County Councils all over the country already in 1995–1996, were further established during the government's-SALAR's patient safety initiative 2011–2014, and continues to cooperate with each other and with the Public Health Institute of Sweden (up until 2014 SMI)

Multi-disciplinary collaboration

A range of different competencies interact in the local Strama groups. One of the important members is the infectious disease specialist, whose work is centred on the use of antibiotics. General practitioners and family doctors treat the majority of patients with infections and prescribe the bulk of antibiotics, and are thus essential participants. Other categories that are often involved due to their antibiotic-intensive work are specialists in otolaryngology (ear nose and throat doctors) and paediatricians. The clinical microbiologists with bacteriological knowledge and resistance data also has a given place. Pharmacists contribute with their pharmacological and pharmacoepidemiological knowledge. Prevention of hospital-acquired infections has, at least recently, become increasingly more prominent in the work on the containment of antibiotic resistance, and representatives of infection control are now often part of

local Strama groups. The local pharmaceutical committee is also often represented. In other respects, the composition of the group may vary considerably.

One important criterion, and probably an important factor for success, has been the fact that the group members are committed to the issue of resistance. A shared commitment and the broad and combined competencies of the group have made it possible to envisage alternative paths towards the common goal – to safeguard the efficiency of antibiotics.

The local Strama groups have played a central role in the work towards the rational use of antibiotics. Their tasks involve communicating and discussing the local use of antibiotics and the national and local resistance conditions with prescribers in the county. Feedback on the situation in the county, in hospitals or health centres in relation to other parts of the country may serve as a wake-up call that developments are going in the wrong direction. The groups also maintain a dialogue with prescribers regarding new treatment recommendations. In addition, they provide training for healthcare professionals, patients and the general public. The strong commitment of local groups anchored in day to day practice is fundamental for the effective implementation of national recommendations and other measures.

The local groups work on the implementation of national goals and campaigns, but also on independent initiatives that are adapted to the changing local situation. The close ties between local Strama and the organisation for communicable disease control has also made it easier to monitor the more serious forms of resistance, since an increasing number of MRB (multi-resistant bacteria) have been made notifiable by the Communicable Diseases Act (chapter 3).

Initially, one group was established per county and County Council, often headed by the County Medical Officer for communicable disease control. The need for differentiated efforts in inpatient and outpatient care has in many places led to the establishment of a separate group for Hospital Strama, and in some cases even an ICU Strama group for intensive care. On a national level this is reflected on the Strama.se website, where information has been gathered under the separate headings Strama hospital care and ICU Strama, in addition to the general information focusing on the quantitatively more significant work in primary healthcare.

Activities central to national and local work

While some activities are specifically local or national by nature, much work is carried out on a local and national level, although on a different scale. Some key components of Strama's work on both levels are presented here.

Monitoring and analysis of the use of antibiotics and resistance

SMI and later the Public Health Agency of Sweden is responsible for the national monitoring and analysis of antibiotic consumption and resistance. *Data* is required to carry out meaningful and effective work, both on the prescription of antibiotics and

with respect to resistance conditions. This data is necessary for monitoring developments, discovering threats, implementing countermeasures and following up on already implemented measures, and last, but not least, as an impetus and motivation in the continuous discussion with prescribers and other parties. Collating, analysing and communicating data on the prescription of antibiotics and resistance conditions are important tasks for Strama on a national level. Over the years, different systems and methods for the monitoring of resistance (chapter 3), use and consumption (chapter 4) have been constructed and developed. In 2002, the first SWEDRES report was published, an overall report with data on the prescription of antibiotics and resistance, containing an analysis and description of interventions. Since 2003, this report has been produced in collaboration with SVARM, Swedish Veterinary Antimicrobial Resistance Monitoring, which provides a corresponding image of the situation within veterinary medicine. Statistics on the prescription of antibiotics and resistance are also continuously published online and in newsletters to provide quick feedback to relevant target groups.

The local Strama groups monitor, analyse and give feedback on national and local data regarding both antibiotic consumption and resistance (see the example on ESBL at the end of section 3.5).

Treatment recommendations

Data is meant to be *used*, after analysis, as the basis for the development of national and local recommendations and guidelines, which are instrumental in the rational use of antibiotics.

National treatment recommendations are of great value since they are founded upon a solid base of evidence. When working to eliminate the unnecessary prescription of antibiotics "just in case", it is also essential to give the doctors support to refrain from prescribing antibiotics. It is easier for the doctor to avoid a prescription when there is solid evidence to support the fact that antibiotics has no proven effect on the given condition, and that only the negative effects of an unnecessary treatment remain.

To gain wider acceptance, treatment recommendations must often be developed in consensus, with a multi-disciplinary approach and through the participation of several authorities and experts. Early on, Strama and the Medical Products Agency initiated expert group meetings at national level for many common infection diagnoses, primarily in outpatient care – otitis, tonsillitis, pneumonia, sinusitis, urinary tract infection, infections of the skin and soft tissue, etc. Such meetings include representatives from a number of specialist associations, for example ear, nose and throat doctors, paediatricians, infectious disease specialists, clinical microbiologists and pharmacists. The meetings result in the publication of national treatment recommendations, based on the Medical Products Agency, which in turn often form the basis for local guidelines – the latter often bringing about actual change in prescription habits.

It is important to note that it is not only the medical *treatment*, strictly speaking, that may be subject to new guidelines, but rather the *management* of a condition, including diagnostic procedures, patient flows and telephone advice services, aspects which may prove just as critical for the total consumption of antibiotics. One important example is optimising the use of simple diagnostic facilities such as rapid throat tests for group A streptococci or urine tests for nitrite and leukocytes when UTI is suspected.

The recommendations are communicated through national channels and publications, hand in hand with dissemination via local Strama groups, and often in collaboration with local pharmaceutical committees.

The recommendations for major outpatient diagnoses (UTI; various respiratory tract infections) have been formulated, often on a national level, in accessible reference manuals, folders, laminated cards that can be kept in one's breast pocket, etc. The basic idea is that new information must reach the end-user. The material is then disseminated in different ways, via direct mail to prescribing physicians, and often through local Strama groups. The information is passed on to clinical practitioners, preferably at a Strama meeting with a local health centre, where there is room to discuss the diagnoses and treatments concerned. A good example is the folder below, in which national guidelines for important diagnoses of infections are summarised in 16 pages.

Figure 2.5 Summarising brochure: National treatment recommendations for common infections in open care

An easily distributed brochure with treatment recommendations for common infections has been produced to facilitate the new recommendations actually reaching out to every prescriber in every primary health care centre.

"Rational use of antibiotics" has been a slogan in Strama's work. The phrase puts emphasis on the treatment being *correct*, adequate – and evidence-based. Over-prescribing is common and should be prevented, but should not be replaced by under-prescribing. Alongside the task of increasing compliance with treatment guidelines, a critical review is being conducted of the evidence for current treatment procedures. When important new evidence is published, the treatment recommendations are revised. In cases where no sustainable evidence can be found, the procedure should be scrapped. In other cases, studies may be required to provide a basis for new

guidelines. As an example, the indications for the antibiotic treatment of a number of common respiratory tract infections (acute bronchitis, uncomplicated sinusitis, etc.) have been re-evaluated since studies have proven that antibiotics have no, or at most marginal, effect.

Conducting studies

It is of importance that the best available evidence is compiled and used as the basis for decision-making, treatment recommendations and interventions, as well as policy statements and for responding to questions. A small selection of studies is presented here, the results of which are valuable in the context of the Swedish work to safeguard the effectiveness of antibiotics. A more detailed presentation of significant studies can be found in annex 1.

Strama has access to a large network of experts which has given it high credibility that is of importance for discussions in articles in national media as well as with colleagues at local level. Over the years, Strama has initiated several studies in areas where scientific knowledge has been lacking. Some studies have been funded by Strama alone while some have been co-funded by other actors.

A number of smaller projects and studies have been carried out, often organised by the local Strama groups. From 2000 to 2009, between 8 and 22 such studies were carried out annually. While the results of these local studies/projects have sometimes provided very valuable information, the local commitment generated in the process has been equally valuable – examining a factor or variable of importance in a particular local context has contributed much enthusiasm.

Some important examples of larger studies and projects that have provided valuable knowledge of how antibiotics are used and infections are handled are "diagnosis-prescription studies", which were relatively early studies carried out in primary care in the early 2000s, and point prevalence studies of the use of antibiotics in hospitals (chapter 4). Another example is how Strama, in cooperation with infectious disease clinics around the country, carried out an independent clinical trial looking at treatment with ciprofloxacin for pyelonephritis (kidney infection) in women. The study which was published in the *Lancet* (24) showed that 7 days of treatment was as effective as a 14-day course. Since the publication of the study, most County Councils have changed their treatment recommendations to 7 days of treatment. A range of surveys and studies concerning the use of antibiotics in ICUs have also been carried out by ICU Strama (25–29).

There have also been surveys concerning the general public's knowledge of antibiotics, which is important since this is likely to influence decisions regarding antibiotic prescription in outpatient care. Other studies have focused on preventive measures. In pre-schools, infections are easily transmitted since many children are grouped closely together. Efforts to reduce the transmission of disease may reduce both the incidence of disease and the need for antibiotics. A major study carried out in pre-schools in

southern and central Sweden investigated the effect of hand disinfectant. The study showed that the use of hand disinfectant containing ethanol gel reduced the children's absence due to sickness by twelve percent (30)

It is also important to investigate effects on the resistance condition following interventions. A study carried out in Kronoberg county clearly illustrates the complexity by demonstrating that antibiotic resistance is not always easily reversible in society after a decrease in the use of antibiotics (31). Although the use of trimethoprim was drastically reduced in the county during 2004–2006 (by 85 percent), no clinically useful effects were noted on the resistance to trimethoprim in *E. coli*, to give one example.

ESBL resistance is increasing significantly in Sweden and is prevalent in bacteria from both animals and humans. National studies are being carried out today in a collaborative project between a number of authorities in different sectors in order to investigate channels of transmission for ESBL. The collection of stool samples will also provide valuable information regarding the prevalence of ESBL in a randomly selected part of the healthy population.

International monitoring

Monitoring of external developments has long been an important source of internal knowledge development within Strama. This involves a systematic monthly review of relevant academic literature for the purpose of making summaries of important articles connected with antibiotic resistance, but also a more mass media-related search which is regularly carried out and compiled weekly, "Web Scan Strama-Public Health Agency Weekly" highlighting any relevant new national and international policy documents and other events that have caught the attention of the media. This task is assigned to the Public Health Agency of Sweden, but the results are also disseminated directly to the local groups, who are then spared this time-consuming task. The reports from international monitoring have given both national and local Strama actors access to broad and updated information on international developments, early knowledge of the transmission of new resistant forms, as well as the attempts made to counteract these and the outcome of different measures.

Shaping opinions – information – training

Since its foundation, Strama has helped to shape opinions on matters concerning antibiotic resistance, thereby ensuring that these issues are put on the agenda and discussed in different forums, through opinion articles in medical journals and newspapers and by actively contacting the media to submit important information. The mass media in Sweden have also provided much coverage over the years and plays an important role in communicating the problem of antibiotic resistance to the general public.

Statistics on use and resistance, results from surveys, reports and major meetings are continuously communicated in press releases and press conferences both nationally and locally. Chairmanship of the local Strama group is often held by the County

Medical Officer for Communicable Disease Control. As such, he/she is a trained spokesperson and often has a well-developed network of media contacts, which facilitates reaching the general public with information regarding antibiotics.

The attitude of the general public to antibiotic treatment is of major significance – the greater the level of knowledge in the population, the easier it will be for people to accept the physician's assessment that the condition does not require antibiotic treatment. The physician, who is often under time pressure, cannot be solely responsible for providing this information – the focus must be that the patient is coming for an assessment and not for a prescription. Local Strama groups are thus in frequent contact with the local medical advice service/telephone advice service, to ensure that patients primarily expect an assessment when they come to see their GP. Since the advice service has been largely centralised with the introduction of a nationwide telephone number and internet service (1177), it is important that this quality assurance of the information continues.

Over the years, a wide range of information and training materials has been developed by former national Strama as well as by local groups. As previously mentioned, local groups have disseminated material through presentations at Strama days, through the Strama.se website and occasionally via the formalised international monitoring service (whenever Strama material has been featured in the media).

The material can be categorised into that which is aimed at the general public and that aimed at healthcare professionals. The latter category can be further sorted into material aimed at prescribers/physicians and that aimed at other healthcare professionals. The box below describes the different types of material developed for different target groups. A more detailed description can be found in annex 2. A selection of material has also been translated into English.

The fact that locally developed materials are often actively shared between counties has obviously multiplied the overall impact. Through this document, there is now a similar opportunity to use the Swedish material across national borders. Local adaptation of material may obviously be required, in addition to purely linguistic translation. Even within a particular country, a certain piece of material may be relevant in the south but not in the north, and as such may require adjustments.

Here follow some examples of information materials on antibiotics directed at different target groups. Each section contains a range of materials developed by various organisations, including local Strama groups.

The general public

- Patient information about common infections published in folders and on posters and websites
- Information material for school pupils, parents and pre-school staff (including the "Emma-project")
- Training for parents on infections and antibiotics used by paediatric nurses
- Short films on antibiotics and resistance aimed at the general public
- Information about infections aimed at the elderly population

Healthcare

- A national 10-point programme to reduce the prevalence of antibiotic resistance in hospital care
- National and local treatment recommendations for common infections in outpatient care
- National and local recommendations for the treatment of infections in hospital care

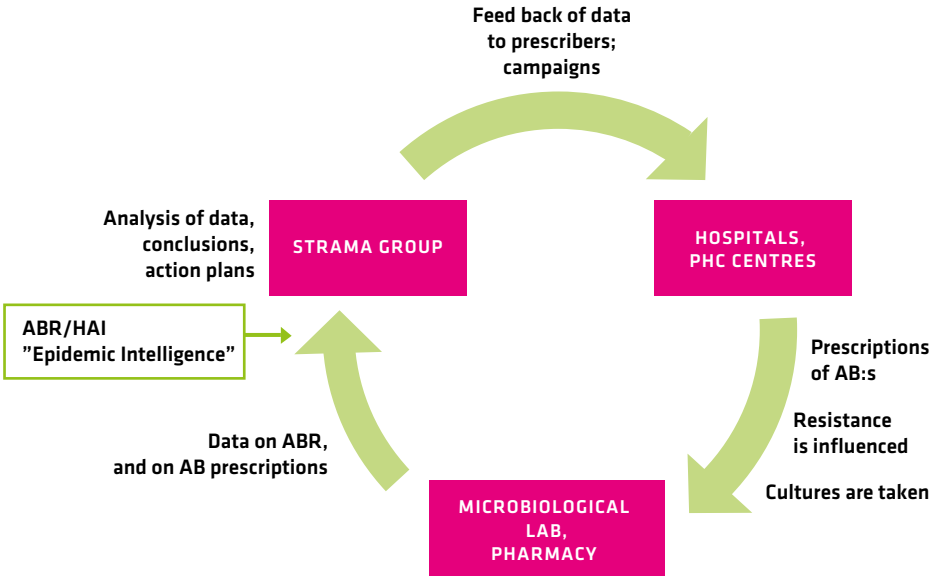
The cyclical process involved in local work

Experiences from local initiatives, working methods and campaigns are widely shared laterally with the other local groups. In many respects, the work in a local group resembles the work at national level – a number of committed experts meet regularly and analyse new data for their geographic area of responsibility (the county and the country respectively), both with regard to antibiotic resistance and prescription patterns. External information is brought in (from the national level or from other countries) and tendencies, threats and consequences are assessed. Action plans/campaigns are developed and implemented – and at the subsequent meetings, the effect and experiences of these efforts are evaluated, maintaining a continuous exchange of experiences both laterally and vertically within the network.

The cyclical process is key; it is not *one* single effort, but rather a recurrent follow-up of the situation with dynamic adjustments. On a local level, quarterly or six-monthly meetings can provide opportunities for analyses. On the national level, the focus is mainly on analysing annual data on resistance and prescription. On both levels, outbreaks may call for extra analyses and more rapid actions.

A simple diagram can illustrate essential parts of the work process:

Figure 2.6 The cyclical process of the Strama work



Improved antibiotic prescription requires continuous work.

An indispensable aspect of the local Strama groups' work is the direct dialogue with prescribers. Developing new treatment guidelines through good national and local consensus is not sufficient, unless they are applied in practice. This may indeed be the most important role of Strama – and is commonly referred to as classic Strama work. In the typical scenario, 1–3 individuals with competence in antibiotics, often an infectious disease specialist, a primary care physician and a pharmacist, members of the local Strama group or associated to it, will visit healthcare centres for discussions with the staff in small groups. Several studies and experiences show that this system of face-to-face discussion is the method most likely to change prescription habits. The work is very resource-intensive but has greater potential impact than simply providing advanced training or lectures, which are nevertheless also organised. At such events, it is vital to present up-to-date data on resistance conditions and the prescription of antibiotics – in an international and national, but preferably also in an as local context as possible. Comparative data is often used successfully – comparing data between units and healthcare clinics. In addition, "burden data" (data that shows the increased cost of infections with resistant bacteria, both in terms of an increase in mortality and morbidity, but also in economic terms) and the results of interventions are used – all in order to boost local commitment.

To clarify the work process, a few examples are presented here that also demonstrate the interplay between Strama at a local and national level, as well as the interaction with many other actors.

Working method – illustrated with examples from a Strama perspective

A few examples may help to illustrate how the work has been carried out. The examples as such are not complex, nor are the measures unique to the rest of the world. However, many of the measures were implemented at an early stage in Sweden. The following examples primarily show that *focused work* has been carried out in these issues: from the early identification of the problem, through analysis of possible measures, to implementation and follow-up. The examples also illustrate the multidisciplinary nature of the work, where interaction between many competencies is required to achieve the set goal. As the examples show, Strama is rarely alone in tackling the problems faced.

Thanks to the national and local overview provided by Strama, and to the coordinated measures from the many parties involved, countermeasures have often been developed more rapidly in Sweden than elsewhere. Despite the problematic nature of preventive work– it being difficult to mobilise resources against a threat that has not yet materialised – efforts such as effective international monitoring may strengthen the awareness that it is easier to retain a low prevalence of MRSA in a society (Sweden), than to bring it back down from a sky-high level (France, Great Britain). The example of $ESBL_{CARBA}$ (carbapenem-resistant *Enterobacteriaceae*, CRE) may today be even more relevant.

To illustrate this holistic approach to different resistance issues, the examples below will be presented in a simplified, stripped-down form without all the details – it is the broad outline that should stand out.

The example of increased resistance in pneumococci

This example, which was also the impetus for the creation of Strama, illustrates the force behind the initiatives that were taken. It also says a great deal about the societal climate at the time, and about the responsiveness of the authorities – that it was possible to gain support for responsible long-term measures.

Starting point/signal: Resistance monitoring detects a significant increase in pneumococci with resistance/reduced sensitivity to penicillin in southern Sweden. There are also many examples of an increasing international prevalence.

Analysis: The over-consumption of penicillin should be reduced. A large proportion of penicillin/antibiotics are prescribed for diagnoses on which they have no effect, i.e. viral infections. Over-prescription also occurs for the diagnosis of tonsillitis, since viral throat infections are generally over-diagnosed as bacterial.

Measure 1: Reduce the antibiotic pressure

a. Develop treatment guidelines together with the Medical Products Agency. The recommendations underline the fact that viral infections are not an indication for antibiotic treatment. Furthermore, recommendations are developed for management of tonsillitis.

b. Establish Strama groups that can communicate new guidelines and handle the discussion with the prescribers.

Measure 2: Limit the transmission of existing resistant pneumococci

c. Act to bring about a change in the Communicable Diseases Act (to class PRP as a public health hazard), so that transmission by confirmed carriers is reduced, by ensuring that they stay home from childcare/pre-school facilities at the most infectious stage (32).

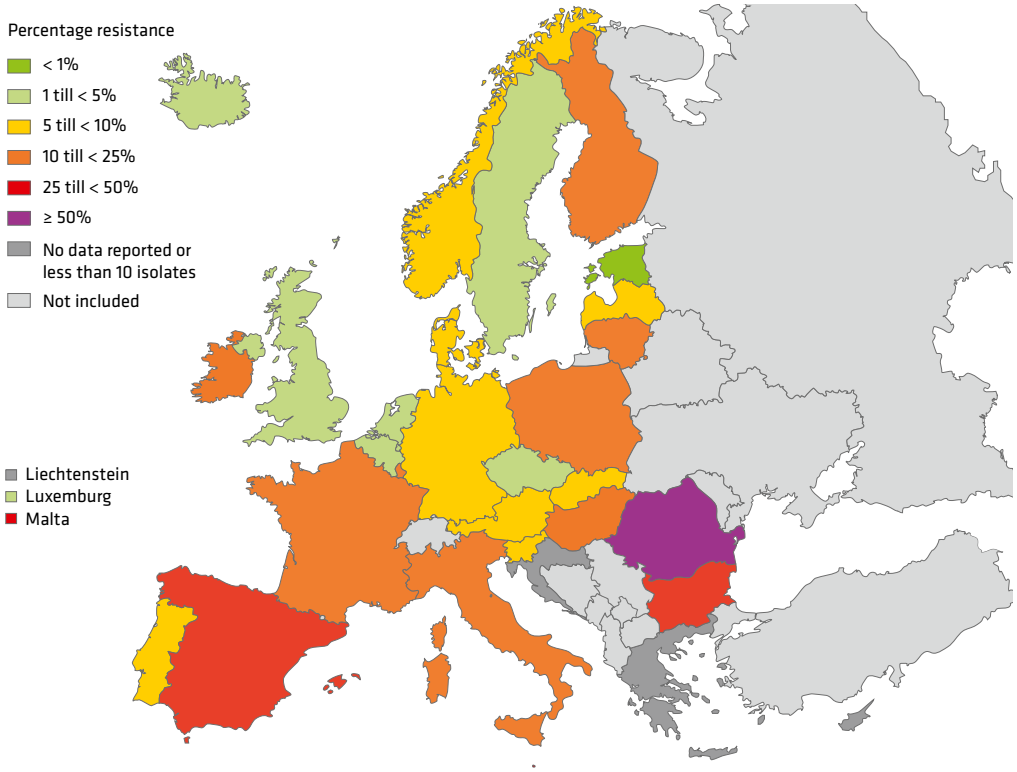
   Develop recommendations to pre-schools regarding "anti-infection prophylaxis" – measures aimed at reducing the transmission of disease and the incidence of children contracting upper respiratory tract infections (20).

The results are followed up:

The general use of antibiotics is followed up via data on prescriptions and sales for the total consumption and for respiratory tract antibiotics in particular by local Strama groups and nationally, and results are consistently brought back to the prescribers.

A careful follow-up is made of the number of notified cases as well as an ongoing analysis/evaluation of different measures for reducing transmission. After a long period with diverging practices regarding carriers in different parts of the country, the National Board of Health and Welfare has developed a national knowledge base with recommendations on the issue (33). The proportion of pneumococci with reduced sensitivity to penicillin is currently one of the lowest in Europe, and in the world as far as is known. Sweden maintains a favourable situation concerning resistance and reduced susceptibility to penicillin among pneumococci.

Figure 2.7 Proportion of penicillin resistant pneumococci in participating countries 2012. Source EARS-Net.

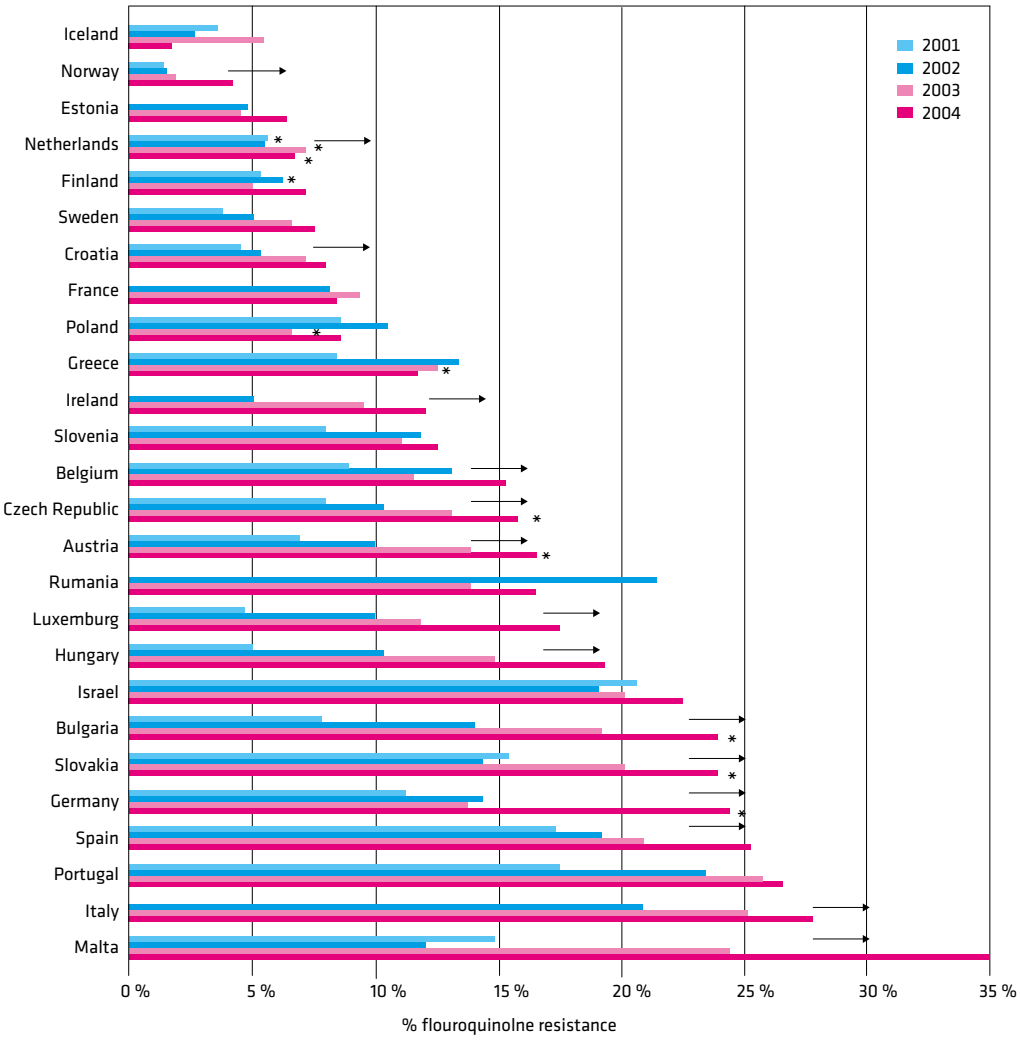


Sweden maintains a favourable situation concerning resistance and reduced susceptibility to penicillin among pneumococci after focused and continuous work to reduce the antibiotic pressure and limit the transmission of existing resistant pneumococci.

The example of quinolone use

Starting point/signal: Strama, which continuously followed the development of resistance and prescription, noted at the turn of the millennium that the antibiotic class of fluoroquinolones, which is effective and valuable for many indications, was increasingly being used, and that quinolone resistance in significant bacterial pathogens was rapidly increasing in European countries (EARSS data) with a similar tendency in Sweden:

Figure 2.8 Increasing resistance against fluoroquinolones in *E.coli* in Europe 2001–2004. Source EARSS.



E. coli: trends of fluoroquinolone resistance by country, 2001–2004. Only the countries that reported 20 isolates or more per year, for at least three years, were included. The arrows indicate significant trends and the asterisks indicate departures from the presented estimates when restricting the analysis to laboratories that reported to EARSS for the entire surveillance period.

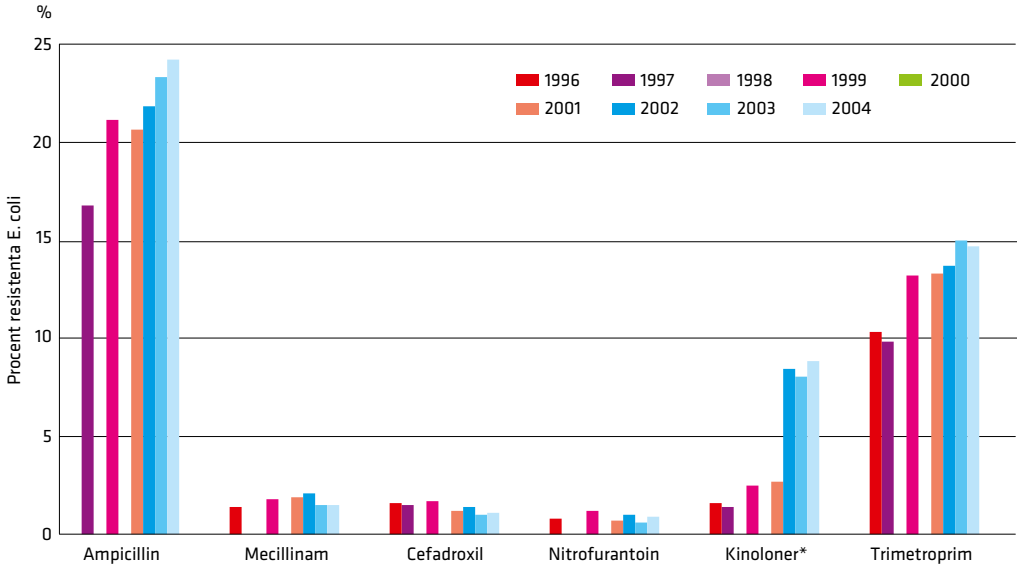
Analysis: The realisation was clear: there was a threat to the effectiveness of quinolones, a group with significant advantages for certain critical indications compared with other antibiotics (for example outpatient treatment of pyelonephritis; oral follow-up treatment of post-operative abdominal infections (34).

To preserve and prolong the effectiveness of quinolones on these indications, unnecessary indications must be reduced. Which are these? At this point in Sweden, quinolones were being used, as they still are in many countries, as a treatment for uncomplicated lower urinary tract infections in women, in itself a very common reason for antibiotic prescription.

What alternatives were available for the relatively easy-to-treat diagnosis of uncomplicated lower UTI in women? Possible antibiotics registered in Sweden were ampicillin, mecillinam, cefadroxil, nitrofurantoin and trimethoprim.

The resistance conditions for these in Sweden were examined for the most important UTI pathogen, *E. coli*:

Figure 2.9 Resistance trends for *E.coli* against possible antibiotics for uncomplicated lower UTI in Sweden around the millennium.*1996–2001 Norfloxacin, 2002–2004. Data from Res-Net.



E. 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. The same was true for trimethoprim. Fluoroquinolone resistance did not show any increase since 2002, but remained on an average of 8 percent. (SWEDRES 2004)

Ampicillin was rejected (the number of resistant strains is too high).

Trimethoprim was a borderline case, with many resistant strains.

Cefadroxil was rejected due to its side-effects/disadvantages (effect on the intestinal flora, selection for ESBL).

Mecillinam was not being used for other indications and resistance conditions were good.

Nitrofurantoin was not being used for other indications and resistance conditions were good.

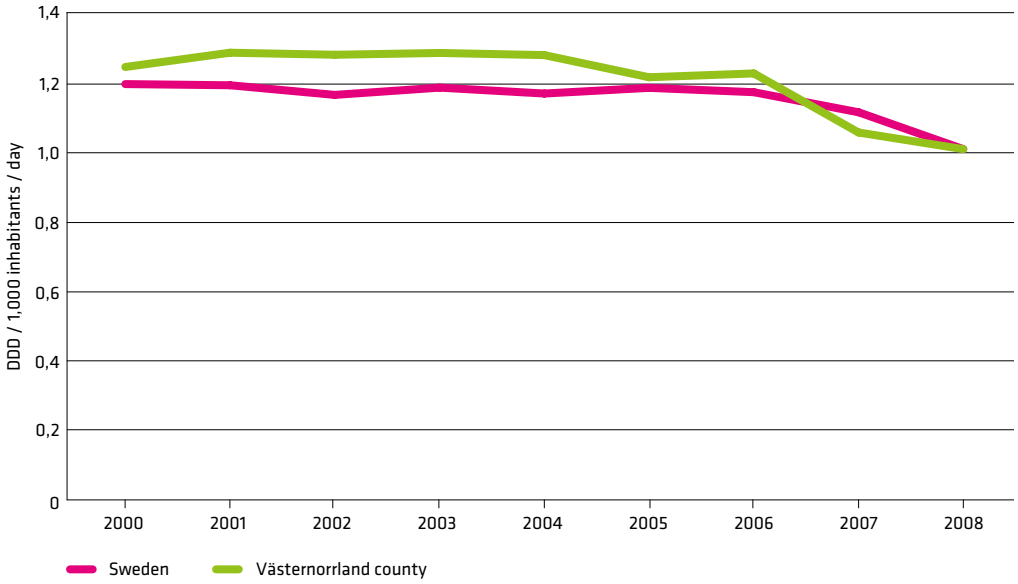
After a comprehensive examination at national level of all available evidence, mecillinam and nitrofurantoin were judged to be adequate means of treatment for uncomplicated lower UTI in women.

Measure:

- A campaign was launched to change treatment practice – use less quinolone and instead increase mecillinam and nitrofurantoin for uncomplicated lower UTI in women
- National guidelines were drawn up in which mecillinam and nitrofurantoin are named as first choice treatment
- The national guidelines were widely adopted into local guidelines and *actively delivered to prescribers* by the local Strama groups in face-to-face meetings. The meetings involved explanations and discussions and took place both in primary care and in hospitals.

The results were followed up: Local and national follow-ups. Campaigns and efforts were repeated (35). An effect is seen on prescription, at local level, which is communicated at regular meetings and eventually an aggregated effect will be noted at county and national levels:

Figure 2.10 Quinolone use in Västernorrland County and in Sweden, 2000–2008. Figure courtesy of Ulf Lindahl, Västernorrland County Council.

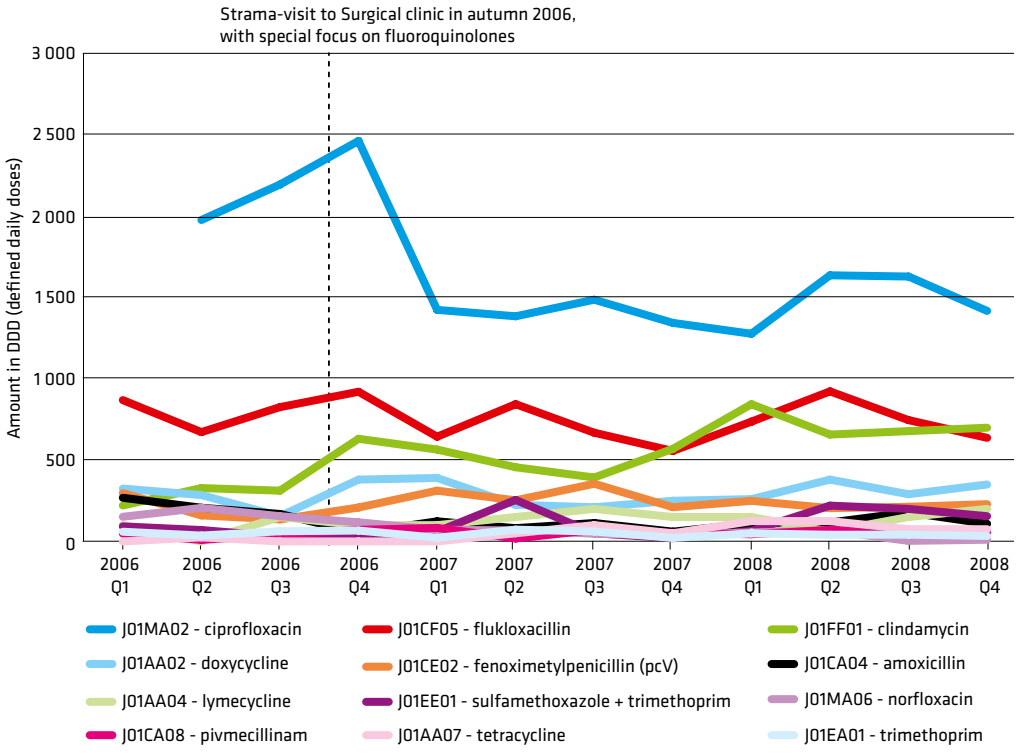


The trend curve for fluoroquinolone use in Sweden as a whole, and in Västernorrland County. Interventions (as the one below) in the County add up to the County trend, and similar interventions in other counties add up to the national trend curve.

The effect at national level is clearly the sum of all the local continuous efforts, mainly by Strama groups and pharmaceutical committees. An example:

Visit to a surgical unit in a county hospital in October 2006, discussion about the prescription of quinolones. It was found for example that quinolone was excessively prescribed in cases of diverticulitis. A dialogue led to the joint realisation that it was used to an unnecessarily large degree for the diagnosis and so it was agreed that the use of quinolone would be reduced. Results are shown in figure 2.11:

Figure 2.11 Antibiotic prescriptions at a surgical clinic before and after a Strama visit. Figure courtesy of Ulf Lindahl, Västernorrland County Council.

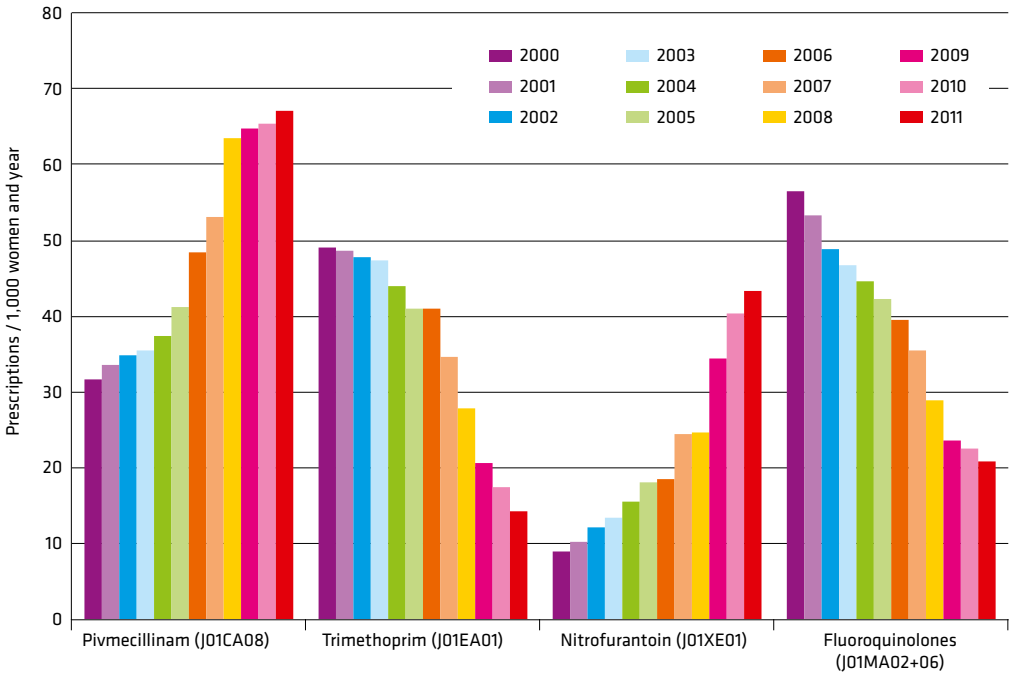


In October 2006 a Strama visit to the Surgical Clinic focused on quinolone use – it was agreed that there was unnecessary use e g for diverticulitis, which was discontinued or reduced accordingly.

Similar initiatives are continuously carried out in other hospital units and in primary care. An aggregated effect can be seen at County Council level. Similar initiatives from all local Strama networks are summarised, and the result shows an effect at national level.

Even if quinolone is over-prescribed in cases of UTI, the use of other substances is likely to increase when quinolones decrease. The substances recommended for uncomplicated lower UTI are thus primarily nitrofurantoin and pivmecillinam. The success of the continuous work to bring about this change across the country that has been ongoing since the millennium is clearly demonstrated in the image below:

Figure 2.12 Exchange of fluoroquinolones for mecillinam and nitrofurantoin for uncomplicated lower UTI. SWEDRES 2012.



The continuous work to bring about a change from an extensive use of fluoroquinolones for uncomplicated lower UTI across the country, to recommendations to use primarily nitrofurantoin and pivmecillinam has proven successful

An important and quantitatively important indication for quinolones is the treatment of pyelonephritis/febrile UTI. This indication represents a considerable consumption. The question was raised whether the course of treatment could be shortened. Previously, the standard course was at least two weeks, more due to tradition than on grounds of solid evidence. The study that Strama initiated on the treatment of uncomplicated pyelonephritis (see the above section on studies) showed that the course of treatment could be halved to 7 days, which also led to the revision of treatment recommendations (the study was published in the Lancet (24)).

The example of the ESBL increase

The increase in ESBL is part of a worldwide tendency and is not unique to Sweden. Here, the problem was however noted at an early stage and active countermeasures were taken comparatively soon. Although the increase of ESBL in Gram-negative bacteria in Sweden is of concern, the prevalence remains lower than in many other countries. The active approach described below may have contributed (see also the detailed description of local work on containment of ESBL at the end of chapter 3).

Starting point/signal: By means of national resistance monitoring and international monitoring, the problem is discovered early. An increase in the country is noted.

Analysis: To stem the increase of ESBL resistance, comprehensive measures are required. Strama acts swiftly to compile the available evidence for effective measures in the form of a national knowledge base about ESBL, which will also form the basis for new recommendations. These were developed, by Strama and SMI/the Public Health Agency of Sweden.

Measures: The national measures are implemented across the country through the local Strama groups, along with units for communicable disease control and units for infection control, mainly in hospitals but also in primary care campaigns.
The most important measures are to strengthen the argument for restrictive use of extended-spectrum antibiotics (cephalosporins, quinolones), and for improved infection control in many areas.

Summary

Sweden has very favourable resistance conditions from an international perspective. The total antibiotic pressure is also unusually low, both quantitatively and qualitatively (of the antibiotics in use, a relatively large proportion is made up of narrow-spectrum penicillin). The total use of antibiotics has decreased since the mid-1990s. This coincides with the founding and first active years of Strama. It is reasonable to assume that the intensive work led by Strama and others has had an effect.
What are the keys to success? Some of the watchwords that define Strama's work are cooperation, network, credibility, multi-disciplinary groups, commitment, local implementation and direct dialogue with the prescribers.

Data on prescription and **data on resistance** form an essential basis. Data on the resistance consequences ("burden data") also supports the argument for improved compliance with new treatment guidelines. **Treatment guidelines** must be created and updated in line with new evidence. The **flow of new knowledge**, e g. studies showing different "antibiotic-minimising" methods, and the disadvantages of unnecessary use of antibiotics, even on an individual level, are increasing and must be **communicated** to prescribers and, to some extent, to the general public. An important success factor has also been the possibility to disseminate simultaneous information to all recipients through interaction with the media.

One way to stretch limited resources in the work towards the rational use of antibiotics is to channel the commitment of the various professional groups that observe and understand the effects of antibiotics and antibiotic resistance. As the lack of effective antibiotics becomes increasingly apparent, and multi-resistant strains become more common, the importance of hygiene and cleaning procedures (infection control) becomes even greater.

Interview with Professor Otto Cars

Otto Cars is a Professor of Infectious Diseases at Uppsala University and was one of the founders of the Swedish strategic programme against antibiotic resistance, Strama, in the 1990s. Since 2004, Cars has been engaged in building an international network focusing on the global aspects and consequences of antibacterial resistance, Action on Antibiotic Resistance, ReAct.

Looking back over the past 25 years, Otto Cars can identify a number of factors that have contributed to Sweden's comparatively low levels of antibiotic resistance, including geographical and cultural aspects. "Sweden is a small country with a history of cooperation. We've also benefited from a high level of awareness within veterinary medicine, where practitioners have long since recognised the ecological implications of increasing resistance", says Otto Cars, referring to the 1986 ban on growth-promoting antibiotics in animal feed.

As one of the founding member of Strama in the mid-1990s, Otto Cars points to its role in promoting rational prescription. "Strama did not invent the wheel. Many doctors were already aware of increasing resistance and were making efforts to stem it. Strama provided a platform for such work." Strama's development as a network of local actors was also facilitated by Sweden's decentralised organisation of disease control. This structure has integrated work against antibiotic resistance as an important aspect of disease prevention.

During its first years Strama was largely a product of idealistic effort and it was not until year 2000 that the network received funding from the state. In 2011 support increased when the Swedish Ministry of Health and Social welfare launched a reform for improved patient safety, identifying use of antibiotics as a key aspect. Since then all county councils are obliged to have a local Strama unit to benefit from specific funding. "This reform has provided much needed resources and increased the legitimacy of Strama", says Otto Cars.

Still, much remains to be done to achieve rational use of antibiotics. Otto Cars and his colleagues have long called for reliable methods to compare prescription data. Showing differences between prescription practices at a regional, hospital and community level is an effective way to make people start looking for possible explanations. But, as Cars points out, discussions about rational use must be based on a diagnosis, pure statistics don't suffice. "We've voiced the need for diagnosis-linked data for years, but the computer systems in most counties are still not designed to meet the requirement of continuously delivering diagnosis-linked data. Such information is also lacking on a national level", says Cars.

In his opinion, many politicians and county councils still have not grasped the magnitude of the problem. Short term budget cuts are made at the expense of long term investments in prevention. Shortage of space and single rooms means temporary placements in hospital corridors and paves the way for new outbreaks.

Otto Cars argues that more efforts should be made to calculate the cost of antibiotic resistance – on an individual, national and international level. "Perhaps we must argue in terms of money, not just morbidity and mortality. One Swedish study showed that a single case of MRSA generated a price-tag of 1 million SEK, only for health care. Imagine the price of a large-scale outbreak", says Otto Cars who believes that the true cost of previous outbreaks in Sweden have been grossly underestimated.

He points to the positive example of Thailand, a country with a high level of antibiotic consumption and resistance. Calculating the actual and potential cost of antibiotic resistance has kick-started preventive measures including a national "*Smart Use Campaign*", where efforts to reduce prescription are rewarded in terms of investments in improved health care facilities etc.

Looking ahead, Otto Cars believes that no country can escape the reality of increased antibiotic resistance. "Sweden *does* have a favourable starting point in an international context, but this only means that we may be able to stem the pace and limit the consequences of resistance", says Cars.

As Otto Cars sees it, necessary measures in Sweden include: investing in new laboratory technology, improving interaction between clinics and laboratories to speed up diagnostic procedures, learning to combine existing antibiotics for synergic effects and increased efforts to prevent transmission within hospitals by providing single rooms and designated staff to infected patients – as well a further strengthening the capacity of the Strama network.

"This all presupposes political will and the allocation of sufficient funding", says Otto Cars. He emphasizes that lasting solutions to the problem of resistance require international cooperation. Joint efforts must be made to develop new kinds of antibiotics and alternative preventive methods such as vaccines and medication that "disables" harmful bacteria without killing them and thereby promoting selection of resistant clones.

"International political cooperation at the highest level is needed to achieve a global ban on antibiotics in animal feed and to phase out all sales of antibiotics without a prescription. We must aim at the stars so to speak – be it a UN convention or international commission on the issue", says Cars.

Cars points to the fact that antibiotic medication is a resource like others, limited and largely unavailable to people in many low-income states and regions such as Sub-Saharan Africa. "Meanwhile, the rest of us have been lulled into a false sense of security, believing that we will always be able to treat a simple case of pneumonia. The blatant truth is – that if we go on like this – we will not."

Chapter 3. Resistance monitoring

National and local monitoring of antibiotic resistance are necessary in order to observe and analyse the development of resistance, to implement countermeasures and to measure the effect of interventions. Purposeful monitoring also forms the basis for the development of recommendations, and for a rational and patient-safe empirical antibiotic treatment of acute infections. Monitoring is also needed to assess the effect of implemented measures. The extent of the sampling for different types of infections, transmission tracing, screening and mapping of outbreaks have great impact on the results when monitoring antibiotic resistance,

Resistance monitoring is largely based on clinical cultures

In Sweden there is a tradition of quite freely taking cultures from patients. Cultures are generally taken from the majority of hospital patients prior to antibiotic treatment. Studies have shown that cultures are taken from around 2 in 3 patients prior to antibiotic treatment in inpatient care, whereas the figure is significantly lower in outpatient care. In primary care, samples are taken from a smaller proportion of patients with infections such as sexually transmitted diseases, complicated urinary tract infections and wound infections. The taking of cultures is not recommended in cases where results are unlikely to influence the choice of treatment (diagnoses such as uncomplicated urinary tract infection in women and upper respiratory tract infections). Resistance monitoring is based on data generated from these clinical cultures and to some extent on cultures from screening, monitoring and tracing the transmission of antibiotic-resistant bacteria monitored according to the Communicable Diseases Act (CDA).

Common breakpoints and a quality-assured methodology

Comparing the prevalence of antibiotic resistance between different laboratories over time requires common breakpoints for the interpretation of results in testing resistance to antibiotics, as well as a quality-assured methodology.

The EUCAST breakpoints for resistance testing have been used in Sweden for many years. EUCAST (European Committee on Antimicrobial Susceptibility Testing) is a European breakpoint committee that establishes SIR-limits for most of the European countries and also functions as the official breakpoint committee for the European Medicines Agency (EMA). Sweden is represented in EUCAST by the Swedish Reference Group for Antibiotics (SRGA). The SRGA is an independent expert group, previously the external reference group of SMI and the Swedish Society of Medicine for antibiotic issues and has worked towards a rational use of antibiotics since 1976. Its tasks include the production and communication of information that is evidence based and manufacturer-independent. The SRGA works to define the sensitivity and resistance of the bacteria to antibiotics (SIR limits), and to analyse the consequences of resistance development on the choice of antibiotics for various patient categories. The SRGA conducts systematic literature reviews and has during 2013 produced a benefit/risk analysis for adults in respect of aminoglycoside treatment of the following

indications: severe sepsis, progressive severe sepsis and septic shock, pyelonephritis and endocarditis.

The SRGA participates in the processes developed by EUCAST and EMA for the determination of breakpoints for new antibiotics, and in the process developed by EUCAST for the revision of breakpoints in respect of pre-existing antibiotics (www.srga.org).

EUCAST describes a standardised disc diffusion method. This is the most common method for testing resistance in Sweden. Over the past few years, however, automated resistance testing has become more common. In spite of their different methodologies, all laboratories use the EUCAST breakpoints, which ensures the comparability of resistance data. The Nordic reference group, Committee on Antimicrobial Susceptibility Testing (NordicAST), provides recommendations that are freely available online on other support methods in resistance testing. This also helps to standardise resistance testing. All clinical microbiological laboratories have been accredited.

Resistance monitoring is mainly done on a voluntary basis and has good geographic coverage

Sweden has four systems of resistance monitoring with national coverage: ResNet, SmiNet, EARS-Net and Svebar. All of the systems except for SmiNet depend on laboratories participating voluntarily and entering their local data into the systems.

3.1 ResNet: To ensure adequate resistance monitoring with comparable data, the methods used for resistance testing by laboratories must be quality-assured continuously. Since 1994, during a set period every year, participating laboratories submit resistance data to the Public Health Agency of Sweden regarding certain combinations of bacterial species and antibiotics via a particular programme. The Public Health Agency of Sweden compiles and feeds back the data through the web-based programme ResNet. The results are used to observe resistance conditions, and by laboratories to continuously assess the quality of their diagnostic methods. The design of ResNet provides country-wide resistance monitoring thanks to the participation of all laboratories.

3.2 EARS-Net: Sweden also takes part in the European monitoring programme EARS-Net which includes invasive isolates (mainly isolates from blood) from seven bacterial species. Data from EARS-Net show the number of resistant isolates in the overall number of isolates in a certain bacterium, for example the proportion of MRSA in all *S. aureus* taken from blood cultures. The microbiological laboratories report data to the Public Health Agency of Sweden that corresponds to a level of coverage of about 80 percent of the Swedish population. The Public Health Agency of Sweden compiles the results for the European Centre for Disease Prevention and Control ECDC. EARS-Net has an important role in informing about the prevalence and spread of antibiotic resistance in Europe. Only results concerning serious infections, from blood cultures for example, are reported in EARS-Net. This provides a smaller statistical base but the resistance that is reported is important in clinical terms.

3.3 SmiNet. Four types of antibiotic resistance are notifiable in line with the CDA. The notification is made to both The Public Health Agency of Sweden and to the County Medical Officer for communicable diseases. SmiNet is a web-based programme that receives and manages notifications in line with the CDA from treating physicians and from laboratory physicians. An advantage of SmiNet is that resistance is reported sooner and can be monitored continuously, unlike in EARS-Net and ResNet.

3.4 Svebar: The above monitoring systems are all based on a selection of important bacterial species and resistance mechanisms. Apart from to SmiNet, resistance is not continuously reported. Svebar is a national IT system that was developed to expand and improve national and local resistance monitoring. The system is based on all results from cultures being transferred on a daily basis from microbiological laboratories to a system managed by the Public Health Agency of Sweden. Svebar is designed to give an early alert on serious antibiotic resistance or suspected disease transmissions by means of pre-set alert functions. An increasing number of laboratories are joining Svebar and all remaining have communicated their intention to start participating within the next few years.

Epidemiological typing is carried out on all notifiable forms of resistance

Epidemiological typing is required to confirm or dismiss a suspicion of disease transmission of the same bacterial strain between people. In an outbreak, epidemiological typing can also be used to confirm new cases or dismiss suspected chains of transmission.

Epidemiological typing of prioritised bacteria should be carried out continuously to gain knowledge of how the prevalence of virulent or resistant strains varies over time between different geographic areas and populations. Long-term monitoring is also required to evaluate findings of certain strains and in the investigation of outbreaks. Without a baseline of the common types in a population, it may prove difficult to evaluate the results of the epidemiological typing in an outbreak situation.

In Sweden, epidemiological typing is carried out in some form for all types of antibiotic resistance that are notifiable according to the CDA, either in the Public Health Agency of Sweden or in the County Council laboratories. In some cases, continuous typing is carried out and in other cases only point prevalence surveys. In addition, further epidemiological typing of bacteria is done in connection with suspected outbreaks or other suspected epidemiological changes.

Analysis and communication is conducted both nationally and locally

To ensure that resistance monitoring leads to adequate measures it is crucial that the results reach laboratories, physicians, hospital management, decision-makers, authorities and concerned organisations as well as the wider public.

The Public Health Agency of Sweden analyses and compiles national data on antibiotic resistance and the use of antibiotics in human medicine, and publishes them

in the SWEDRES annual report. The report is co-published with SVARM (Swedish Veterinary Antimicrobial Resistance Monitoring) that shows corresponding results in veterinary medicine and is produced by the National Veterinary Institute. Statistics on antibiotic resistance that are notified according to the CDA are also continuously posted on the Public Health Agency of Sweden website. The weekly the Public Health Agency of Sweden newsletter also publishes important news and summaries of scientific articles and events on the subject.

National and local resistance data and data on antibiotic prescription form the pillars of Strama activities at a local level (chapter 2 and section 3.5) and is used in discussions with prescribers in order to demonstrate resistance development and to decide upon the focus of local interventions

The extent to which laboratories provide detailed local resistance data to Strama groups, disease prevention and control units, infectious disease clinics and pharmaceutical committees varies. In many County Councils it is possible to obtain reports on individual hospitals or follow the development in particularly critical activities such as intensive care or urology. The expansion of Svebar will involve the introduction of automatic feedback of local resistance numbers in standardised formats to laboratories, which can then forward them to other local users.

3.1 ResNet – annual resistance monitoring and quality assurance online

Since 1994, all laboratories in Sweden have participated voluntarily in a national scheme for resistance monitoring and quality assurance which is carried out once a year. The laboratories compile quantitative data (zone diameters) of at least 100 consecutive clinical isolates from a selection of commonly occurring bacteria and commonly used antibiotics. ResNet is an internet-based programme that has been used since 2002 to collect and present this data.

In ResNet it is possible to check the prevalence of resistance in a specific bacterial species to a selection of antibiotics both on national and local level. It also shows the distribution of measurement data (MIC values and zone diameters). This allows laboratories to compare the distribution of their measurement data against the normal distribution and discover potential errors and method shifts. ResNet thus offers laboratories the possibility to continuously assure the quality of their measurement methods.

Implementation

The basis for current resistance monitoring in ResNet was initiated by RAF-M, which was a method group consisting of microbiologists under the authority of SRGA, the reference group for antibiotic issues. The monitoring was later taken over by the Public Health Agency of Sweden.

The bacteria chosen for monitoring has varied over the years depending on signs of increased prevalence of resistance in certain bacterial species. Continuity has

been sought in order to discern tendencies over time. Certain pathogens have almost always been included: (*Streptococcus pneumoniae and Haemophilus influenzae* from respiratory tracts, *Staphylococcus aureus* from wound cultures and *Escherichia coli and Klebsiella pneumoniae* from urine cultures). Species that have been tested more infrequently include *Streptococcus pyogenes*, *Pseudomonas aeruginosa*, *Enterococcus faecalis*, *Enterococcus faecium* and *Enterobacter*. The number of antibiotics that they are tested against varies between two and six and corresponds to common treatment options.

The two criteria that influence the choice of bacterial species for the annual measurement are:

1. clinical relevance
2. commonly occurring bacteria in the routine activities of laboratories so that they quickly can establish a basis.

It is important to adapt the approach of the measurement to the daily activities of the laboratories to avoid unnecessary extra work.

ResNet has simplified the management of data and reduced the amount of work

SMI developed the internet-based programme ResNet in 2002 to simplify the submission of data and the feedback of results. Initially, paper forms, and later Excel files, were used but through ResNet the laboratories can submit the results of their resistance testing in a web form (http://resnet.folkhalsomyndigheten.se/ResNet/).

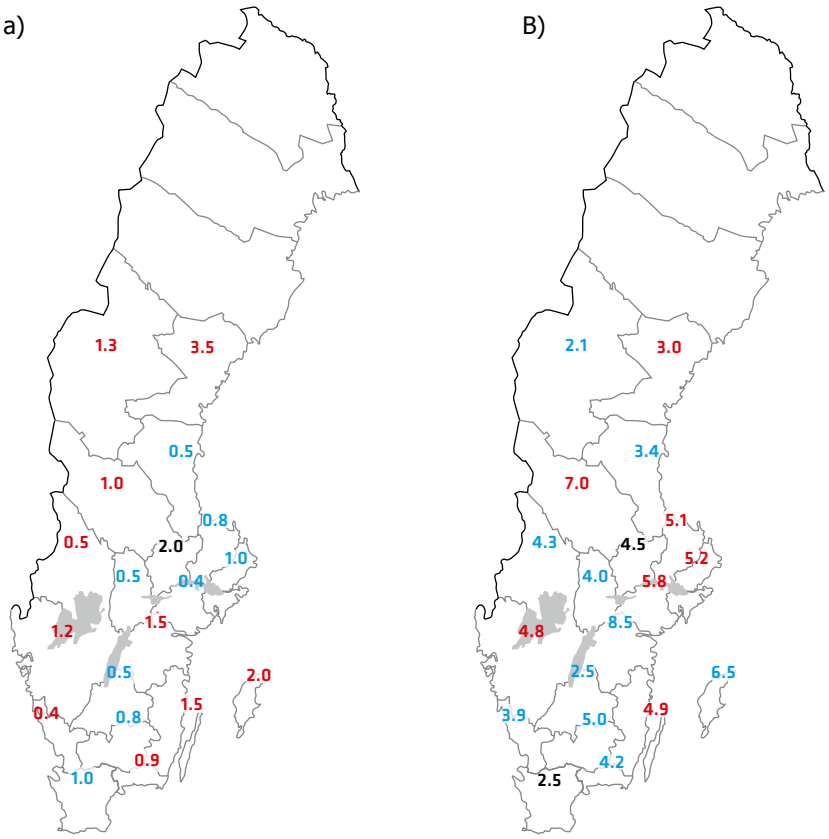
The data is based on cultures included in the laboratories' routine activities. Some smaller extended analyses may be required. There is also the need for a resource to coordinate ResNet nationally. The work involves going through reports from the individual laboratories to ensure that the data has been submitted correctly. In addition, some time must also be spent on communicating the results (see below).

Results

ResNet is a point prevalence measurement and as such, is only representative of the time period in which the measurements were carried out. Since the measurements are repeated annually, it is however possible to see tendencies over time. The design of ResNet gives the resistance monitoring country-wide geographic coverage thanks to the participation of all the laboratories. The basis for the measurements (normally more than 3,000 items of measurement data per species and antibiotic per year) is larger than in most international studies.

The programme uses a map of Sweden for the geographic representation of resistance frequency.

Figure 3.1 a and b Map generated from ResNet of resistance levels for *E. coli* against a) nitrofurantoin and b) mecillinam for 2012.



Numbers in black represent unchanged resistance frequencies compared to previous year, blue decreased and red increased numbers. Based on data from ResNet, the Public Health Agency of Sweden presents the national average for resistance for a specific bacterial species against selected individual antibiotics. These diagrams are available on the Public Health Agency of Sweden website and in the annual report SWEDRES.

Resistance to nitrofurantoin remains low whilst resistance to mecillinam has increased slightly in recent years (figure 2.9). Both nitrofurantoin and mecillinam are first choice treatments in national treatment recommendations for lower urinary tract infections in women in outpatient care. By continuously following the development of resistance in ResNet it is possible to see the effects of antibiotics that are suggested in the national treatment recommendations for outpatient care. For increased user-friendliness on a local level, each laboratory/County Council may also have their results summarised in a table.

Conclusions and lessons learned

Since the laboratories contribute measurement data to ResNet every year, they are now able to continuously ensure the quality of their measurement methods. From this perspective, it has been particularly useful for them to generate their own measurement data. (An alternative would have been to send cultures to a national organisation that would generate measurement data for all laboratories.)

ResNet has given laboratories, decision-makers, authorities, Strama groups and other concerned organisations access to resistance data for clinically important bacteria and enabled them to see tendencies over time. The total amount of data from all cultures is large enough to draw conclusions about changes over time on a national level. Data on a local level must, however, be interpreted with caution since the basis may be too small for drawing reliable conclusions about change.

One of the limitations of ResNet is that the software receives and presents aggregated data per laboratory, bacterial species and antibiotic. This means that it is not possible to see the prevalence of multi-resistant strains in the material, information that is sometimes desirable when developing or following up on local treatment guidelines. So far, such information has had to be retrieved directly from the computer system of the local laboratory, but it will now also be made available in Svebar (section 3.4).

In addition to the collection of resistance data, a central and important aspect of ResNet is that it enables quality-assurance of data. Good national cooperation between the local laboratories, the national/Nordic method group and the Public Health Agency of Sweden has made this possible. Another precondition for the design of ResNet is that cultures are taken from patients quite frequently in Sweden, making it possible for laboratories to carry out resistance testing and provide the healthcare sector with information.

Anyone who wishes to develop a similar programme should begin by establishing good cooperation within a laboratory network. A resource is also required on a national level to coordinate the cooperation and to collate the data and provide feedback.

3.2 EARS-Net – European resistance monitoring of invasive infections

EARS-Net (the European Antimicrobial Resistance Surveillance Network) is a European network of national monitoring systems, which is led by the European Centre for Disease Prevention and Control, ECDC. EARS-Net plays an important role in documenting the prevalence and development of antibiotic resistance in Europe.

The monitoring includes seven bacterial species from invasive infections: *S. aureus, S. pneumoniae, E. faecalis, E. faecium, E. coli, K pneumoniae* and *P. aeruginosa* as well as Acinetobacter species which have been included since 2012.

Implementation

EARS-Net is the largest publicly funded monitoring system for antibiotic resistance in the European region. EARS-Net has achieved a status and a commitment from the participating countries which has enabled the monitoring to continue for almost 15 years.

The current EARS-Net originated from a European collaboration led by the Dutch National Institute for Public Health and the Environment, RIVM, which was insti-

gated in 1998. From the start it was agreed that each country's results from the resistance testing of invasive infections (mainly from blood) should represent at least 20 percent of the country's population.

Initially there was a focus on *S. aureus* which would reflect hospital-related infections and *S. pneumoniae* which would represent society-related infections. Later on, the programme was broadened to include more pathogens and more countries joined. ECDC took over the coordinated efforts in 2010 and the programme changed its name from EARSS to EARS-Net. The work is supported by a steering group in which experts from a number of participating countries rotate.

There are currently 27 EU countries as well as Norway and Iceland participating in EARS-Net. More than 900 laboratories serving over 1,400 hospitals provide EARS-Net with data. The participating hospitals and laboratories provide services for an estimated population of 100 million European citizens.

Each country is responsible for gathering and collating their data and reporting it to a central database at ECDC once a year. The data that is reported is the total number of blood cultures for the seven bacteria included and the prevalence of resistance to two or more antibiotics, which are defined by species. Details regarding the laboratory taking the sample, sample date, age of the patient and which hospital and unit the sample comes from are also included.

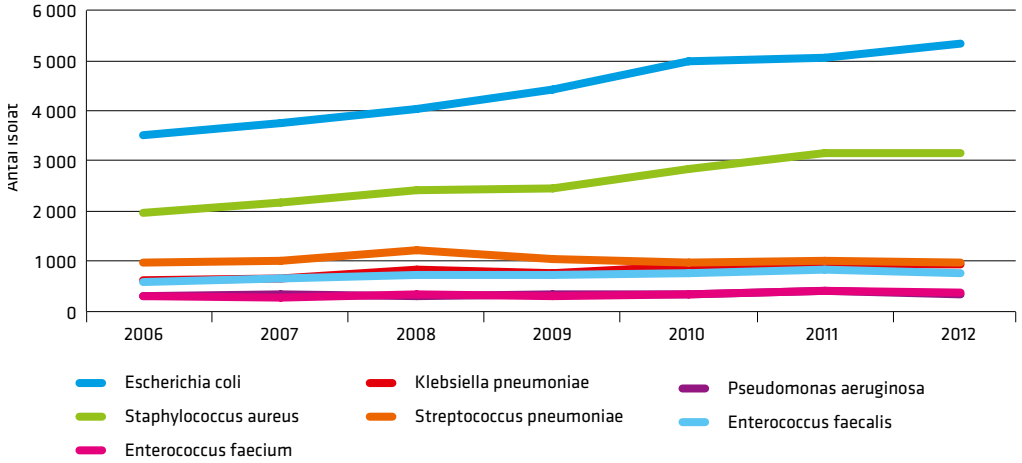
In Sweden, the reporting is coordinated by the Public Health Agency of Sweden. The Swedish laboratories were very interested in joining EARS-Net right from the start. Three quarters of the laboratories in the country currently participate, which corresponds to a level of coverage of about 80 percent of the Swedish population. Extensive work is required to validate data and to supplement and format the reports. The WHO's Whonet software is a valuable tool and is available free of charge. Depending on the IT system of the local laboratory, their need for manual work will vary. Some can automatically generate a file including all isolates for a particular year, whilst others continuously enter their data in a report file (often in a format that is compatible with Excel).

Results

ECDC collates the data and publishes an annual report with an analysis of developments in Europe. Statistics by country are illustrated with maps, diagrams or tables and are available in a database on the ECDC website. Statistics have often been made available for the European Antibiotic Awareness Day on 18 November and have thus helped the participating countries to raise awareness in the media or in activities organised on the day. Sweden and the other Scandinavian countries have comparatively good resistance conditions. Sweden is one of the few countries where less than 1 percent of all *S. aureus* are cases of MRSA. However, Sweden also has a notable prevalence of *Enterobacteriaceae* with ESBL or other resistance in gram-negative bacteria. A few cases of invasive infections with carbapenem resistant *Enterobacte-*

riaceae have been discovered so far in Sweden. The Public Health Agency of Sweden is responsible for ensuring that data from Sweden is reported to EARS-Net and it also publishes the Swedish results in the annual report SWEDRES.

Figure 3.2 Total yearly numbers of bloodstream infections by seven pathogens reported to EARS-Net from Sweden (20 laboratories, covering approximately 80 percent of the population). Source SWEDRES 2012.



The numbers of isolates of *E. coli* and *S. aureus* in bloodstream infections were much greater than the other pathogens, and they also showed increasing trends over the years, whereas the numbers of the other five pathogens were stable. Still, the percentages of resistant strains in bloodstream infections were relatively low (SWEDRES 2012).

An increase in the number of carbapenem-resistant *Enterobacteriaceae* has been noted in a growing number of European countries over the past years. In the light of this serious threat, ECDC and CDC in the USA have published risk assessments and recommendations to control and prevent the development (36, 37).

On the other hand, the proportion of MRSA bacteraemia has decreased or stabilised in most EU countries (38). Targeted interventions in several European countries may have had an effect on this development. In England for example, several radical reforms were introduced, which in 2011 had led to an 84 percent reduction in cases of MRSA bacteraemia compared to 2002 (39). However, many EU countries still have a high incidence of MRSA which shows that it remains a serious problem.

Conclusions and lessons learned

Although data from EARS-Net only includes resistance in invasive infections, and thus is likely to reveal only the tip of the iceberg, it still provides information that shows tendencies over time. Comparisons of resistance in EU countries must be interpreted with caution since varying sampling procedures may affect the results. Some countries take blood cultures more frequently from patients whilst others only focus on complicated cases, which may give a distorted image of the resistance situation.

For quality assurance purposes, all countries participate in external quality mailing lists organised by UK-NEQAS, an organisation that provides service for external quality control. The introduction of the EUCAST system and its breakpoints in a growing number of countries in Europe (and outside Europe) makes the comparison of data between countries more reliable.

There is significant interest in participation in EARS-Net and, thanks to the participating countries, monitoring has continued successfully for almost 15 years. In compilations produced by the RIVM in the Netherlands and the ECDC, all countries have been able to see their own data in relation to other countries. Every year the participating countries meet to exchange experiences and discuss possible expansions of the programme.

In Sweden, statistics from EARS-Net have proven a valuable tool, used both nationally and by local Strama groups, to demonstrate the increasing importance of the rational use of antibiotics and disease prevention as resistance is becoming more prevalent.

3.3 SmiNet – continuous monitoring of resistance in accordance with the Communicable Diseases Act

SmiNet is a system for national and local monitoring of diseases in accordance with the Communicable Diseases Act. The system was developed by the Swedish Institute for Communicable Disease Control, now the Public Health Agency of Sweden, and the County Medical Officers for communicable diseases.

Some forms of antibiotic resistance are notifiable in accordance with the CDA. This applies to *Enterobacteriaceae* (intestinal bacteria) with the ESBL resistance mechanism, methicillin-resistant *S. aureus* (MRSA), penicillin-resistant pneumococci (PNSP) and vancomycin-resistant *E. faecalis* and *E. faecium* (VRE). SmiNet reports cases both in real time and continuously, where appropriate. Reporting is done both by the clinically treating physician and by the laboratory. For ESBLA/M only laboratory reporting is required.

Implementation

The Swedish Communicable Diseases Act aims to prevent and stop the transmission of disease. Approximately 60 diseases are notifiable according to the CDA. This means that physicians are obliged to notify each diagnosed case of such a disease to the County Medical Officer for communicable diseases and to the Public Health Agency of Sweden. The County Medical Officers for communicable diseases constitute an independent authority, coordinating disease prevention and control in their respective County Council and providing information on how different cases should be handled.

Some of the notifiable diseases are deemed to be particularly serious and also oblige the physician to trace the transmission. The treating physician shall also inform the patient/carrier of particular rules of conduct in order to avoid further transmission of the disease. The laboratories are also obliged to report the discovery of a notifiable

disease. The double notification by physicians and laboratories greatly increases the sensitivity of the monitoring.

SmiNet is a web-based programme that receives and manages notifications in line with the CDA from treating physicians and from laboratory physicians. Over the course of a year, SmiNet receives about 75,000–80,000 notifications for the roughly 60 diseases that fall under the CDA. The system is designed to collect the information needed to continuously monitor the prevalence of the diseases locally and nationally, in order to prevent and stop disease transmission, in accordance with the CDA.

Since 1969, Sweden has had a notification system which at first only involved notifications on paper. Today, notifications are made electronically by treating physicians and by laboratories (it is still possible to send a paper form). Some laboratories also have automatic transfers from their IT systems to SmiNet.

The local communicable diseases units can see and supplement information on cases in SmiNet in their own County Councils. Authorised persons within the Public Health Agency of Sweden can access the information logged in the shared databases from all the County Councils, and thereby gain a national overview.

Information can be supplemented gradually

All people who have registered residence in Sweden are given a civic registration number as a form of identification. This makes it possible to link up different notifications regarding the same case in SmiNet. Each notification must include a diagnosis, some details about the patient and the treating physician. The laboratories have case criteria that define necessary components for the case to be classified as a discovery of ESBL or MRSA. Notifications from laboratories must include the species, data regarding the patient and the laboratory physician in charge.

To facilitate speedy reporting, the number of mandatory fields to be filled in by a laboratory or physician must be kept to a minimum. To obtain the details necessary for subsequent measures, additional information may be added gradually; this includes the likely source of transmission, the channel of transmission and details regarding resistance. Most of the fields in SmiNet are drop-down menus with multiple choice options in order to facilitate searches and statistical summaries.

Most of the notifiable forms of resistance are notified by both the physician and the laboratory. *Enterobacteriaceae* with $ESBL_A$ and $ESBL_M$ are the exception, as they are only notifiable for the laboratory, which in these cases makes the epidemiological information limited. All notifiable forms of antibiotic resistance involve the obligation to trace the transmission, except for $ESBL_A$ and $ESBL_M$. In SmiNet, the notifications from laboratories and clinical units are linked up, thus gathering all information on a particular case in one place. This also applies if there are many notifications from clinical units or laboratories concerning the same case. As such, epidemiological summaries of antibiotic resistance may avoid double notifications and can be based on unique cases alone.

To gain an overview of the epidemiological situation and understand the transmission of disease, epidemiological typing of isolates in the notifiable bacteria is conducted, either at the Public Health Agency of Sweden or in the laboratories. For some species, only point prevalence measurements are conducted and for others, epidemiological typing of all isolates is carried out. This information is also submitted in SmiNet and is added to the case in question.

The communicable diseases units act locally and the Public Health Agency of Sweden acts nationally

The local units for communicable disease control work on all cases within the County Council according to the CDA, to prevent further transmission of disease. They support the treating physician in tracing disease transmission. They also supplement the notifications in SmiNet as more information on each case becomes available and monitor the local development. They monitor the local development and assure local actions are taken, by for example healthcare givers.

The Public Health Agency of Sweden carries out national monitoring and communicate the information on its website and in annual reports. An important task is to identify possible sources of transmission across County Council borders, carry out an epidemiological typing, and provide information and support to the communicable disease units. The freely available CASE software, which was developed by the agency, is used to make statistical analyses. CASE uses different algorithms to calculate whether the number of notifications deviates from the expected level, over time and by area. Deviations are automatically reported to the administrator in charge at the agency.

Before issuing annual reports, units for communicable disease control go through the notified cases and add missing information. The units also contribute information regarding ongoing disease transmissions or experiences from their handling of outbreaks in the electronic newsletter produced by the Public Health Agency of Sweden which has country-wide coverage. There are also networks concerning specific agents through which people from all County Councils and from the agency meet and exchange information and experiences.

Results

A country-wide spread of VRE is a clear example of a quickly arising problem. In 2008, 618 cases were reported, which is nearly 12 times as many as the previous year. An epidemiological typing showed that the main strain being spread in several counties was *E. faecium* with the resistant gene *vanB*. Screening and comprehensive local disease prevention measures and controls in the affected counties led to a decrease in the spread in 2009-2010. Since then, the Public Health Agency of Sweden has developed a knowledge base about VRE with suggested measures to prevent transmission. Monitoring of MRSA has clearly shown how paths of transmission can change. As in many other parts of the world, MRSA in Sweden is no longer mainly transmitted

in healthcare settings but out in society at large. In 2012, 2,097 cases of MRSA were reported. Of all the cases contracted in Sweden, 68 percent were community-acquired and the afflicted were younger than those acquiring MRSA in healthcare. Changes in epidemiology present new challenges in preventing community-acquired MRSA and preventing further transmission to hospitals and other healthcare environments.
The most serious threat is posed by the significant increase in Enterobacteriaceae with ESBL in Sweden and other countries. ESBL leads to increased mortality, prolonged care periods and increased costs for the hospitals. Swedish healthcare has seen several ESBL outbreaks, such as those in neonatal units, where they have caused deaths. Enterobacteriaceae with ESBL is the most common notifiable resistant bacteria in Sweden. In 2012, 7,225 new cases were reported. The number of cases has increased by 14–33 percent every year since they became notifiable for the laboratories in 2007. $ESBL_{CARBA}$ cases are, so far, rare in Sweden and the majority of discovered cases have been among patients who have previously received healthcare abroad. In the light of the rapid spread in many countries, an obligation to notify and trace the transmission was introduced for treating physicians regarding Enterobacteriaceae with $ESBL_{CARBA}$ (carbapenemase-producing Enterobacteriaceae – CPE) in March 2012. The measure helps to identify cases of Enterobacteriaceae with $ESBL_{CARBA}$, to limit disease transmission in Swedish healthcare, and to follow developments in order to implement adequate countermeasures.

Conclusions and lessons learned

SmiNet has enabled communicable disease units and the Public Health Agency of Sweden to continuously monitor notifiable forms of antibiotic resistance. The extensive data facilitates good monitoring of these bacteria both nationally and locally. SmiNet makes it possible to discover and map outbreaks and transmissions and to study the epidemiology for different patient groups. Data from SmiNet is also important for the work on the rational use of antibiotics (see the example in section 3.5)

However, SmiNet only includes positive culture findings and no denominator data. It is therefore not possible to find out through SmiNet whether a change in resistance conditions is due to changes in sampling procedures since the system does not show if the overall number of cultures has increased or decreased.

An organisation is needed to work actively with the system both in terms of technology and content. The Public Health Agency of Sweden has a project group comprised of County Council representatives that continuously develops SmiNet. They work on adapting the notification forms for the clinical notifications and making the optional questions more specific for each agent in order to shorten forms. An important issue to resolve when developing a similar system is to define what type of information is needed in order to make the monitoring relevant and sufficient to take measures. This should be weighed against the work involved for the person who files the report and supplements it with further information.

3.4 Svebar – an IT system for early alerts and continuous resistance monitoring

An increase in the development of resistance and outbreaks of resistant bacteria in Swedish healthcare has shown that the current systems are too limited and slow and require manual management. Svebar is an IT system that the Public Health Agency of Sweden is developing with representatives of microbiological laboratories in order to improve local and national resistance monitoring. The aim is that all culture findings from the country's laboratories will be automatically transferred to Svebar on a daily basis. Svebar gives an early alert about findings of very serious antibiotics resistance or other undesired changes in resistance conditions. The large amount of data also allows for a continuous and more extensive resistance monitoring locally and nationally.

Svebar should satisfy the increased need for local statistics with aggregated resistance data. Many laboratories currently have difficulties compiling such statistics without manual resource-intensive work, since IT systems are mainly designed to handle individual patient samples. Svebar is designed so that statistic reports can be easily generated for national and local use.

The laboratories' participation in Svebar is voluntary. The aim is for all of the laboratories to be connected by 2015.

Implementation

The Public Health Agency of Sweden is responsible for running Svebar. There is an initial cost to the laboratories, in the form of time and money to develop the file that is to be introduced into the system. After that, reporting is automatic.

Every night each connected laboratories automatically send a file with the culture findings from the past 14 days to the system, and the file is saved in a short-term storage. The pre-set alerting algorithms search through the storage and issue an alert when there is a hit. An alert is generated when there is a finding of a bacterial species that is resistant to one or more antibiotics, for example for findings of *E. coli* resistant to carbapenems. There will also be an alert if the system discovers a trend, for example if more than 30 percent of *E. coli* in a laboratory is resistant to ampicillin. National alerts are sent by e-mail to the contact person at the local laboratory and to administrators at the Public Health Agency of Sweden and if needed they can discuss the alert. Local alerts only reach the contact person in the local laboratory.

Since Svebar receives data continuously, the system can react to findings that may come to change since they have not yet been fully analysed by the laboratory. For this reason, Svebar has been divided into a short-term storage that can react quickly and a long-term storage that receives more processed data. Every night, the short-term storage receives data from the past 14 days, which means that there is one day's shift compared to the previous day and an overlap of 13 days. The long-term storage saves the oldest day from the previous night's report. This means that culture findings are

kept in short-term storage for 13 days before being transferred to long-term storage. This creates a good margin for the culture finding to be fully analysed in the laboratories before it is stored permanently in Svebar.

Data reported by the laboratories to the short-term storage includes:

- Sampling year
- Sex and age of the patient (year and month of birth)
- Laboratory number (the ID number of the referral)
- Type of test (Test material)
- Analysis (i.e. urine culture, blood culture, etc)
- Sample-taking laboratory
- Microorganism (or the reporting of a negative finding in a culture)
- Resistance pattern (SIR and MIC)

Details about the laboratory number enable the laboratories to go back and follow up on a patient sample that has generated an alert in Svebar. According to Swedish rules on storing data, those details are erased before the results are stored in the long-term storage since it would otherwise be possible, nationally, by linking local registers, to connect a finding to a specific person. In other words, data in long-term storage is anonymous.

There are definitions for how data is reported to Svebar. When a laboratory is connecting to Svebar, there is a need for a mutual standardisation of the nomenclature and file format that will be sent to the system every night.

Results

Svebar facilitates early discovery and a short response time to outbreaks through its alert function. This may help put a quick stop to the transmission of disease, which in turn saves money for the healthcare system and reduces the number of patients afflicted. The system requires the Public Health Agency of Sweden or the local laboratory to define in advance what findings should generate an alert. By continuously following the development of resistance it is possible to discover changes at an early stage, changes which may motivate altering the settings of the alert system.

The large amount of data from all the culture findings provides a good statistical basis for national and local resistance monitoring. The fact that reporting is done automatically saves time and resources and the system is designed to produce statistical reports quickly. As such, Svebar will improve access to local aggregated resistance data required for the development of treatment recommendations and to facilitate local work on the rational use of antibiotics. The possibility to follow development of multi-resistance in Svebar is also essential for the designing and revision of treatment recommendations.

All laboratories have access to their local data and to aggregated national data. The Public Health Agency of Sweden is responsible for regularly feeding back national and local resistance data in reports to the laboratories. Together with the laboratories, it makes suggestions on particularly important matters to follow and compile in the standard reports. In addition to this, Svebar makes it possible to individually analyse aetiology and the prevalence of resistance for a certain patient group, locally or nationally. An example of a question that the system can answer is: How many cases of bacteraemia were discovered during a year in children, which bacterial species were the most common and what proportion of these bacteria were resistant to one or more antibiotics?

Svebar contains denominator data, i.e. the number of both negative and positive cultures. It can also show if differences in the prevalence of resistance, during a period or between laboratories, can be attributed to a difference in the sampling frequency. In other words, it forms a better basis for clarifying whether there is an actual increase or decrease.

One of Svebar's current limitations is that resistance reported to the long-term storage reflects the whole catchment area of the laboratory, which includes different types of care activities for which resistance conditions may vary. For legal reasons of personal integrity there is currently no opportunity to go more in-depth and analyse the prevalence of resistance in health centres, in individual hospitals or surgical and haematological units, which is important for the development of more targeted treatment recommendations and in order to direct the empirical treatment. It is likely that the risk of contracting a urinary tract infection caused by resistant bacteria differs between an otherwise healthy woman visiting a health centre and a woman suffering from cancer in a haematological unit who has previously undergone several antibiotic therapies. Svebar has, however, been developed to receive resistance data on a health centre, hospital or unit level (referred to as HSA ID or originator information). In the long term, it should therefore be possible to extract such information provided that the storing procedure conforms to Swedish rules on data storage. Another condition is that laboratory reporting of originator information becomes standardised and follows the same format. A national project is currently in place to promote such standardisation.

Conclusions and lessons learned

By means of Svebar, Sweden has improved its capacity to stem the development of resistance and to prevent disease transmission, capacities that benefit the entire population.

It was important to invite all of the laboratories early on in the process in order to inform them about Svebar and to reach a joint agreement on how data from Svebar would be used. The system relies on the voluntary participation of the laboratories. To avoid using data on a national level without the consent of the local laboratories that have submitted the data, there is a mutual agreement on use between the Public Health Agency of Sweden and the laboratories.

Anyone aiming to develop a similar monitoring system should keep in mind the value of reaching a common agreement on standardised nomenclature for test material, names for analyses and antibiotics, and the reporting format. If the laboratories lack IT systems, it is beneficial to introduce the same system in all the laboratories participating in the monitoring programme.

3.5 Examples of how resistance data is used as a tool to change prescription in hospitals

Over the course of a few years, the number of ESBL findings rapidly increased in Sweden and several outbreaks were reported. In February 2007, compulsory reporting of ESBL was introduced in accordance with the Communicable Diseases Act, in order to gain a good national overview. This worrying development was noted across the country and efforts were made to handle the problem.

In Skåne, the southernmost county of Sweden, the local Strama group (Strama Skåne) summoned all hospital physicians to meetings in 2007. By using local resistance data from urine and blood cultures together with national and European data from SmiNet and EARS-Net, the group was able to clearly illustrate the threat and suggest necessary measures. Below follows a description of this initiative, based on an interview with Eva Melander, the chief physician for disease prevention and control, and chairman of Strama in Skåne.

Implementation

Strama Skåne initially met with all of the chief physicians for the hospitals in Skåne and received their support, which made it easier to subsequently reach the clinical directors and the physicians in the hospitals. The chief physicians ordered all physicians to attend one of the meetings held by Strama Skåne at each hospital.

Resistance statistics were presented at the meetings, demonstrating the increasing prevalence of ESBL in Skåne and Sweden. Maps showed that the development had accelerated further in other parts of Europe. Strama informed the physicians about the few existing treatment options in case of serious infection with ESBL-producing bacteria. Besides breaking down beta-lactam antibiotics, they often carry resistance to other groups of antibiotics such as quinolones and aminoglycosides. The fact that ESBL threatened to lead to increased mortality and morbidity made many agree that vigorous efforts were required to counteract this development.

Strama Skåne had also compiled data on the prescription of antibiotics in hospitals which showed a high and unbalanced use of cephalosporins and quinolones. It indicated that these substances were strongly associated with the development of ESBL. A proposal was then presented to change the empirical treatment by reducing the use of cephalosporins and quinolones and increasing the use of penicillin.

Some of the main messages from Strama Skåne to the physicians were:

- Reduce the general use of cephalosporins and quinolones
- Do not use quinolones for lower urinary tract infections in women
- Use benzylpenicillin for respiratory tract infections
- Contact an infection consultant when a patient with ESBL requires antibiotic treatment

Resistance data was also used to emphasise the importance of applying basic procedures for infection control (chapter 1) to prevent disease transmission. Strama Skåne also informed the physicians about routines for screening and care of patients with ESBL. Initially the bar was set high and it was recommended that all patients with ESBL were to be cared for in single rooms. Since ESBL has unfortunately become increasingly common, this requirement has gradually had to be dropped in the local guidelines for disease prevention. Meanwhile, compliance with procedures for infection control has become all the more important.

Eight staff from Strama Skåne spread these messages in the 10 hospitals in Skåne during 2007. In each hospital a number of meetings were arranged, ensuring that all physicians would have the opportunity to attend. At the meeting, Strama Skåne distributed a reference manual on the empirical antibiotic treatment of patients with community-acquired infections. The recommendations were developed by representatives of infectious disease clinics in the hospitals involved in the Strama work. Many physicians also received e-mails with the same information and a link to the local recommendations.

Results

Strama Skåne felt that the meetings elicited great support from the physicians. The serious threat and the rapid development of resistance made it easier for many to take the messages on board. The prescription of antibiotics changed drastically. The use of parenteral cephalosporins measured in DDD fell by 45 percent and the use of PcG rose by a corresponding 45 percent in hospitals in Skåne between 2006 and 2008. The use of piperacillin/tazobactam rose by nearly 50 percent whereas the use of carbapenems remained relatively unchanged. The use of quinolones fell by 25 percent.

The efforts in Skåne coincided with a national effort to call attention to ESBL. Compulsory reporting of ESBL was introduced in accordance with the CDA, which helped to emphasise its importance. National Strama drew up a report suggesting measures (40, 41). National data on use also showed a shift from cephalosporins and quinolones to penicillins.

Strama Skåne has also since continuously organised meetings in hospitals and emphasised rational use of antibiotics. The shift in prescription routines remained constant in Skåne in the following years. However, in the past year, the use of cephalosporins and quinolones has increased somewhat in certain hospitals.

Conclusions and lessons learned

The commitment from the chief physicians was crucial to the work of Strama Skåne. Their support encouraged a greater attendance at the meetings. The serious threat that could be demonstrated with resistance data made many people realise that the revised therapy recommendations were reasonable and important. Some were critical, however, and thought that they would result in an increased number of complications, and in the worst case scenario, deaths. Some perceived the message as an indication that they should stop all use of cephalosporins, which was not the case. The aim was rather to reduce unbalanced use. For this reason, it was vital to emphasise that the recommendations were primarily aimed at the treatment of large patient groups with community-acquired infections, patients who had no underlying diseases. The revised recommendations were thus not aimed at immuno-suppressed cancer patients or seriously ill patients in intensive care units.

As a result of the information campaigns in the hospitals in Skåne, prescription patterns changed dramatically. This may have led to a reduced prevalence of ESBL in hospitals, since the use of cephalosporins and quinolones was reduced. However, it is not possible to prove the extent of such a relationship. As with other preventive measures, it is difficult to know what the situation would be like if prescription had not changed.

The transmission of ESBL in the community and around the world is probably not influenced significantly by the local use of antibiotics in the hospitals. The fact that ESBL is increasing rapidly has posed a certain educational challenge for Strama Skåne, which has to continuously carry the argument that it is important to reduce unnecessary prescription of broad-spectrum antibiotics, since otherwise there is a risk that the situation will worsen.

Interview with Professor Gunnar Kahlmeter

Gunnar Kahlmeter is a Professor of medical microbiology and operations manager of Kronoberg county council. He is president of European Society of Clinical Microbiology and Infectious Diseases (ESCMID), and former chairman of the Methodology subgroup of the Swedish Reference Group for Antibiotics (SRGA-M) and of the European Committee on Antimicrobial Susceptibility Testing (EUCAST).

"There are no short cuts to success. The reason for Sweden's relatively low prevalence of resistant bacteria can be found in the structure of our society, our economic wealth and our history", says Gunnar Kahlmeter, an international authority in the field of antibiotic resistance, including methodology, standardisation and surveillance.

Gunnar Kahlmeter has been part of the 'antimicrobial scene' since the 1980s. As former chairman of SRGA-M and EUCAST, Kahlmeter has been a leading advocate of harmonising laboratory methods and antimicrobial susceptibility testing in Sweden and internationally. "We must know our starting point if we are to get anywhere", he says referring to the need for standardised definitions of susceptibility and resistance. He has been instrumental in building a completely new system of harmonised break-points in Europe, a system countries outside Europe are now adopting. In Sweden, Kahlmeter has been the driving force behind the development of several national surveillance systems, one of which is Svebar, the Swedish system for early warning and surveillance of antimicrobial resistance.

Kahlmeter is rather pessimistic when it comes to the future of antibiotics and efforts to overcome resistance on a national and international level, hence the title of his popular lecture '*Multi-resistant bacteria – up the creek without a paddle*'. He compares the issue of resistant bacteria to the global climate crisis, alluding to the magnitude of the problem and the fundamental changes required to overcome it, not least in terms of political will.

Even so, Kahlmeter believes that lessons learned in Sweden may be useful in a broader context. Countries facing the major public health threat imposed by multi-resistant bacteria can and must work on many levels to reduce this threat. In the long run this involves improving general nutrition and health, health care systems as well as child care and care of the elderly. It also involves investments in public infrastructure, general hygiene, water supplies, managment of latrines, sewage and waste and not least education. Kahlmeter concedes that the task may indeed seem overwhelming.

"A good starting point is to set up a national infrastructure consisting of a network of **high standard laboratories**, using standardised methods and harmonised breakpoints to detect and define resistant bacteria. It is crucial that these national, public health laboratories agree on methods and standards."

Simultaneously, great efforts must be made to **improve general health care** and to actively **reduce the transmission of bacteria** within health care facilities. “This task is far more expensive and time-consuming and even well-to-do Sweden has a long way to go here, not least to improve disease control in homes for the elderly and day care facilities for children”, says Kahlmeter.

From this follows efforts to develop protocols and systems for rational use of antibiotics, such as the work done by Swedish Strama since the mid-1990s.

The war on resistant bacteria is far from won, even in a country like Sweden. Like all experts in the field, Kahlmeter points to the need for international solutions to a problem that knows no borders. As an example, he emphasises the need to develop **improved diagnostic procedures**. This requires costly investments but will in turn allow doctors to eliminate the unnecessary use of broad spectrum antibiotics in favour of targeted therapy.

Gunnar Kahlmeter describes Sweden as a well-organised, uniform society with comparatively small gaps in income and education. “During the past century we have been able to afford the necessary investments in infrastructure, health services and high quality laboratories with standardised methods. These general developments, not isolated efforts in themselves, can explain why Sweden, as perhaps the only country in the world, has been able to break the trend of increasing antibiotic consumption”.

And yet, it is too early to say what this break actually means and what impact it will have in the long run. “Reduced consumption in Sweden has mainly a symbolic value in a global context. But this should not be underestimated”, Kahlmeter concludes.

Chapter 4. Monitoring the use of antibiotics

Virtually all use of antibiotics gives rise to bacterial resistance. Therefore, to minimise the development of resistance, the use of antibiotics must be optimised. This work requires effective surveillance and follow-up of consumption, at a local and national level.

To be effective in the long run, work to optimise use of antibiotics must influence the prescribing practices of individual physicians. The goal is "rational use", i.e. the correct patient receives the correct antibiotic at the correct dose and for the correct duration of treatment, in accordance with evidence-based guidelines. Over-prescribing should be avoided without resulting in under-prescribing. Swedish experience has found that such work should also be carried out close to the prescriber, something which also requires high resolution prescription data, down to the clinic and health centre level or better still at the level of individual prescribers. Data of this kind has been, and is, an essential ingredient in the local work of Strama. At the national level, the Public Health Agency of Sweden is responsible for the surveillance, analysis and feedback of statistics on antibiotic consumption in human medicine.

This chapter describes the systems that have gradually been developed in Sweden, from the relatively simple diagnosis-prescription studies of the 1990s to today's increasingly sophisticated instruments, such as the Anti-Infection Tool. By way of introduction, an overview is also provided of how antibiotic management and sales are regulated in Sweden as well as some basic methodological aspects.

The sale of antibiotics is regulated

All sales of pharmaceuticals in Sweden are regulated by the Medicinal Products Act, which is applicable to their use both in human and veterinary medicine. Under this Act, a medicinal product may not be sold before it has been approved for sale. The approval of new pharmaceuticals is now a European matter. Approval can be granted via three alternative procedures; the centralised procedure, the mutual recognition/decentralised procedure and the national procedure. The centralised procedure is administered by the European Medicines Agency, EMA. In Sweden, the Medical Products Agency is responsible for the scientific examination of pharmaceuticals in the approval process. Although the procedures are different, the scientific requirements are the same. If a pharmaceutical is not approved in Sweden, the Medical Products Agency can grant a licence, that is, a special permission for use. A licence can be granted to a specific prescriber, to an individual patient or to a clinic with a particular patient group (general licence).

A patient can only obtain antibiotics via prescription in outpatient care or via prescription by a physician at a hospital (in some rare cases, specific preparations for specific diagnoses, also via prescription by a nurse with prescribing rights). There is thus no sale of antibiotics without a prescription, known as over the counter, OTC, directly to patients. Antibiotics and other prescription drugs must be distributed through pharma-

cies. Prescribers (physicians or veterinarians) may not own a pharmacy or sell pharmaceuticals for personal gain.

All pharmacies in Sweden are obliged to supply daily statistics on all sales of medicinal products to the Swedish eHealth Agency, which is responsible for maintaining a database of statistics on pharmaceutical sales in Sweden. These statistics are supplied to authorities, County Councils and other stakeholders.

The statistics are based on the ATC Classification System and on DDDs

Sweden uses the Anatomical Therapeutic Chemical (ATC) Classification System for statistics on antibiotics, as recommended by WHO. (In veterinary medicine, ATCvet is used). In human medicine, the WHO's metric DDD (defined daily doses) is also used to measure antibiotic consumption. The defined daily dose for a given antibiotic is based on the assumed average maintenance dose per day for a drug used for its main indication in adults. The Swedish eHealth Agency annually updates its databases regarding ATC codes and DDDs in accordance with WHO recommendations (42).

Surveillance is necessary both for antibiotic consumption and for prescription causes

In Sweden, all sales statistics from the Swedish eHealth Agency are used for the surveillance of antibiotic consumption, both nationally and locally in County Councils. Pharmacy sales data is given either as the number of DDDs per 1,000 inhabitants and day or as prescriptions per 1,000 inhabitants (section 4.1). These statistics are general, but provide, among other things, valuable information about the total antibiotic consumption over time, in different age groups and between different geographical areas.

In order to secure the rational use of antibiotics, one must also evaluate how antibiotics are used for different diagnoses. Among other things, it is necessary to see how treatment recommendations are followed and to evaluate any possible need for and effects of training measures and interventions. At present, the sales statistics from the Swedish eHealth Agency do not contain such diagnosis-linked data, although in the past there have been manual diagnosis-prescription surveys based on prescription sales (section 4.1).

To gain access to diagnosis-linked data, Strama has conducted repeated manual diagnosis-prescription studies in outpatient care (section 4.2) and point prevalence measurements in inpatient care (section 4.5). The studies have provided important knowledge about how antibiotics are used. Their design, however, means that only a limited period during the year is studied and a substantial level of work by the participating prescribers is required as all registration is done manually. Processing the data also involves a lot of manual work and the results are completed only after several months of compilation. For this reason, in recent years, several initiatives have been taken to set up registers and systems that automatically generate diagnosis-linked data in outpatient care (section 4.3). Projects have also been initiated in inpatient care, with IT systems registering antibiotic prescriptions and healthcare-associated infec-

tions (sections 4. 6 and 4.7). Within intensive care, a special project has been running since the year 2000 to systematically register and analyse the problem of infection in intensive care units (section 4.8).

Sweden also participates in ESAC-Net, a European network for the surveillance of antibiotic consumption (section 4.10). In addition to the systems described in this chapter, there are several local systems developed by various County Councils.

Targets and quality indicators

In human medicine, the prescribing of antibiotics in outpatient care constitutes 90 percent (of which primary healthcare accounts for approximately 60 percent) of all prescribing of antibiotics (measured in DDD/1,000 inhabitants/day) in Sweden. There are national targets and quality indicators for antibiotic treatment in primary healthcare. These partly relate to total antibiotic consumption and partly to the selection of antibiotic preparations as different types of antibiotics drive resistance to varying degrees. Based on national treatment recommendations, the Swedish Association of General Practice has developed indicators for diagnostics and antibiotic treatment. These show, for example, that fewer than 20 percent of all cases of acute bronchitis should be treated with antibiotics and that over 70 percent of all patients treated with antibiotics for pneumonia should receive penicillin V. Furthermore, the proportion of women treated with quinolones for the diagnosis of cystitis should not exceed 3 percent. The same applies to the proportion of women with cystitis treated with cephalosporins. These targets are based on diagnosis-linked data and are primarily intended as an aid for the individual physician or health centre to be able to evaluate their own results, such as in the review of medical records (section 4.4 on PV-quality). Strama has also proposed national targets that are based on sales data without any link to diagnosis. These are used as more general measurements for monitoring and comparing counties in Sweden. Two targets focus on major diagnosis groups, urinary tract infections in women and respiratory tract infections in children, and they advocate the high use of narrow-spectrum antibiotics according to national treatment guidelines. Another target concerns the total use of antibiotics in outpatient care (section 4.1).

Methods for detecting signs of complications or under-prescribing

In parallel with efforts to reduce the unnecessary and inappropriate prescribing of antibiotics, it is important to continuously evaluate whether there is an increase in complications for common infections, such as acute mastoiditis in the case of otitis. In Sweden, there is a register that has examined such issues, and specific studies have also been conducted (section 4.9).

Analysis and communication

Data from surveillance is only valuable when used. The Public Health Agency of Sweden analyses and publishes national statistics on antibiotic consumption on the Public Health Agency of Sweden's website in quarterly and annual reports and in press releases and in the agency's newsletter.

A main task for Strama groups in the County Councils is to analyse and provide feedback on local antibiotic use. Much of this feedback takes place through discussions with physicians at hospitals and health centres. Within an increasing number of County Councils, systems are now being constructed so that feedback can be given on an individual level to enable every physician to compare their prescribing with that of their closest colleagues (section 4.11 and chapter 2). Statistics are also communicated through local websites and newsletters. National and local activities are often coordinated through press releases and press conferences in order to reach both national and local media.

4.1 Pharmacy statistics on antibiotic consumption

The Swedish eHealth Agency is a state-owned company responsible for maintaining pharmaceutical statistics in Sweden. Sweden's pharmacies daily supply statistics on all sold pharmaceuticals, including antibiotics, to the Swedish eHealth Agency, which compiles the statistics. Data is sorted and processed to match its designated recipient. Through a subscription, national authorities may access data on sales aggregated at the national level, by County Council or municipality. Local actors such as County Councils, pharmaceutical committees and Strama groups also have access to statistics broken down to the activity level, for example at health centres or hospital clinics. The Public Health Agency of Sweden is responsible for compiling and analysing data regarding the overall antibiotic consumption in Sweden.

Implementation

Since 1975, pharmacies in Sweden have regularly produced statistics on sales of pharmaceuticals. Until the mid-1990s, these statistics were based on a sampling of prescriptions. Until 2002, national surveys of prescription causes, known as diagnosis-prescription surveys, were also conducted in a joint project between national public organisations. For a specific period each year, a random selection of physicians made a copy of all their prescriptions. They attached details regarding the diagnosis and indication for treatment. The surveys were resource-intensive and came to an end with the setting up of computerised medical records systems.

Since 1996, pharmacy statistics include all antibiotics sold on prescription, outpatient requisition, Apo-dos and on prescription to hospitals. However, these statistics do not include diagnoses and there is therefore no data regarding indications for antibiotic treatment.

Statistics on antibiotic consumption in outpatient care

In Sweden, approximately 90 percent of antibiotic sales take place in outpatient care. In the Public Health Agency of Sweden's statistical compilations, the term outpatient care covers all sales of antibiotics prescribed on prescription, Apo-dos (dose-dispensed medication) and outpatient requisition, for example, from primary care and outpatient specialist clinics.

When patients present their prescription at the pharmacy, information is registered in the pharmacy's pharmaceutical register. A large proportion of all prescriptions are now electronic, and registration in the pharmaceutical register is then automated. The information is automatically forwarded to the Swedish eHealth Agency on a daily basis. Information registered from the prescription includes product name, quantity (DDD, number of sold packages), patient fee, total cost, patient age, sex and domicile. In addition, a workplace code is recorded indicating where the prescription was issued (County Council, municipality, or healthcare unit) and a unique prescriber code for each prescriber. The unique prescriber code enables the Swedish eHealth Agency to categorise prescribers in various prescriber categories. Authorities and local organisations may only view the statistics broken down by prescriber category (veterinarian, physician, dentist and district nurse), while prescribers and unit managers are able to order statistics on the prescriptions of individual physicians.

Pharmacy statistics on antibiotics in outpatient care are expressed either as DDD per 1,000 inhabitants or the number of sold prescriptions per 1,000 inhabitants. The information registered makes it possible to gain knowledge of consumption over time, across regions and of the average consumption among different age groups.

In July 2005, based on data from the Swedish eHealth Agency, former Apotekens Service AB, an individual-based pharmaceutical register was started that is provided by the National Board of Health and Welfare. The register allows for analysis of antibiotic purchases at the individual level and thus complements the sales statistics of The Swedish eHealth Agency. One may, for example, study what percentage of the population has purchased antibiotics or how many prescriptions for antibiotics each individual has retrieved annually.

Statistics on antibiotic consumption in inpatient care

Approximately 10 percent of antibiotic sales are made via requisitions, primarily to hospitals. Clinics and departments at hospitals purchase antibiotics from hospital pharmacies on requisition. Sales information is then transferred daily from hospital pharmacies to the Swedish eHealth Agency's database. The information registered from requisitions includes product name, quantity (DDD, number of sold packages), total cost. There is also information on customer numbers that indicate the hospital and healthcare unit that has ordered the medication. Authorities may only view the statistics aggregated at the county level, while County Councils have more detailed information and are able to monitor their own statistics by customer number (hospital and clinic/section level). Local Strama groups from the County Councils make annual contributions of local statistics to the Public Health Agency of Sweden's national compilations. For example, they contribute data on antibiotic sales to emergency hospitals only, where municipal, elderly and care homes are excluded.

The use of antibiotics in hospitals is reported as DDD per 1,000 inhabitants and day. When the Public Health Agency of Sweden compiles statistics on consumption in hospitals, DDD is also given per 100 patient days (the number of days that *all* patients

are admitted) or per hospitalisation (each new admission registered as one hospitalisation), data that is obtainable from a register managed by the National Board of Health and Welfare. These latter parameters with healthcare-producing denominator data, give a better picture of the antibiotic pressure in a hospital.

The analysis of antibiotic use in municipal homes for the elderly and special care homes is problematic due to national variations in how people in such homes receive antibiotic treatment. They can either receive antibiotics by prescription or Apo-dos and thus be included in the outpatient statistics or from pharmaceutical supplies where medication has been purchased via requisition, which falls within inpatient consumption. This leads to an uncertainty in analyses and comparisons of inpatient sales in different counties, including outpatient sales to patients 80 years of age.

Analysis and communication of data

At the Public Health Agency of Sweden, pharmacists are responsible for the regular monitoring, analysis and feedback of statistics on antibiotic consumption in outpatient and inpatient care. Supporting this work is an analysis group consisting of representatives from various parts of Sweden with expertise in healthcare, pharmacy and pharmacoepidemiology.

The Public Health Agency of Sweden's statistical reports monitor and present the status of each county with respect to three targets previously proposed by Strama. These are also reported annually by the National Board of Health and Welfare and the Swedish Association of Local Authorities and Regions in "Open Comparisons" where health services across the entire country are compared with respect to various indicators.

The first target is that the ratio of penicillin V (J01CE02) to all antibiotics commonly used for respiratory tract infections should be 80 percent in outpatient care among children 0–6 years. The second target is that the ratio of quinolones (J01MA02+06) should not exceed 10 percent of all typical urinary tract preparations for women in outpatient care in the 18–79 age group.

The third target states that the total antibiotic consumption in outpatient care should be 250 prescriptions per 1,000 inhabitants and year. This is a long-term target adopted under a special initiative for patient safety initiated by central government.

Evaluating and securing rational antibiotic treatment requires knowledge of how antibiotics are prescribed and, at best, in relation to diagnosis. However, the targets from Strama stated above are based solely on sales data for various antibiotic preparations and are not linked to diagnosis. They constitute benchmarks for reference and comparison but may need to be reconsidered in relation to diagnosis-linked data.

Antibiotic consumption statistics are published in quarterly reports via the Public Health Agency of Sweden's newsletters and in an in-depth annual report, SWEDRES/SVARM. Statistics, quarterly reports and the annual report are available on the

Public Health Agency of Sweden's website in the form of ready-made tables and diagrams, as well as in interactive Excel tables where the user can perform their own data searches. Local Strama groups analyse and provide feedback on local data on antibiotic use to health centres and hospital units in their respective County Councils (see introduction of chapter 4, section 4. 11 and chapter 2).

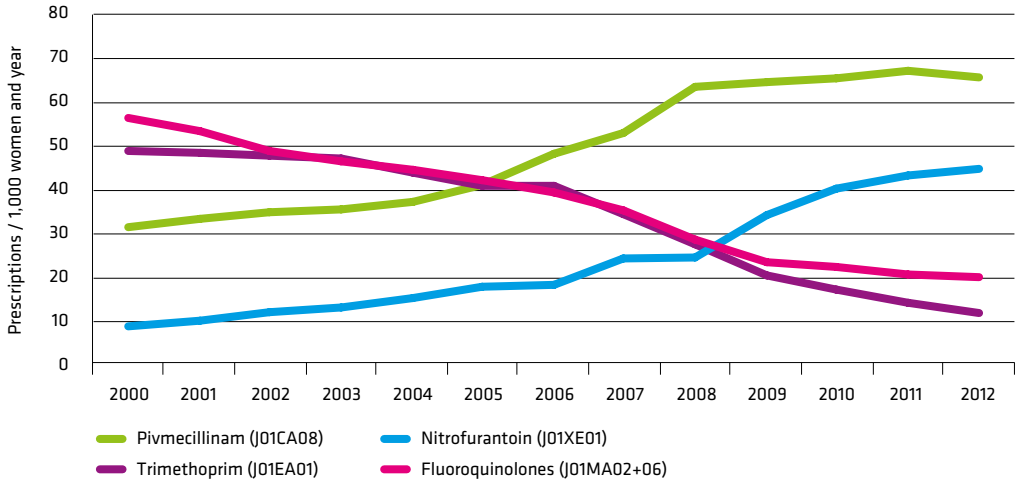
National and local press releases and press conferences are also used to communicate news about antibiotic consumption to the media, which means that information also reaches a wider public.

Results

The results from the national surveillance show that antibiotic usage varies greatly between different regions in Sweden, both with regard to the total quantity of antibiotics and to the types of antibiotic preparations used. Since 1992, the use of antibiotics in outpatient care has decreased from an average of 560 prescriptions per 1,000 inhabitants and year to the current 374 prescriptions per 1,000 inhabitants and year (chapter 2 and below).

Data from the National Board of Health and Welfare's individual-based pharmaceutical register shows that in recent years, one in four to one in three children have received at least one course of antibiotics per year. As with the rest of the population, children in the metropolitan areas receive the most antibiotics. Since the beginning of the 2000s, there has been an improved adherence to treatment recommendations for lower urinary tract infections in women. The use of the first-choice preparations nitrofurantoin (J01XE02) and pivmecillinam (J01CA08) has increased significantly.

Figure 4.1 Sales of commonly used antibiotics to treat UTI in women 2000–2012, prescription/1000 women and year. Data from SWEDRES.



The compliance to recommended therapy for lower uncomplicated uti in women seems to have increased, as reflected by these graphs: ecologically less beneficial quinolone use has been reduced, and instead we see an increase in pivmecillinam and nitrofurantoin, with less disturbance of the bacterial ecology. Simultaneously, use of trimethoprim goes down, much because resistance levels have climbed

In recent years, there has also been a shift in inpatient care where the use of narrow-spectrum penicillins (J01CE02) has increased and the use of cephalosporins (J01DB-DE) has decreased. This is in line with proposed measures for counteracting the selection of ESBL. The Swedish Society of Infectious Diseases has also published therapy recommendations for community-acquired pneumonia where penicillins are indicated as the first choice for uncomplicated cases.

Conclusions and lessons learned

The sales statistics collected by the Swedish eHealth Agency provide a continuous and comprehensive picture of the quantity of antibiotics consumed in Sweden. The statistics form the basis for comparisons between counties and for interventions and advanced studies. They also constitute bases for discussions with prescribers conducted by Strama groups and pharmaceutical committees.

The opportunity to analyse sales of antibiotics as measured by prescriptions per 1,000 inhabitants is very valuable. This measure is a better reflection of reality than DDD since DDDs are not adapted for different age groups where dose adjustment must be made. There are also certain differences between countries and between counties in how medication is dosed, for which reason DDDs can be misleading. For example, penicillin V (J01CE02) is mostly dosed as 1 gram 3 times a day in Sweden, while the DDD for penicillin V is 2 grams, which was previously also used as the standard dose for many years. A standardised measure like DDD is useful for comparing consumption between countries or over time. DDDs are mostly used in the analysis of antibiotic consumption in inpatient care in Sweden. An even better measure of inpatient consumption would be to measure the doses actually prescribed, PDD (Prescribed Daily Dose), or the number of patients treated.

In preparing national compilations, the Public Health Agency of Sweden has found it essential to have access to an external analysis group with broad expertise and knowledge of local conditions in order to understand the significance of statistical changes. If the statistics are to constitute a basis for discussion and advocacy, it is important that these are published continuously in quarterly reports and made available on the Public Health Agency of Sweden's website. The quarterly reports contain the same recurring figures to reflect consumption in a clear and accessible way. In addition, the annual reports provide the opportunity for in-depth analyses.

As of 2013, Apotekens Service AB/ the Swedish eHealth Agency has also developed a special prescriber profile for antibiotics in outpatient care. Physicians at health centres and their managers are able to order data on the antibiotic prescribing of individual physicians in relation to that of the health centre. This allows for direct feedback with respect to the individual physician's prescribing.

One limitation of pharmacy sales statistics is that they do not contain diagnosis-linked data. For this reason, there has been a need to generate such data through studies and other systems.

4.2 Diagnosis and prescribing studies in primary care

In the early 2000s, the Medical Products Agency and Strama developed national treatment recommendations in outpatient care for acute otitis media, pharyngotonsillitis and sinusitis.

To gain knowledge about how common infections are dealt with in primary care and the extent to which the recommendations were followed, Strama implemented diagnosis and prescribing studies on three occasions (2000, 2002 and 2005) (43). The studies covered counties with a total of approximately 1.2 million inhabitants.

Implementation

During one week in November, week 47, all the general practitioners in five counties were invited to register all patients seeking treatment for symptoms of an infection. The five counties had been selected in advance to represent both high and low-prescribing areas. The week in November was chosen so as to reduce the risk of an epidemic of influenza or respiratory syncytial virus affecting the results.

Using a paper form with fixed options, the treating physicians registered information on sex, age, symptom period prior to the visit, first and subsequent visits, diagnosis, use of diagnostic methods and their results. Furthermore, physicians registered whether or not antibiotics were prescribed. The selection of antibiotic and duration of treatment were stated in free text. The physicians were to complete the form even if antibiotics were not prescribed, among other things, to gain knowledge about the proportion of patients treated with antibiotics for a particular diagnosis. It was also possible to specify whether a prescription was issued that could be collected by the patient later if the symptoms did not disappear within a set period.

One person at each health centre was responsible for distributing and collecting the forms, which were then sent to the contact persons in each County Council. The results were quality-assured by a national project group and compiled in a national database. A working group consisting of contact persons from each County Council as well as experts from healthcare and from Strama groups met to discuss the significance of the results and how they would be communicated.

Data on a county level was fed back to prescribers, primarily by Strama groups and pharmaceutical committees. The results were also communicated at national and international meetings and constituted bases for the development of national treatment recommendations. In addition, articles were compiled for scientific journals and for "Läkartidningen", a magazine for physicians in Sweden.

Results

Approximately 155 health centres and 600 physicians participated in the study. During the study period, the number of registered visits for respiratory tract infections decreased significantly, especially for throat infections. A corresponding decrease in the number of visits for respiratory tract infections was also reported from another survey carried out in one of the County Councils also participating in this study.

Penicillin V was dominant in the treatment of respiratory tract infections in line with national recommendations for the treatment of respiratory tract infections. The number of patients with a respiratory tract infection decreased over time, while the proportion of patients receiving antibiotics decreased significantly from 54 percent to 49 percent. The greatest change was seen among children. However, the diagnoses sinusitis and otitis saw no significant decrease in the proportion of patients treated with antibiotics. For the diagnosis otitis, antibiotics were prescribed in more than 90 percent of the cases. For all the years, there was also a high proportion, about 50 percent, of patients with acute bronchitis who received antibiotics.

A significant change was seen in the choice of antibiotics for women with lower urinary tract infections. An increased resistance to trimethoprim and quinolones had led to calls to reduce the prescribing of these preparations in the treatment of women with urinary tract infections, among others from local Strama groups. (National recommendations were published later in 2007.) The study showed that the use of the recommended first-choice preparations nitrofurantoin and pivmecillinam increased significantly, while the use of trimethoprim and quinolones decreased. A similar change was also seen in sales statistics from Apotekens Service AB/ the Swedish eHealth Agency (section 4.1).

Conclusions and lessons learned

These studies provided important insight into how common infections are dealt with in primary care and also pointed out areas where increased information was needed by way of treatment recommendations and training initiatives. The studies provided a basis for discussion on infection management with physicians at health centres. They also illustrated the large proportion of patients with infection symptoms in primary care.

The results showed that general practitioners to a relatively great extent followed recommendations for increased use of penicillin V and revised procedures in the treatment of urinary tract infections. However, results also pointed at a need for improvement with regard to treatment of otitis and acute bronchitis.

To achieve a high level of participation, it was important for the person coordinating the study in each county to have a good network of contacts at health centres.

One weakness of the studies is that there was no control over how many patients with infection symptoms that were not registered. Furthermore, manual measurements are resource-intensive. However, the fact that the studies were limited to one week probably contributed to the participating physicians perceiving this as reasonable. The protocol for the study may well be used for a few weeks at a health centre as a basis for local quality work.

However, to save resources and obtain more reliable data, systems are required that support data searches in medical records and continuous data supply without any intermediate manual handling, as is for example the case in PRIS (4.3). In such

systems, it is however difficult to extract equally detailed information about data not registered systematically in the medical records.

More examples of important studies are found in appendix 1.

4.3 PRIS – register for management of infections in primary care

PRIS (Primary care Register of Infections in Sweden) is a register for documenting how infections are dealt with and treated in primary care. The register is based on data automatically retrieved from patients' medical records and includes diagnosis-linked prescribing data.

PRIS makes it possible, for example, to obtain answers about how great a proportion of acute bronchitis is treated with antibiotics at a health centre in a year, which antibiotic preparations have been prescribed for various diagnoses and how rapid tests for streptococci and C-reactive protein (CRP) are used. Since 2007, approximately 60 health centres from different parts of Sweden, about 50 percent from Stockholm, with around 600,000 listed inhabitants, have contributed data to PRIS each year.

Implementation

The lack of diagnosis-linked data in pharmacy sales statistics (section 4.1) and the experience from the manual and resource-intensive diagnosis-prescription studies (section 4.2) highlighted the need for methods to automatically extract data from medical records. In 2006, the Primary Care R&D unit in Jönköping and Strama therefore developed the register PRIS. At present, participation is open to all health centres that have "RAVE", a specific search engine, connected to their medical records systems.

In January each year, health centres are invited to submit data to PRIS from all visits with infection diagnoses during the previous year. In addition, all visits without an infection diagnosis where there is an antibiotic prescription are retrieved. From these visits, information is collected on the date of visit, encrypted personal identity number, patient age and sex, any laboratory tests (Strep A, CRP and culture) as well as prescribed antibiotics (with ATC code). The health centre also submits information on the total number of visits to physicians and the number of listed patients.

There is no charge for the health centres' participation in PRIS, and data searches are performed automatically. The health centre or the County Council does however have a subscription cost for the RAVE search engine, which is owned by a company. The operation of PRIS is currently financed by Jönköping's Primary Care R&D unit and the Public Health Agency of Sweden.

Analysis and communication

It takes about three months to process data from the health centres and this is handled by a nurse at the Primary Care R&D unit in Jönköping with the support of a physician who sets aside a few weeks' working hours.

If multiple conditions are diagnosed during a visit, the most critical indication for antibiotics is selected according to guidelines. Over the years, PRIS has been developed to improve access to the information. When new procedures have been introduced, data from previous years has also been supplemented.

Each participating unit receives a report showing how various infections have been dealt with at that particular health centre compared with other health centres and with national treatment recommendations. In addition, all the data from the health centres is compiled and analysed in comparison with data from the previous year. Pooled data from PRIS has been presented at annual meetings for all Strama employees, in connection with the training initiatives for general practitioners and in the SWEDRES annual report. Via the Strama network website, presentations from PRIS are available to the Strama groups. PRIS data has also been forwarded to the European network ESAC-Net (section 4.10). Compilations for national and international journals are also currently in progress.

Results

In 2011, all infection-related visits to physicians were registered from health centres with a catchment area that includes a total of 680 000 inhabitants. A total of over 1 200 000 health centre visits for infections were registered for 2007–2011.

The results have shown that infections account for approximately 25 percent of all physician visits in primary care. An analysis of the 2010 data shows that antibiotics were prescribed in 44 percent of all infection-related visits. 10 diagnoses accounted for 90 percent of prescribing, of which the top three are cystitis 20 percent, tonsillitis 17 percent and acute otitis media (AOM) 15 percent. Procedures regarding the management of infections vary greatly between the health centres. The results also show that there is good adherence to national recommendations for the treatment of urinary tract infections in women. However, adherence to recommendations for tonsillitis and acute bronchitis is poorer, resulting in over-treatment with antibiotics.

Conclusions and lessons learned

PRIS serves two important purposes. First, general practitioners can receive feedback on how their own health centres deal with infections and adhere to treatment recommendations, which in turn may serve as a basis for discussion and improved procedures. It is important for the individual health centres to receive feedback on their submitted data so that they see the benefits of participation and are able to draw conclusions about their own practices.

Second, the large body of data from the participating health centres provides an overview of how infections are dealt with in primary care in Sweden and of adherence to national recommendations at present and over time. It is also possible to see changes in the prevalence of various diagnoses at visits to physicians, something which may signal that patients have changed behaviour with respect to seeking medical care for these complaints, or changes in the practices of physicians in diagnosing certain

conditions. Data from PRIS can also be used in international comparisons to study the significance of cultural and organisational factors.

In PRIS, it is however difficult to examine in detail how well the management of certain diagnoses follows recommendations as these are based on data that is not registered in the patients' medical records in a structured and searchable manner. This relates, for example, to visual assessments of skin lesions, perforations of eardrums in the case of otitis or complicating, underlying patient factors.

One difficulty with respect to automatically searching data in medical records in Sweden is that different County Councils have different types of medical records systems. Since it is only health centres with RAVE that have so far been able to participate in PRIS, the sample has been geographically limited, with a majority of health centres from the Stockholm area and Västra Götaland. Lately, however, more County Councils have developed other search engines for automatic extraction of data from medical records. In future, therefore, more County Councils will have the opportunity to participate in PRIS. Parallel to this, work is also in progress for health centres with RAVE to automatically have their processed data returned in real time, which will reduce the need for manual work and provide faster feedback.

4.4 PV-quality – tool for improved prescribing in primary care

PV-quality is a register that all health centres in Sweden are free to use for local quality work. PV-quality provides a picture of how infections are dealt with and shows the prescribing of antibiotics for various diagnoses of infection. Besides infectious diseases, PV-quality also includes other diseases not discussed in this section.

Implementation

PV-quality began as a partnership between County Councils in south-eastern Sweden in 2007 and has since 2008, been available to health centres throughout the country.

The Swedish Association of General Practice has developed quality indicators relating to diagnostics and the antibiotic treatment of infections, and it is mainly these that are used as yardsticks in PV-quality.

The infection diagnoses included in PV-quality are:

- Acute exacerbation of chronic obstructive pulmonary disease (COPD)
- Acute bronchitis
- Tonsillitis
- Pneumonia
- Lower urinary tract infection in women >18 years
- Acute otitis in children 1–12 years

For the diagnosis to be studied, a review is made of 10–20 randomly selected medical records per physician/nurse or 50–60 records per health centre. For lower respiratory tract infections, the following is recorded, among other things:

3. Proportion of patients with acute bronchitis receiving antibiotics
4. Proportion of patients with antibiotic-treated pneumonia receiving penicillin V
5. Proportion of patients with pneumonia or exacerbation of chronic bronchitis/ COPD where respiratory rate is registered in the medical record

The level sought in PV-quality is for: 1) under 20 percent; 2) over 70 percent; 3) over 70 percent.

PV-quality is based on selecting a random sample of medical records for a chosen diagnosis, which are reviewed according to a form adapted for each diagnosis. The aggregated results are then entered via the website pvkvalitet.se. The results are shown within 10 seconds and can be directly compared with guidelines or with results from other health centres in the local area or elsewhere in the country. Units can also use them to monitor their own activities over time. For each diagram, written feedback is provided with explanations for a reasonable level, and there are also links to treatment recommendations and other references.

Administering PV-quality does not involve a great workload, and is currently handled by a physician at Jönköping's Primary Care R&D unit. The manual review of medical records does, however, give rise to a certain amount of work for the participating health centres.

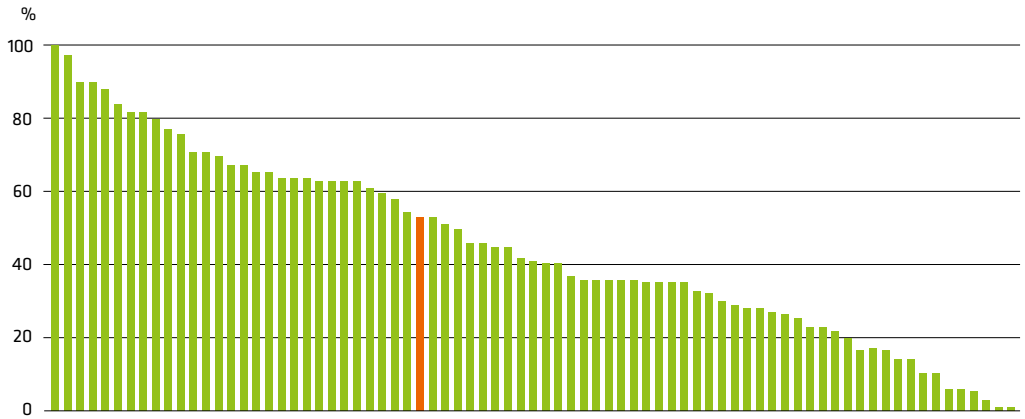
PV-quality is free of charge for health centres, and they need only have access to the internet in order to participate. Operating PV-quality does not constitute a great cost and in recent years it has been financed by the Swedish Association of Local Authorities and Regions. The technological development of PV-quality has been managed by the Swedish company Otimo Data AB.

Results

320 health centres are connected to PV-quality, representing approximately 25 percent of all health centres in Sweden. Their level of activity varies.

PV-quality is primarily intended as a tool for local quality work at a workplace. Output data is anonymous, and the health centres own their data. However, anonymous aggregated data shows that different health centres vary greatly in how they deal with infections. An example is shown in the diagram:

Figure 4.2 The proportion of all patients diagnosed with acute bronchitis and receiving antibiotic treatment varied between the participating health centres. (Each column represents one health centre). Target <20 percent.



A cough occurs naturally during and after most colds caused by a virus. An unaffected patient with a cough, without known COPD, chronic bronchitis or asthma is likely to have acute bronchitis. In these cases, discoloured sputum lacks value as an indicator for infections requiring treatment. Irrespective of whether the acute bronchitis is caused by a virus, mycoplasma or classical bacteria, the patient has no benefit from antibiotic treatment. (Medical Products Agency treatment guidelines 2008).

Conclusions and lessons learned

PV-quality is a tool that provides instant feedback and that is easy to use at a health centre. The results provide a good basis for discussions between colleagues about keeping medical records, dealing with infections and prescribing antibiotics. They can thus provide a basis for improvement.

The database for PV-quality has been easily constructed and does not require access to electronic medical records, but is equally suitable for paper records. However, established quality indicators are needed that can serve as a gauge of good quality.

Reviews and compilations of data from the medical records are performed manually, which is more resource-intensive when compared, for example, with PRIS and other systems that automatically search data in medical records. A major advantage of reviewing medical records manually is that important information that is often not documented in a structured way becomes available. Among other things, facts that should be a basis for decisions on antibiotics, such as the presence of purulent sputa in exacerbations of COPD, the number of days with earache due to otitis or the presence of certain clinical criteria (Centor criteria) in the case of tonsillitis.

PV-quality is based on a random sample of medical records, which provides an adequate basis for the health centre to evaluate and discuss its results. However, PV-quality is not intended to provide thorough systematic comparisons between health centres. It has therefore been important to spell out that the health centres own their data and that this will not be used for public evaluations. PV-quality is thus not intended to provide a comprehensive picture of how infections are dealt with in primary care.

4.5 National point prevalence measurements of antibiotic use in hospitals

Between 2003 and 2010, Strama conducted five national point prevalence measurements of antibiotic use in hospitals in Sweden in order to increase knowledge about indications and prescribing patterns.

Implementation

The reason behind the studies was that there was no national diagnosis-linked data on prescribing practices in Swedish inpatient care, something which was needed to be able to evaluate therapy patterns. The first national measurement was conducted in 2003 and was then repeated in 2004, 2006, 2008 and 2010. The protocol for the measurements was prepared by Strama together with a reference group and was based on the experiences from local studies (see the protocol in annex 1). For the reporting of data, a web-based reporting system was developed by a Finnish company, Neotide Oy.

Participation was offered to all Swedish hospitals through the local Strama groups. Involvement was voluntary, and the participants were free to themselves allocate resources in terms of working hours.

Antibiotic use was registered for all patients admitted at the participating hospitals. Data collection was performed during the course of one day. The measurements were in progress for a period of two weeks in November and the data was registered by an infectious disease specialist, often with links to the local Strama group. At one participating clinic, all patients prescribed antibiotics at 8 am on the day in question were included. The patients' medical records were reviewed, among other things with respect to the patient's age and sex, choice of preparation, quantity of antibiotics/anti-fungals, indication and whether a relevant culture was taken. Treatments were registered in relation to nineteen predefined diagnosis groups and were categorised with respect to whether it was a prophylactic measure or treatment for a community-acquired or healthcare-associated infection. The registration was estimated to take between three and five minutes per patient. In addition, the total number of admitted patients was recorded (even those who did not receive antibiotics), which was used as denominator data. The registering infectious disease specialists entered their results into the web-based reporting system.

Data from all hospitals was quality-assured and analysed by a national steering group. Antimicrobials were classified according to the WHO's ATC system. Defined daily doses were calculated according to WHO definitions based on the quantity of antibiotics in grams prescribed per day. Defined daily doses were not calculated for children under 18. Prescribed daily doses, PDD, could also be calculated.

Analysis and communication

The national steering group compiled the results in the form of presentations that the participants received for discussion purposes, in a training context and for comparison with each other. Furthermore, the participating Strama groups and hospitals were themselves able to immediately obtain their own and national results through a searchable report generator.

The results of the first survey indicated a need for special training in order to improve antibiotic use in accordance with treatment recommendations. Prophylactics in connection with operations included far too many doses, and the use of quinolones was too high for women with lower urinary tract infections. Furthermore, intravenous broad-spectrum preparations were dominant in the treatment of community-acquired pneumonia despite national guidelines from the Swedish Society of Infectious Diseases specifying penicillin G and V as first choices.

Prior to new measurements, information leaflets were also sent out to all physicians at hospitals with an overview of the previous results calling attention to the need for changes in prescribing practices within the identified areas. The results from the studies were also highlighted in the media and raised at national and international conferences as well as in the Swedish annual report SWEDRES.

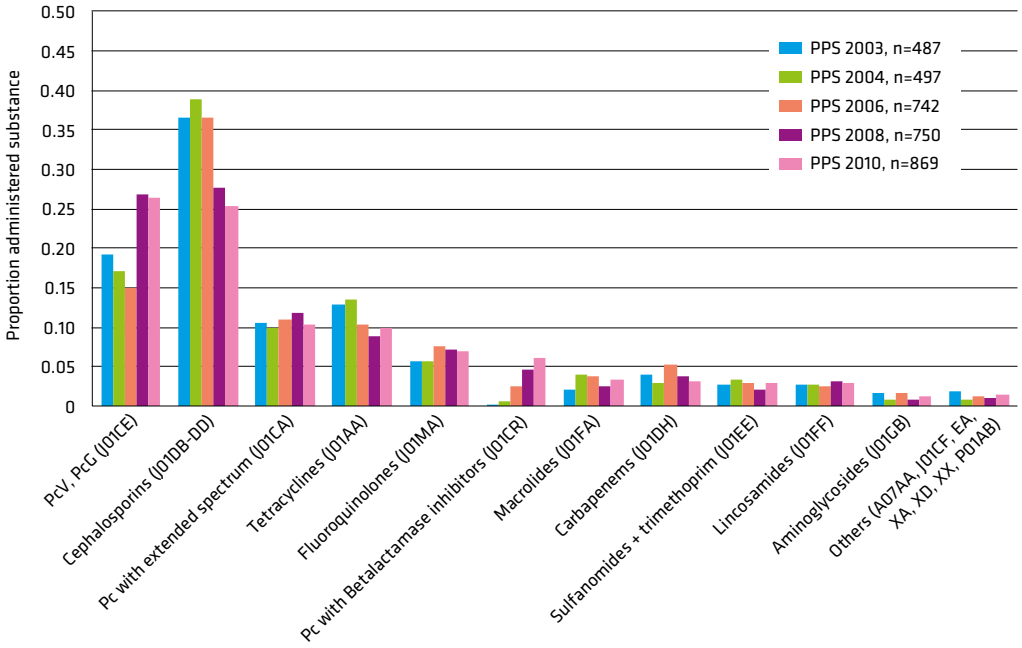
Results

Participation in the nationwide point prevalence surveys was high. The measurements included just over 13 500, 11 300, 17 100, 16 300 and 17 600 admitted patients, representing 50–80 percent of all hospitalised patients in Sweden on one day. The results showed, among other things, that about a third of all hospitalised patients received antibiotics.

During the study period, there was an improvement in adherence to the recommendations for cystitis in women. The proportion of the recommended first-choice preparations nitrofurantoin and pivmecillinam increased, while the proportion of quinolones decreased. The same trend was also seen in outpatient care in other studies.

The treatment for community-acquired pneumonia also improved through a shift from cephalosporins to an increased use of narrow-spectrum penicillins, see figure 4.3. The use of cephalosporins, however, remained too high according to national recommendations. Approximately 35 percent of all treatment consisted of PcV, PcG and amoxicillin (J01CA) in the latest measurement. The duration of the prophylactic use of antibiotics in connection with operations continued to include far too many doses throughout the study period, although there were improvements.

Figure 4.3 Proportions of antibiotics for treatment of community acquired pneumonia in adults. Antimycotics and drugs for tuberculosis excluded. Source Strama:s PPS 2003–2010



For community acquired pneumonia in adults a continuous shift from cephalosporins to narrow spectrum penicillins was seen. At the same time there was an increase in the group J01CR (mainly piperacillin with tazobactam). Around 35 percent of all treatments were PcV, PcG and amoxicillin (J01CA) in the latest measurement.

Conclusions and lessons learned

The point prevalence measurements were successfully carried out five times, and participation was high, despite the fact that they were resource-intensive. The results yielded requested and valuable information on the proportion of patients treated with antibiotics in Swedish hospitals and diagnosis-linked data on antimicrobial use. They also provided insight into the need for training and information efforts.

It is likely that training conducted by Strama groups and pharmaceutical committees over these years contributed to improved antibiotic use for cystitis in women and for community-acquired pneumonia. However, the results showed that there is still room for improvement.

Healthcare-associated infection was included as a cause of antibiotic treatment. These were thus the first nationally comprehensive measurements that could provide a gauge of the prevalence of admitted patients treated for healthcare-associated infection. These results have been verified through the Swedish Association of Local Authorities and Regions in subsequent targeted point prevalence measurements of healthcare-associated infections.

One success factor in the measurements was that many employees at the County Councils contributed with the registration of data, something which greatly facilitated

collection compared with everything being handled centrally. Furthermore, the review of medical records gave the Strama members direct contact with ward personnel and an insight into various other problems associated with antibiotics. However, as mentioned above, the method is resource-intensive and time-consuming and also does not provide as rapid feedback as would be desirable. Various initiatives have therefore been undertaken to develop IT systems that automatically register data on antibiotic use and healthcare-associated infections in hospitals in real time (sections 4.6 SAI and 4.7 The Anti-Infection Tool).

The protocol from the Swedish PPS study has also been used by the European network ESAC-Net (European Surveillance of Antimicrobial Consumption) with participating hospitals in Europe (section 4.10). ESAC-Net has subsequently developed its own more comprehensive study protocol that is currently used in Europe.

Protocols for the Swedish point prevalence measurements are found in annex 1.

4.6 SAI – Local IT system for continuous registration of healthcare-associated infections and antibiotic prescriptions

SAI (Sjukvårdens Antibiotika och Infektionsuppföljningssystem - Healthcare Antibiotics and Infection Tracking System) is an IT-based tool for the real-time tracking of healthcare-associated infections and diagnosis-related antibiotic prescriptions. This in turn makes it possible to provide rapid feedback on adherence to guidelines on antibiotic treatment. The system has been in use at Södra Älvsborg Hospital in Borås and Skene since 2008, and during that time, the hospital's use of antibiotics has improved considerably.

The Anti-Infection Tool is a similar IT-based tool that is planned to be introduced in the whole of Sweden (section 4.7).

Implementation

SAI is a Finnish system developed by the company Neotide Oy. Södra Älvsborg Hospital has integrated SAI with the pharmaceutical module in Melior, the medical records system used at the hospital.

When physicians at the hospital prescribe antibiotics in group J01 (according to WHO's classification system ATC), they must answer two compulsory questions displayed in a pop-up window on the screen.

1. Does the treatment concern a community-associated infection, healthcare-associated infection or prophylaxis?
2. What is the treatment cause? Here, the physician may make a selection from a dropdown menu containing a number of predefined indication areas.

Registration by physicians normally takes 10–15 seconds, and follow-up has shown that they consider the registration meaningful, easy to perform and not too time-consuming. The information is stored in a database and is immediately available for

processing in Microsoft Excel. In addition, information can be retrieved from other IT systems at the hospital, such as positive culture results from the microbiological laboratory, thus reducing the need for duplicate documentation. The system is adapted to generate reports easily and these can also be created as templates for repeated use.

A project group with experts in infectious diseases, infection control, microbiology and IT worked to implement the system at South Älvsborg Hospital. Initially, several information activities were conducted for both hospital management and physicians in order to promote understanding and acceptance with respect to registration. A contact physician was appointed from each unit and given the task of feeding back data to their respective units. Guidelines for antibiotic treatment had also been developed and presented in training sessions for the physicians. Among other things, the guidelines advocated a reduction in the use of cephalosporins.

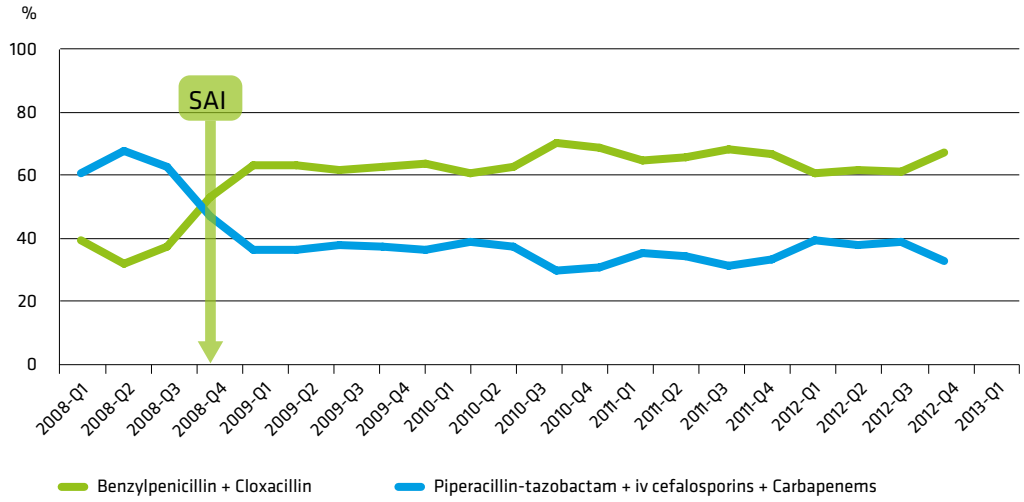
Analysis and communication

Hospital staff specialised in infectious diseases and infection control have set aside time to work continuously on analysing and communicating statistics from SAI. Furthermore, the organisation with contact physicians ensures that data is fed back to the units. Reports are published monthly and are fed back at clinic and hospital level through meetings, e-mails and on the hospital intranet. In addition to this, reports are produced examining specific processes at the hospital in order to improve quality, such as the management of pneumonia and sepsis.

Results

SAI registers almost all antibiotic prescriptions, although a small percentage may be lost for technical reasons. Since the system's introduction, there has been a drastic reduction in cephalosporins in accordance with the local guidelines. In 2008, the proportion of intravenous cephalosporins constituted 15 percent of all defined daily doses at the hospital. In 2013, this proportion decreased to 1 percent. During the same period, the proportion of benzylpenicillin increased from 9 percent to 17 percent. There has also been an increased use of piperacillin-tazobactam, which in the local guidelines is a recommended alternative to cephalosporins in the treatment of serious infections. Since 2008, the incidence of reported healthcare-associated infections has also decreased from 5.6 to 4.0 per 100 hospitalisations. The focus of prevention has been on healthcare-associated urinary tract infections, which have dropped by about 30 percent.

Figure 4.4 Proportion of two different groups of intravenous antibiotics compared to each other in relation to time of implementation of SAI



In 2008 SAI was implemented at Södra Älvsborgs hospital together with updated treatment guidelines. The shift from antibiotics with more broad spectrum to those of more narrow spectrum was obvious and large and has maintained over time.

There is still a need to increase adherence to guidelines, such as those regarding the total use of antibiotics.

Conclusions and lessons learned

SAI generates continuous statistical information on the use of antibiotics in a hospital. As antibiotic prescribing can be related to diagnosis, improper use can be detected and the need for information efforts identified. SAI is also a valuable tool for monitoring the incidence of healthcare-associated infections, which is necessary in order to gauge the effect of measures taken against such infections. It is thus a powerful tool to systematically promote the rational use of antibiotics and improve patient safety.

To ensure that data is used, it has been crucial that people be appointed with working hours set aside for SAI. Also significant is the support of hospital management and the fact that the work with healthcare-associated infections and antibiotics has been integrated into the general organisation at the hospital.

In order to gain a high reporting frequency, it has been important for registration to be compulsory when a physician prescribes antibiotics. As registration is quick and easy, it has not been perceived as burdensome. The significant changes in prescribing patterns may be due to the fact that registration itself raises awareness and reminds prescribers of the importance of choosing the correct treatment in line with current recommendations the very moment they issue a prescription.

A weakness in SAI might be that a the number of diagnoses is limited to the most common and, from Strama's perspective, most relevant, as registration was designed to be brief and not too time-consuming for physicians to manage. This explains why some clinics often have to register "other infection".

The main goal has been for SAI to be a means towards systematic improvement work. However, it is not a tool for generating scientific data or for comprehensive registration.

4.7 The Anti-Infection Tool – national IT system for continuous registration of healthcare-associated infections and antibiotic prescriptions

The Anti-Infection Tool is a national IT system for the registration and feedback of information on healthcare-associated infections and antibiotic prescriptions. The Anti-Infection Tool is based on the same basic principle as SAI, whereby registration is performed in conjunction with the physician's prescribing of antibiotics in a medical records system (section 4.6). However, the Anti-Infection Tool has undergone further development with respect to searching patient data and microbiological data, which is done automatically and continuously for all admitted patients, including those not prescribed antibiotics. This reduces the need for supplementary manual searches compared with SAI and generates continuous denominator data so that it is, for example, possible to calculate the proportion of healthcare-associated infections or antibiotic prescriptions among all admitted patients.

All healthcare providers may introduce the Anti-Infection Tool since it can be integrated with various types of medical records systems and other IT systems. The purpose is for the Anti-Infection Tool to be used in the local work to reduce healthcare-associated infections and improve antibiotic use. The positive experience from SAI shows what potential there is in a similar tool.

Two pilot projects have been implemented at a few clinics in Region Västra Götaland and Uppsala County Council. In 2013, pilot activities were initiated in all County Councils. The goal is for all County Councils to have introduced the Anti-Infection Tool throughout inpatient care in 2014. Below follows a description of the Anti-Infection Tool along with experiences from the pilot project in Region Västra Götaland.

Implementation

The Anti-Infection Tool was initiated by the Swedish Association of Local Authorities and Regions and is based on a specific initiative for patient safety that seeks, among other things, to reduce the number of healthcare-associated infections. The decision to introduce the Anti-Infection Tool in Sweden was made in 2010 by the directors of the County Councils. The national part of the project has been run and financed by the Center for eHealth in Sweden (CeHis), working on behalf of the County Councils. The individual County Councils are responsible for adapting the transfer of information to the Anti-Infection Tool from the local IT systems and also finance the local connection.

The Anti-Infection Tool consists of a national data warehouse that collects information from healthcare providers. A healthcare provider connecting to the Anti-Infection

Tool must meet certain requirements in order to be able to search and deliver defined information to the national data warehouse. The information gathered is standardised and is based on a unified national terminology. Reports can then easily be produced by authorised persons at the respective healthcare unit by means of a web-based report generator.

The Anti-Infection Tool is linked to healthcare providers' electronic medical record systems. Registration in the Anti-Infection Tool is compulsory and takes place in a medical records system when the physician prescribes antibiotics. The physician states whether the reason for the prescription is a community-acquired infection, healthcare-associated infection or prophylaxis. A healthcare-associated infection is further categorised as urinary tract infection, pneumonia, sepsis, postoperative wound infection, infection with *C. difficile* or "other healthcare-associated infection". There is also the opportunity for healthcare providers introducing the Anti-Infection Tool to add prescription causes in the case of community-acquired infections, but this is not a requirement. It takes about 10–15 seconds for the physician to answer these questions by clicking on defined response options.

A healthcare provider connecting to the Anti-Infection Tool must also meet requirements of being able to automatically search data on all patients' identity, when and where they received treatment, diagnosis codes, medical measures, certain risk factors for healthcare-associated infections, and laboratory tests. The source of this information may vary between healthcare providers depending on the local medical record systems, laboratory systems and systems for administrative data that they use. The main point is that the information is supplied to the national data warehouse in a predetermined manner via standardised messages. Experience from the two pilot projects shows that it has been technically challenging to ensure that this information is automatically transferrable from the local IT systems to the national data warehouse.

The Anti-Infection Tool also includes additional features such as detection of certain healthcare-associated infections that are not prescribed antibiotics. For example, the national data warehouse automatically considers the laboratory detection of *C. difficile* to be a healthcare-associated infection. Similarly, a healthcare-associated infection is automatically registered for certain categories of diagnoses, such as for postoperative wound infection, regardless of whether the infection is treated with antibiotics.

The Anti-Infection Tool is part of the four-year patient safety initiative that the Swedish government launched in 2010 through an agreement with the Swedish Association of Local Authorities and Regions (chapter 1). The County Councils can receive allocated stimulus funds if they take significant steps towards introducing the Anti-Infection Tool in hospitals, provided they also meet certain other requirements. In the long term, it will be possible to expand the information searched via standardised messages to the Anti-Infection Tool. Primary care centres will also have the opportunity to connect.

Conclusions and lessons learned

Both the incidence of healthcare-associated infections and resistant bacteria pose a threat to patient safety in healthcare. The Anti-Infection Tool gives healthcare providers throughout Sweden enhanced capacity to reduce the number of healthcare-associated infections and to follow up and optimise the use of antibiotics. The Anti-Infection Tool makes it possible to continuously set improvement targets and to evaluate the degree to which these are attained.

The experience from pilot projects at two surgical units at Sahlgrenska University Hospital in Region Västra Götaland has been positive. Physicians consider the registration in conjunction with antibiotic prescription to be performed simply without interfering with their regular duties. It is also easy to use the report generator to produce reports tailored to different purposes.

Surveys have shown that the registered indications for prescription are sufficiently reliable for use in the local improvement work. However, shortcomings have emerged in the quality of the reported information, partly due to registration errors by users (physicians). Since it is easy to use the registration module, there is a risk of inadequate familiarity with the case in question when choosing – for example, that an infection is to be categorised as healthcare-associated. For this reason, it is important to continuously validate the quality of registered data and to train physicians in proper registration in order to improve the quality. As there is a potential for varying interpretations in the registration procedure, data from the Anti-Infection Tool is primarily suitable as a tool for local improvement. There may well be major differences in registration practices between different hospitals and County Councils, which might also make comparisons precarious.

It has been important that both IT experts and end-users from the clinics have participated together in the work of introducing the Anti-Infection Tool so as to ensure that the content provided is accurate and relevant.

One conclusion from the pilot project in Region Västra Götaland is that the Anti-Infection Tool will be able to serve as a powerful tool for local improvement work. However, it is still too early to report the effects of having used data from the Anti-Infection Tool within the different units.

4.8 Surveillance of consumption and resistance in intensive care units

The problem of resistance is particularly evident in intensive care units, where critically ill patients receive care. Many of these patients have impaired immune systems and are thus at greater risk of becoming infected or colonised with resistant bacteria. Complicated infections are common, something which contributes to a high use of broad-acting antibiotics that drive resistance.

ICU Strama – a group focusing specifically on intensive care – was formed in 2000 (Chapter 2). Its goal is to systematically register and analyse the problem of infection in intensive care units. The purpose is for this data to be used as a tool to reduce healthcare-associated infections at ICUs, optimise antibiotic use and reduce the emergence and spread of antibiotic-resistant bacteria.

Implementation

The collection of data has evolved over the years. Initially, ICU Strama compiled aggregated consumption and resistance data from intensive care units based on information from Apotekens Service AB/ the Swedish eHealth Agency (section 4.1) and on data submitted from microbiology laboratories. Hospitals were asked to provide supplementary information regarding patient days to get a clearer picture of how many patients there are at different ICUs. Consumption data was thus stated in DDD/1,000 patient days. A survey was also conducted of basic infection control procedures at the intensive care units.

The initiation of ICU Strama's collaboration with the Swedish Intensive Care Registry (SIR) in 2005 meant that it gained access to information on individual patients (data based on personal identity number) with respect to diagnoses, care periods and complications (CVC infections, ventilator-associated pneumonia (VAP), discovery of multi-resistant bacteria and diarrhoea caused by C. difficile). Especially valuable is the ability to obtain patient-based information on mortality, which is registered weekly for all patients. SIR is a quality register which comprises approximately 95 percent of all general intensive care units in Sweden. The register aims to monitor and raise the quality of Swedish intensive care in selected areas.

One limitation, however, is that it has not been possible to link microbiological findings to patients' diagnoses. To study, among other things, complications and mortality from infections linked to discoveries of various pathogens, ICU Strama developed a pilot version of a database in which microbiological data based on personal identity number can be linked to individual hospitalisations. This project is being further developed with SIR, building up a database that will be able to collect such information from all laboratories. The database will be based on a nomenclature and structure that is harmonised with the Public Health Agency of Sweden's surveillance system Svebar in order to reduce the workload for the laboratories (section 3.4 on Svebar).

Results

When ICU Strama initially compiled aggregated consumption and resistance data from intensive care units, it presented the results to intensive care physicians at regional and local meetings. The results aroused interest since there had previously been inadequate knowledge at many intensive care units regarding resistance conditions. It was seen that antibiotic consumption varied greatly between different units. Via a web application, the intensive care units were able to compare their consumption and their resistance conditions over time. A commitment evolved to use data for local quality work, and local ICU Strama groups were formed.

In 2008, there was also a combined intervention at 12 intensive care units based on a method of the type »push« and »pull«. This consisted, among other things, of visits to ICUs with lectures and discussions (»push«) and a follow-up activity with questionnaires (»pull«). The intervention showed promising results with the introduction of better diagnostic methods and an impression of increased motivation among employees following a visit.

A major compilation of antibiotic use in intensive care units between 1999 and 2009 showed that the use of cephalosporins decreased, while the use of piperacillin-tazobactam increased, a welcome development in line with Strama's messages to counteract the development of ESBL. At the same time, however, use of carbapenems also increased, which is less desirable as carbapenem-resistant Gram-negative bacteria are also on the increase in Sweden.

Data from Swedish intensive care units has also been presented at European meetings organised by ESCMID (European Society of Clinical Microbiology and Infectious Diseases) and *is* also used as a basis for the work to validate Swedish treatment recommendations for pneumonias requiring intensive care.

Mortality from sepsis caused by various pathogens has also been studied using the pilot database, whereby microbiological findings from laboratories are linked to patient hospitalisations. 1416 patients were included in the analysis, and the outcome was 30-day mortality calculated from admission to the intensive care unit. The highest mortality rate (> 30 percent) was seen in patients with sepsis caused by *S. aureus and Candida spp*. The results point to the importance of correlating mortality to causative pathogens in the analysis of risk factors for sepsis mortality in intensive care units.

ICU Strama is now also working on developing a system to integrate digital antibiotic prescriptions in SIR-micro, meaning that it will be easy to map the precision of antibiotic treatment and to counteract incorrect antibiotic choice, dosage and treatment duration.

Examples of studies are found in appendix 1. See also section Conducting studies in chapter 2.

Conclusions and lessons learned

The initial basic compilations of aggregated consumption and resistance data provided valuable information on antibiotic pressure in intensive care units as well as knowledge of resistance conditions that has been useful both nationally and internationally. This approach has also formed the model for a similar European project (CARE-ICU), which was a sub-project in IPSE (Improved Patient Safety in Europe) financed by DG-SANCO (43) and an ongoing Sida-funded intensive care project at 16 hospitals in Vietnam (44).

Together with SIR, ICU Strama has created an opportunity to analyse risk factors for mortality due to sepsis, pneumonia and postoperative infections. The system also

facilitates analysis of the disease burden of antibiotic resistance in intensive care and is able to identify improvement needs and propose interventions.

Examples of studies are found in appendix 1, see also chapter 2, section on Conducting studies.

4.9 Indicators to detect the under-prescribing of antibiotics

Since the mid-1990s, the use of antibiotics has decreased significantly in Sweden, and considerable work over the years has also been devoted to the reduction of over-prescribing. However, it is also important to ensure that a reduction in use does not lead to increased complications as a result of under-prescribing. For this reason, searches have been performed in a national inpatient register in order to study the incidence of complications that could indicate the omission of antibiotic treatment.

The national inpatient register is maintained by the National Board of Health and Welfare and includes all patients discharged from hospital. The register has had full national coverage since 1987 and currently registers more than 99 percent of all discharges from somatic and psychiatric care. One of the variables is personal identity number, which makes it possible to link a patient to each hospitalisation and to main and secondary diagnoses based on the WHO classification system ICD.

Strama conducted a major search of the register for patients in different age groups with acute sinusitis, peritonsillar abscess and acute mastoiditis for the years 1987–2003. The purpose was to see if hospital admissions for these diagnoses had increased, which might indicate the undertreatment of respiratory tract infections. However, the results showed that the number of children who were hospitalised with these diagnoses was stable or decreased during the period.

In addition to searches in the inpatient register, a more in-depth national study has also investigated the incidence of mastoiditis between 1993 and 2007 through a retrospective review of medical records. The purpose of the study was partly to map whether the publication of more restrictive treatment recommendations in 2000 might have increased the risk of children developing mastoiditis. All medical records with cases of mastoiditis were reviewed. A comparison was made of children suffering from acute mastoiditis 7.5 years prior to the publication of the recommendations with children diagnosed 7.5 years after publication. The results showed no statistical difference in the frequency of acute mastoiditis, antibiotic prescribing before acute mastoiditis, complications or number of mastoidectomies (46).

In 2012, SMI conducted a review of the number of cases of retropharyngeal abscesses in the national inpatient register (2001–2011) in conjunction with an update of the national treatment recommendations for pharyngotonsillitis in outpatient care. Retropharyngeal abscesses are a rare complication that primarily affects adults. The review showed an increase in the number of cases per 100,000 inhabitants (total number of cases 94 in 2001 and 172 in 2011). This increase was observed in all age

groups except among children 0–4 years old and among those older than 80, where a decrease was seen. It is not possible to comment on the cause of the recorded increase without studying the cases more closely. One hypothesis is that an increase in the number of patients with diabetes and poor dental status might play a role as these conditions are risk factors for retropharyngeal abscess.

The national inpatient register is a valuable tool for studying the incidence of various diagnoses over time since it is a comprehensive register and since reporting from inpatient care has been conducted over many years. However, a covariance between a reduction in antibiotic consumption and an increased incidence of registered complications may be difficult to interpret as this could be due to undertreatment, but also to other factors such as epidemiological changes (e.g. modified virulence among pathogenic bacterial strains) or altered procedures for diagnosis and dealing with infection. For this reason, a time series analysis comparing the incidence of a number of diagnoses with consumption data may primarily serve as a means to signal the need for further analysis.

Nevertheless, the major review of medical records and the searches carried out in the inpatient register can provide valuable insights, and the Public Health Agency of Sweden has thus begun work to develop improved methods to systematically detect and analyse signs of under-prescribing at the national level. In addition, more targeted case-control studies may be needed in order to identify factors underlying potential increases in complications due to the undertreatment of prior primary infection.

The Public Health Agency of Sweden aims to create a national electronic system, to be able to continuously monitor the incidence of unusual but serious infections and to study the use of antibiotics for infections in primary care and its effect on incidence of serious infections. The new model would make it possible to link the registers for open- and hospital care and thereby be able to follow the patients through the care system. The model could also give access to continuous data instead of the yearly compilations that are presently available.

4.10 ESAC-Net – European surveillance of antibiotic consumption

ESAC, and subsequently ESAC-Net (European Surveillance of Antimicrobial Consumption Network), is a European project that has run since 2001 to collect data and compare the consumption of antibiotics, anti-fungals and antivirals between countries. 27 EU countries are participating as well as Iceland and Norway. This section deals only with data on antibiotic consumption.

Implementation

ESAC-Net (formerly ESAC) was initially coordinated by the University of Antwerp. In 2011, the European Centre for Disease Prevention and Control (ECDC) assumed responsibility for this work. Each country organises its own network of experts responsible for collecting data.

Over the years, the work has focused on improving and quality assuring data since different countries have different methods for data collection. Sweden contributes antibiotics statistics based on data on the sales of all antibiotics from pharmacies (section 4.1), that is, total data. In some countries, the statistics are not comprehensive and may instead be based on the sales of pharmaceutical companies, while others report statistics in relation to insurance and high-cost protection.

In the early years, reports from the countries were submitted to the University of Antwerpassociation using Excel spreadsheets in a standardised format. Today, the participating countries annually report statistics to ESAC-Net via a web-based database where they can upload their own data. The Public Health Agency of Sweden is responsible for Sweden's reporting. To facilitate comparison, all countries must submit their reports according to a standardised protocol, which entails a certain amount of work to adapt the data being supplied. Among the information registered are preparations stated as DDD per 1,000 inhabitants and number of packages per 1,000 inhabitants. Antibiotic consumption gauged using these measurements are analysed and compared between the countries. The registration of both of these measurements provides a possibility to calculate average DDD/package. Among other things, this may indicate varying traditions of treatment duration for different preparations in different countries. The reported pharmaceuticals are categorised according to the WHO classification system ATC.

A number of in-depth studies and sub-projects have also been initiated over the years in order to gain access to more detailed data. More examples of studies is found in appendix 1.

Within ESAC, point prevalence measurements have also been conducted at hospitals and homes for the elderly. The first measurement of antibiotic use in hospitals was conducted in 2008 and was based on Strama's PPS protocol and web-based data tools (section 4.5). Data was collected primarily to answer the following questions: What different trends exist in antibiotic consumption in Europe? What is the effect of using different denominator data (patient days or care occasions)? What is the relationship between DDD and PDD (prescribed DD) in a hospital? In 2012, a further point prevalence measurement was carried out at hospitals in Europe. This measurement studied both antibiotic prescriptions and healthcare-associated infections.

In 2009, a PPS was conducted in which antibiotic consumption was for the first time measured in special care homes in 21 European countries using a common protocol developed in collaboration with participating countries. The protocol was based on Strama's protocols for the diagnosis-prescription study in outpatient care, the week 47 study (section 4.2). The project has been further developed into a PPS that also includes a survey of healthcare-associated infections. This survey was carried out in 2010 and 2013.

Results

The results from the annual surveillance are made available on the ESAC-Net website in the form of annual reports and presentations. In an interactive database, the participating countries can also perform searches in their own data. The results show that use varies greatly between different countries in Europe, both with respect to total consumption and to the selection of narrow-spectrum and broad-spectrum preparations. The lowest consumption in human medicine is seen in the Netherlands and the Scandinavian countries, while a higher consumption is seen in, for example, southern European countries. The use of narrow spectrum-antibiotics that cause less resistance varies greatly, with Sweden being one of the countries with the highest proportion of narrow-spectrum antibiotics, using more than 20 times as much as some other countries. Surveillance of resistance within the European network EARS-Net (European Antimicrobial Resistance Surveillance Network, see section 3.2) also shows that the Scandinavian countries generally have a lower incidence of resistance compared with countries in southern Europe.

Conclusions and lessons learned

Through compilations of antibiotic use in ESAC-Net, participating countries have been able to view their own data in relation to other countries and gain an overview of the type and quantity of antibiotics used. However, comparisons of consumption data must be interpreted with a certain degree of caution as the methods for data collection vary among the reporting countries. Along with resistance data from EARS-Net, a picture is given of the development of resistance and consumption of antibiotics in Europe.

Each year, representatives from the participating countries meet to discuss results, methods for measuring and reporting antibiotic consumption, strengths and weaknesses of the data and to share experiences. There have also been opportunities within the network to pursue advanced studies and projects.

An integrated effort in Europe highlights the issue and creates commitment in many countries. Joint work and standardised methods of reporting consumption are important in order to be able to compare antibiotic consumption between countries and over time.

4.11 Local example of the feedback of individual prescribing data in outpatient care

Västerbotten in north-eastern Sweden is the County Council with the lowest level of antibiotic prescribing in outpatient care. For several years, the Strama group in Västerbotten has conducted typical Strama work, prioritising direct meetings and discussions with physicians at hospital clinics and health centres.

In 2012, Strama Västerbotten initiated an IT solution that facilitates access to each individual physician’s prescribing of antibiotic preparations in outpatient care. This

provides a better statistical basis regarding each practitioner and makes it possible to discuss procedures at the health centres; for example, how it can be that prescribing varies among colleagues, whether this may be related to treating different groups of patients, or due to other factors.

Since 2013, all outpatient units are also requested to analyse their own prescriber data twice a year and report back to Strama Västerbotten and the County Council management. Units that comply receive some financial compensation from the County Council based on their number of listed patients. Below follows a description of this project, based on an interview with Stephan Stenmark, chairman of Strama and infectious disease specialist in Västerbotten.

Implementation

Antibiotic prescribing differs between County Councils in Sweden. The highest level of prescribing per inhabitant is seen in the more densely populated metropolitan regions. Västerbotten is among the more sparsely populated County Councils and is also the County Council with the lowest prescribing level in outpatient care. In 2012, prescribing in Västerbotten was at a number of 290 prescriptions per 1000 inhabitants and year, while the average for Sweden was 374 prescriptions per 1000 inhabitants and year.

The IT solution initiated by Strama Västerbotten is based on all antibiotic prescriptions being extracted from the pharmaceutical module in the county medical records system (System Cross) to an IT system that is otherwise used for reporting and follow-up (Diver). From there, it is easy to generate reports that show prescribed preparations per county, healthcare unit and individual. However, there is no diagnosis-linked data. In essence, it is the same information that has also been possible to extract from individual prescriber profiles based on data from Apotekens Service AB/ the Swedish eHealth Agency since 2013 (section 4.1). The system in Västerbotten, however, makes it possible to easily produce customised reports to fit particular needs and to illustrate trends over time.

The manager of a healthcare unit is able to view data at the individual and unit level as well as the county's prescribing. The chairman of Strama Västerbotten is able to view data on all prescribing down to the individual level. The report requested twice a year from the units is to include the dates when they fed back prescribing data of the unit and individual physicians and an analysis of volume, trend and distribution of various preparations based on local treatment guidelines. The report should also contain proposed measures.

Results

In 2012, Strama Västerbotten informed all health centres of the reporting procedures. The goal was for all units to perform a regular analysis of their antibiotic prescribing. In 2013, 35 of 38 health centres submitted their first report.

It is still too early to draw conclusions about how the project has influenced prescribing practices. But even in a short time, noticeable changes have been seen. For example, Strama Västerbotten organised meetings with units that had a high prescribing level for doxycycline, after which there was a noticeable decrease in prescribing. Some individual prescribers with a highly divergent prescribing profile have also improved their prescribing after discussions with Strama or their chief medical officer. Other units and prescribers have themselves requested assistance and training from Strama Västerbotten.

Conclusions and lessons learned

Through the IT solution initiated by Strama Västerbotten, every physician in outpatient care is able to easily access information on how he or she prescribes antibiotics compared with other physicians at the unit or compared with other units in the county. One limitation of the IT solution, however, is that it is not possible to generate diagnosis-linked data.

The project for analysis and feedback also aims at the healthcare units themselves taking responsibility for using prescribing data in regular discussions. So far, there has been a high level of participation by the health centres.

Both the organisation and members of Strama Västerbotten are well known among healthcare professionals in the County Council. This familiarity facilitates discussions at health centres and promotes a high rate of participation in the project for reporting prescribing data. The fact that Västerbotten County Council has backed the project and shown an interest in the results has also been of great importance.

Financial compensation to the units that analyse and report their own prescribing data is also of value. In this way, the process of quality improvement is generated within the units themselves. This may in turn lead to improved prescribing.

For Strama Västerbotten, the IT solution has meant that it needs to devote fewer resources to producing local statistics on antibiotic consumption and can instead set aside more time to follow up on the reports from the health centres and to identify those units in most need of support and training.

Interview with Dr Per-Åke Jarnheimer

Per-Åke Jarnheimer is a medical doctor specialised in infectious diseases. He is chair of Strama in the South-Eastern county of Kalmar and responsible for infection control at Kalmar county hospital. As one of the first counties in Sweden, Kalmar has introduced a new computer-based system linking each prescription of antibiotics to a diagnosis and data regarding the patient and prescribing doctor.

"It's too early to evaluate and draw conclusions, but we see a huge potential in this system", says Jarnheimer, who has been active in local Strama since 1996. In his experience, direct feed-back is the key to changing practice on a local and individual level. "Spokespersons for Strama may act as missionaries, telling doctors what to do and why, but in my experience this is not very effective. Presenting data showing actual differences in when and how doctors use antibiotics often generates discussion and positive results."

In his opinion, the potential of feed-back systems such as the one implemented in Kalmar is particularly great among general practitioners. "Most patients in the primary health care system suffer from simple infections and are not as ill as those in need of in-hospital treatment. This allows for standardised protocols on the use of antibiotics", says Jarnheimer. The greatest challenge to quality improvement in Swedish primary health care, as he sees it, is the shortage of general practitioners, with a high turnover among temporary employees brought in to fill the gaps.

Hospital physicians, in comparison, face patients with more serious infections and are often forced to use broad-spectrum antibiotics or combination therapy. Still, Jarnheimer believes that improvements can be made and points to the fact that Sweden, unlike many countries, has specialists in infectious diseases at all major clinics. "Specialists have up to date knowledge on bacterial resistance and therapeutic alternatives and should be used more systematically in early evaluation – for possible alteration or termination of antibiotic treatment." Cutting treatment periods, whenever possible, is a key strategy to reduce the volumes of antibiotics used.

In Kalmar, local Strama consists of three operative individuals. In addition to Per-Åke Jarnheimer, representing hospital physicians, a general practitioner and a pharmacist work part time to improve local routines and guidelines for rational use of antibiotics. Educational outreach, or feed-back in a clinical setting, is an essential component of Strama's strategy. Jarnheimer is convinced that doctors are more likely to listen so someone who knows the ins and outs of clinical practice. Therefore, he deals with issues related to hospital physicians, while his GP counterpart visits health centres for discussions with local GPs.

The new computer systems linking prescription of antibiotics to diagnosis and patient data generate immediate feed-back, allowing doctors to map their clinical practice and compare it to other colleagues. “In the future, we hope to analyse these data to see whether certain groups stand out and are in need of targeted information. Such groups may be young doctors, temporary employees or physicians educated in other countries”, says Jarnheimer.

Strama’s work is facilitated by Sweden’s homogenous health care system and a well-educated public. “Most people know that antibiotics don’t cure viral infections and are aware of increasing resistance.” As an example, Jarnheimer mentions that increasing awareness among parents has reduced prescription of antibiotics for simple infections, such as uncomplicated otitis in children.

“As I see it, Strama functions as a brake on antibiotic resistance. We cannot reverse the development of resistant bacteria, but we can to some degree delay its consequences by reducing the volumes of antibiotics used. We are buying ourselves time, during which improved diagnostic methods and new antibiotics can hopefully be developed”, says Jarnheimer.

Chapter 5. Treatment recommendations

To optimise the prescription of antibiotics, it is important that healthcare personnel have access to information to support their decisions in the form of evidence-based treatment recommendations. For the treatment of infections in outpatient care, national recommendations are published by the Swedish Medical Products Agency (section 5.1). For the management of infections in hospital care, there are national, evidence-based care programmes developed by Infektionsläkarföreningen (the Swedish Society of Infectious Diseases) (section 5.2).

The production of treatment recommendations is a complicated process, on both a national and local level, and the involvement of the profession is important. The compilation of, evidence-based guidelines and treatment recommendations on a national level saves resources and is important to ensure similar administration throughout the country. However, merely establishing national recommendations is not enough – they must also be made known and implemented by the health services. Strama groups and pharmaceutical committees are key players through their systematic work to implement treatment recommendations into the healthcare system (section 5.3 and chapter 2). With national recommendations as the point of departure, local guidelines and memos are often produced and adapted to local requirements, including resistance situations, traditions and information channels.

The Swedish experience is that structured and coordinated work conducted by the profession on a national and local level is essential for healthcare personnel to have access to and knowledge of evidence-based treatment recommendations and follow these to a greater extent.

5.1 Recommendations for the treatment of infections in outpatient care

Since 2001, the Medical Products Agency has been publishing national recommendations for infections in out-patient care. Initially, the focus was on respiratory tract infections where there had been an over-prescription of antibiotics that was brought to attention partly by the work of Strama. Recommendations have subsequently been produced for several other common infection diagnoses in out-patient care, and for dental care.

The recommendations are primarily aimed at general practitioners and dentists, but are also important for physicians working in hospital care with the treatment of many minor infections, primarily in elderly people and in emergency wards. The aim is that the recommendations should provide support in the management of infections in out-patient care. One objective has been to more clearly define when the use of antibiotics is indicated – and when it is not – and to base this on the evidence found in the literature.

Implementation

National recommendations are produced in conjunction with expert meetings organised by the Medical Products Agency and the Public Health Agency of Sweden. The expert meetings were initially organised together with Strama, and then later with the Swedish Institute for Infectious Disease Control (SMI) as well as with 'dental Strama' (a Strama group composed of dentists).

In order to facilitate widespread support for the recommendations, it is essential that experts from various medical specialities participate, who can contribute with their experiences from both out-patient and hospital care. When recommendations for acute otitis media (AOM) were produced, general practitioners, ear, nose and throat physicians, infectious disease specialists, paediatricians, microbiologists and pharmacists took part, among others.

Prior to an expert meeting, the national specialist associations are usually asked for the names of experts with knowledge and experience within the area of infection in question. Inquiries are at the same time made into whether there are any binding obligations or conflicts of interest. The experts must not receive financial compensation from any companies that have an interest in the recommendations drawn up by the expert group.

Prior to an expert meeting, the invited experts are asked to write evidence-based background documents that address the different subjects that the recommendation concerns. The background documents are then sent out to all participants, prior to the expert meeting. Common subjects are:

- Aetiology
- Epidemiology

- Diagnostics (and differential diagnostics)
- Clinical evaluation (symptoms, signs of severe infection, anamneses, status, tests, monitoring)
- Treatment (e.g. painkillers, antibiotics, puncture)
- The effects and safety of antibiotics or other treatment

An expert meeting often goes on for two days. The experts first give a short lecture presenting the conclusions drawn from the various background documents. After this, work is conducted in groups to write various sections of the recommendation, based on the background documents. The statements made in the recommendations are evidence-graded. The discussions conducted during the expert meeting are important to reach consensus in respect of the recommendations, especially when there are no studies available on which to base opinions. It is also important that the formulation of the recommendation is adapted to clinical reality, and to the formulation of questions that physicians and nurses handle in their daily work. After the expert meeting, the recommendation and the background documents are summarised and sent to the participants for comment prior to publication.

The Medical Products Agency and the Public Health Agency of Sweden also have an agreement on the process with regard to the revision of treatment recommendations. The Public Health Agency of Sweden and the Strama Council are to regularly inventory the need for updates, based on the current knowledge situation and in consultation with the Medical Products Agency decide which revisions to prioritise.

The recommendations are communicated both nationally and locally

One challenge is to ensure that recommendations are not just published, but also reach their target groups and are used by the health services. The national recommendations are communicated via several channels, both nationally and locally. Recommendations are promoted via national websites, newsletters and press releases and are often picked up by the media that reach the wider general public. The Medical Products Agency publishes the recommendations in its journal *Information från Läkemedelsverket* [Information from the Medical Products Agency] which is sent to all prescribers. They also inform other relevant national and local actors, such as the pharmaceutical committees and 1177 – a telephone service providing medical information to the general public. Articles are often published in “Läkartidningen”, a journal for physicians in Sweden.

Treatment recommendations for out-patient care have been summarised on pocket-sized plastic cards and in a brochure. The brochure has been sent out to health centres across the country and has also been distributed by the Public Health Agency of Sweden, the Medical Products Agency, Strama groups and other local actors. The brochure presents the overall features of all recommendations and has been asked for by health centres. Concise information sheets that can be handed out to patients by the treating physician have also been designed for several areas of therapy. They provide information about the relevant infection, the treatment that is recommended, whether the patient should come back for a check-up and for which symptoms the patient should re-establish contact with their healthcare provider. The information sheets have been translated to several languages and can be downloaded free of charge from the Public Health Agency of Sweden's website. Most are also available from the respective Strama group's website. If necessary, they can be adjusted to local conditions.

The local work conducted by Strama groups and pharmaceutical committees is central for new recommendations to reach the prescribing physicians. Well-known local spokespersons who have a high degree of credibility are important for the recommendations to have the intended impact. They arrange training courses and also carry on discussions with the prescribers at health centres and clinics. Local (actors)/bodies also work with producing and revising local recommendations, based on national recommendations.

Results

Together with Strama and the Public Health Agency of Sweden, dental Strama and other representatives from the healthcare sector, the Medical Products Agency has produced treatment recommendations for the following infection diagnoses in out-patient care:

- Management of pharyngo-tonsillitis in ambulatory care (2012 revision of the recommendation from 2001).
- Diagnostics, treatment and follow-up of acute otitis media (AOM) (2010 revision of recommendation from 2000).
- Pharmacological treatment of bacterial skin and soft tissue infections (2009).
- Pharmacological treatment of lower respiratory tract infections in outpatient care (2008).
- Lower urinary tract infections (UVI) in women (2007).
- Antibiotics during pregnancy (2006).
- Drug treatment of rhinosinusitis (2005).

In addition to these recommendations, the Public Health Agency of Sweden has during 2013 published data regarding the treatment of urinary tract infections in men. Recommendations that are to be published in the near future include: Antibiotic treatment of odontological infections, Drug treatment of acne, and Managment and treatment of sexually transmitted infections.

The recommendations for infections treated in out-patient care refer in the first instance to the management of patients without severe underlying disease.

To facilitate the new recommendations actually reaching out to every prescriber in every primary health care centre, the numerically most important diagnoses, the one's likely to have the greatest impact on the antibiotic prescription patterns, are summarized in the shorter but more easily distributed brochure "Treatment recommendations for common infections in outpatient care", see more in chapter 2, figure 2.5.

In December 2011, SMI conducted telephone interviews with 100 randomly selected general practitioners in respect of the use and perceived benefit of the treatment recommendations. The interviews showed that several of the physicians interviewed were aware of the treatment recommendations. The majority stated that it was easier to choose the correct treatment and also to refrain from prescribing antibiotics with support from the recommendations.

Conclusions and lessons learned

The production of evidence-based treatment recommendations requires considerable resources; for this reason, it is most efficient to produce them at national level. National recommendations set a standard for when the use of antibiotics is indicated and are important for reaching similar administrations throughout the country. To gain widespread support for the recommendations and for them to have the desired impact, it is important the recommendations are produced with the consensus of experts who represent several medical specialities within both inpatient and outpatient care. Nor must there be any conflict of interest.

The national guidelines form the basis for the local guidelines and have an impact through the local engagement.

The national recommendations should be communicated through many different channels, both nationally and locally. A survey suggests that they are well-known among general practitioners. Training initiatives by well-known local stakeholders such as Strama groups and pharmaceutical committees are of utmost importance for the recommendations to reach the care sector and be implemented.

The treatment recommendations are not mandatory but merely provide support for prescribing physicians. The recommendations can never replace the clinical assessment made in the individual case. It is important, for medical efficiency and resource-optimised healthcare that the recommendations are followed to as large an extent as possible. In order to be able to evaluate compliance, access to diagnosis-linked data is required, for which various IT tools have been developed (chapter 4).

5.2 Examples of a national care programme for Community Acquired Pneumonia in hospital care

In Sweden, a clinical infection speciality with its own, independent clinical structure was developed at an early stage. Antibiotic therapy became a central area and led to a high level of competence that was also backed up by antibiotic research within the speciality. This high level of competence led to an all the more developed role as consultant to other areas concerned with therapy and medical care of infectious diseases. It also became natural to take responsibility for overall therapy recommendations for hospital care and, together with the primary care physicians, also for outpatient care.

The Swedish Society of Infectious Diseases is a nationwide association of, primarily, infectious disease specialists. The association is, with its members, one of the key stakeholders in the national work for rational antibiotic treatment conducted by the work of Strama. The association publishes national, evidence-based care programmes on the management of infections in hospitals. The association appoints programme groups responsible for designing the care programmes. The experts participate on a voluntary basis and are reimbursed by the association for the costs they incur through attending the meetings. The national care programmes include infectious endocarditis, bacterial CNS infections, viral CNS infections, community acquired pneumonia, joint and skeletal infections, urinary tract infections, and severe sepsis and septic shock. These programmes are primarily limited to adult patients. Below follows a description of how the association works with the care programme on how to handle community acquired pneumonia, primarily based on an interview with Jonas Hedlund, infectious disease specialist and chair of the programme group for community acquired pneumonia.

Implementation

The group for community acquired pneumonia consists of nine clinical specialists operating within the field of infectious diseases. The care programme for the management of community acquired pneumonia was first published in 2004 and has since been revised in 2007 and 2011 (47). The guidelines are based on published studies, quality-assessed by the group in terms of relevance and the strength of the evidence they provide.

International guidelines vary a great deal, due to a certain extent to differences in aetiology, epidemiology and resistance status. The Swedish recommendations are therefore adapted to the prevailing epidemiological situation.

The recommendations are a tool for rational treatment with antibiotics

The recommendations adopt an approach where classification is based on the severity of the disease and the expected care need, divided into polyclinical, hospital and intensive care respectively. To help in the assessment of the care level, the prognostic index CURB-65 is recommended. The assessment then also forms the basis for the choice of antibiotic treatment, the scope of the diagnostic measures and other care

measures. There is a clear aim for assessment of probable aetiological agents, to be able to provide optimised antibiotic therapy that is targeted as much as possible with the least potential to induce resistance.

As preventive measures, vaccination of risk groups against influenza and pneumococci is recommended, as is the cessation of smoking.

Phenoxymethyl penicillin, penicillin V, is recommended as the first choice in non-severe community acquired pneumonia in adults. This is in line with the Swedish tradition known as the "penicillin model", which implies that the use of antibiotics with as narrow a spectrum as possible is preferred. Sweden has a favourable level of resistance in pneumococcus and there are good experiences from treating non-severe pneumonia with penicillin V.

Communication and monitoring

Updated care programmes are published on the Association of Infectious Disease Specialists' website, in "Läkartidningen" and in international journals. They are also presented verbally at the association's various meetings.

The association maintains several quality registers where, among other things, the monitoring of the compliance to the care programmes can be studied. Based on the care programme, parameters are registered for all admitted patients with community acquired pneumonia with a coverage of 70 percent.

Compilations show that the variation in compliance with the care programme is considerable between the different infectious disease clinics. These compilations are reported back to the infectious disease clinics and have also been presented at the Association's meetings and on its website. As far as the choice of antibiotics is concerned, there has been an increased usage of narrow spectrum penicillins over the years and a parallel reduction in the use of cephalosporins in the national point prevalence measurements conducted by Strama during the 2000s (section 4.5).

Conclusions and lessons learned

Community acquired pneumonia is a common diagnosis. Around one out of five patients at the infectious disease clinics are treated for this diagnosis. Many with this diagnosis are also treated at other clinics. Evidence-based, rational therapy guidelines for diagnosis are therefore essential. Guidelines must be communicated to other physicians and be easily accessible at the time of prescribing.

Summarising evidence and revising guidelines requires considerable resources, which is why it is important to work systematically and limited to that which is most relevant. The care programme for community acquired pneumonia applies only to the management of adult patients who are not immunosuppressed and who are assessed/treated in hospital.

5.3 Examples of local Strama work with treatment recommendations

Since its formation in 1996, the Strama group in Region Halland has had the task of working towards rational use of antibiotics. Physicians, nurses and the wider public are important groups to reach with information regarding antibiotic resistance and how infectious diseases should be treated. Below follows a description of Strama Halland's work, based on an interview with Mats Erntell, chair of the local Strama group and an infectious disease specialist in the county of Halland.

In 1997, legislation was implemented that required the establishment of pharmaceutical committees in each County Council tasked with working towards a rational use of medical products. In Region Halland, the Strama group has since 1998 been a therapy group within the pharmaceutical committee, with the task of formulating the regional therapy recommendations for infectious diseases in outpatient and hospital care. Through this, Strama Halland has received the mandate and resources to work towards, and to provide training on, rational antibiotic treatment.

Since 2011, the work has been reinforced by the various target formulations of the national patient safety initiative (chapter 1). The group's task has been clarified in the management system and the work has increasingly been directed outwards through the introduction of regular visits to all healthcare providers for dialogue and feedback of antibiotic prescription and resistance data.

Implementation

Region Halland is located in south-west Sweden and has a population of more than 300,000. Strama Halland is made up of the County Medical Officer for communicable diseases as the chair, two general practitioners, a project coordinator, three infectious disease specialists, two microbiologists, a paediatrician, an ear, nose and throat physician, a public relations officer and three pharmacists. A dentist and the county veterinarian are co-opted into the group.

Strama Halland proceeds from national recommendations and care programmes when producing the local recommendations adapted to local routines for diagnostics and administration. Several local information channels are used in the implementation.

The basis for their work towards outpatient care is the pharmaceutical committee's compendium of therapy recommendations published each year. The pharmaceutical committee organises a two-day residential course that provides Strama Halland, one of several expert groups, with time to revise its therapy area.

Fundamental to the work in hospital-based care has been the direct, collegial meetings, with information based on the point prevalence measurements of antibiotic use at various diagnoses that Strama Halland conducted, first on a regional basis and later through its participation in national measurements (section 4.5). Since 2004, Strama Halland has produced and updated an antibiotic guide that contains information on

all preparations on the market in respect of indications, dosages, dose reductions and any applicable remarks. There is also a simple pocket version with recommendations for the first day's initial therapy. They thus focus on achieving rational antibiotic treatment through the correct choice of substance and dosage. The therapy recommendations in hospital care are based, in addition to the recommendations of the Medical Products Agency and Strama, on national documents from the Swedish Society of Infectious Diseases and the Swedish Reference Group for Antibiotics (SRGA), as well as on data from the Swedish Council on Health Technology Assessment, SBU, in respect of pre-operative antibiotic prophylaxis.

Communication

Strama Halland provides information via its own website and in conjunction with the training sessions for physicians and nurses provided under the auspices of the pharmaceutical committee. They also contribute information to the medical product committee's information sheets and through the information sheets that they themselves provide to the healthcare sector.

The governing documents for primary care contain a clear Strama-mission for the clinics to adhere to the therapy recommendations and to analyse their own prescribing. The Strama group supports this through two annual visits at each health centre, where feedback is given on the centre's individual prescription data. The health centre then makes a brief analysis of its own prescription. Each month, Strama Halland sends emails with open/official statistics detailing the antibiotic usage of all health centres to all units and decision-makers, to keep the issue of antibiotic usage alive.

The knowledge and expectations of the general public are also important for decisions regarding the prescription of antibiotics in outpatient care. Strama Halland has regular contact with local media so that information reaches the general public. To facilitate patient-physician encounters, patient information has also been produced based on national data. The information addresses the disease progress of common infections, when antibiotics are required, and what patients can do themselves.

Parents of young children are an important target group since children are often affected by infections and are one of the groups in society that uses antibiotics the most. In Sweden, all young children are monitored by children's health centres (BVC) that also offer education for parents. Strama Halland has developed a training programme, Strama BVC, which is led by a paediatric nurse and which addresses common infections in children and why antibiotics are not always the obvious choice.

Results

Since there is a lack of continuous access to diagnosis-linked prescription data in Halland, it is difficult to study the adherence to treatment recommendations. However, in Region Halland, the total use of antibiotics has fallen substantially since the mid-1990s, just as it has elsewhere in the country.

Halland is one of the County Councils that, for many years, has had a relatively high level of antibiotic prescription. However, during the whole of 2012, prescription was reduced by 3 percent compared with the previous year. On average, 371 prescriptions per thousand residents were prescribed in 2012. Time-wise, the reduction coincides with the introduction of visits to the health centres and the instruction for centres to conduct their own analyses. A continuous reduction of 10 percent has been noted for the second half of 2012 and into 2013.

Conclusions and lessons learned

The extensive national work with evidence-based treatment recommendations is inspiring and important for the regional work. A regional multi-professional organisation with mandate and resources is a prerequisite for the effective implementation of new knowledge, along with adaptation to local conditions and information channels. Strama Halland's experience has been that effective implementation requires professional support, and as a result, the group currently includes a public relations officer.

Interview with Dr Katarina Hedin

Katarina Hedin is a general practitioner with a PhD on communicable diseases among Swedish pre-school children. She has been involved in the Strama network at a local and national level since the late 1990s and is currently chair of Strama in the Southern county council of Kronoberg.

”During my training to become a specialist, I was surprised to meet so many children who were repeatedly treated with antibiotics for common colds and other simple infections. When I began to look into the matter I saw that there were significant national variations in the prescription of antibiotics. I was disturbed to find Kronoberg among the top counties in the country!” says Katarina Hedin.

Her involvement in Strama followed from this realisation. “The great thing about Strama is that it is a network with activities at many levels. Local, national and international meetings and discussions provide inspiration and ideas. A small county like Kronoberg can learn from work done elsewhere. It’s like a smorgasbord where we can pick and choose solutions to match our local needs”, Katarina Hedin says.

Hedin points to the importance of local initiatives, based on common needs and a shared interest to limit antibiotic resistance. As a network of engaged individuals representing different professions, local Strama can function in a semi- independent and pragmatic manner in relation to the general health care system.

In her work for Strama, Katarina Hedin often discusses guidelines for prescription of antibiotics with her fellow GPs at local health centres. “Working in the same field gives me credibility”, she says. “We speak the same language”. In her experience, most doctors see guidelines as helpful tools in their daily practice. However, some practitioners are generally critical of what they see as directives from above, while others just go about business as usual.

“Working for rational use of antibiotics also involves education and changing people’s expectations”, says Katarina Hedin. Over the past decade, she has noticed a clear shift in the expectations of her own patients at the health care centre in Tingsryd. “When I first started out as a GP, most parents demanded a prescription when they brought their sick child to the doctor. Today many parents are relieved and happy when I tell them that their child does not need antibiotics.”

Education and media attention has also improved preventive work in health care facilities and pre-schools. Hedin, who has headed a number of studies on transmission among children, emphasises that disease prevention is a process that must be kept alive, through the involvement and education of parents, teachers and health care staff. Today there are still great variations when it comes to basic hygiene routines and information to children and parents about how to prevent transmission.

As a result of Strama initiatives, political measures and growing awareness among the public, levels of antibiotic prescription have dropped nationally since the peak in the 1990s. However, as Katarina Hedin points out, Kronoberg still had comparatively high levels of antibiotic prescription to children under six until 2010, 15 years after she and other Strama activists raised the issue.

“We must be humble and realistic when it comes to implementing guidelines. Change takes time”, says Katarina Hedin.

Chapter 6. Communicating rational use of antibiotics

In order to attain rational use of antibiotics and counteract antibiotic resistance, extensive communication efforts are needed at national and regional level. It involves both using antibiotics right, and only when necessary as well as reducing the spread of infection in healthcare and society. This chapter gives examples of how these aspects have been communicated and how this information has been used in Sweden.

Fundamental to communication on rational use of antibiotics in Sweden has been the development of networks of multi-professional local Strama groups in the County Councils, a driving force for these issues (chap 2). Since Strama was formed in 1995, it has repeatedly brought up the issue of resistance to the profession as well as the public in media, both on a local and national level. Local Strama groups have cooperated on communication with Strama and the Institute for Communicable Disease Control (now the Public Health Agency of Sweden) at national level. Over the years, the Strama groups have also shared experiences of their work with each other through recurrent Strama Days and the www.strama.se website. One of the Strama groups' core activities is discussions with physicians at health centres and hospital clinics. In 2010 SMI drew up a communication strategy to strengthen the continuing antibiotic efforts. The purpose of the strategy was to lay a foundation for external communication and contribute to the work of attaining the agency's goal. The strategy points to approach and choice of directions and emphasises that close collaboration is needed with local partners to spread new knowledge, follow up the work that is done and create change.

As part of drawing up the communication strategy, interviews were held with representatives of Strama groups, the Strama Council, the Swedish Association of Local Authorities and Regions, SMI and other national authorities, specialist associations and also with two representatives from the ECDC and the WHO Europe. The interviews identified significant factors that can affect the use of antibiotics, including:

- The patient's expectations and prerequisites in the encounter between physician and patient.
- The physician's knowledge and security. It is important to have underlying scientific bases for treatment recommendations that are evidence-based. It is also important to feed back use statistics (where do I and my unit stand in comparison with others?).
- Culture and treatment traditions at different workplaces.

Collaboration between national and local bodies increases the possibility to focus the information on factors that can affect rational use of antibiotics.

Rational use of antibiotics has many target groups

Consumption of antibiotics concerns most people in one way or another. The main target groups for direct communication on the work concerning rational use of antibiotics are prescribers and patients.

In human medicine, physicians have considerable responsibility for a rational use of antibiotics since only they (with a few specific exceptions) can prescribe antibiotics. In Sweden, there are thus no sales of antibiotics directly to patients without a prescription. Work to improve the use of antibiotics therefore needs to first and foremost affect the individual physician's prescribing. Many target groups have been identified who can conceivably affect prescribers' behaviour, including medically responsible nurses and others with specific care competencies in different areas, local Strama groups and decision-makers such as politicians and high-ranking health officials.

The general public's knowledge and expectations may also be of significance for decisions on antibiotics prescribing in outpatient care. GPs say, among other things, that lack of time in the consultation with the patient can contribute to unnecessary prescribing of antibiotics. It can quite simply take time to explain the marginal effect of antibiotics in the case of minor infections and that it is not good to take antibiotics unnecessarily, and that due to lack of time they find it easier to prescribe antibiotics than explain this to the patient.

Nurses also play a central role when they for example give patients advice and recommendations about their care needs. This also applies to the 1177 telephone service and healthcare advisors. Pharmacists are another important category who give both the public and healthcare staff advice on handling pharmaceuticals. They are an important link to the patient since they ensure that information on dosage and intervals and the importance of taking the whole of the prescribed course of medication reaches the user. The dispensing of antibiotics at the pharmacies is also stringently controlled, which contributes to make it difficult to obtain antibiotics in Sweden without a prescription. At the same time, antibiotics are purchased on the Internet and when people visit countries without such strict controls.

Statistics as a basic tool

Statistics on antibiotic consumption and antibiotic resistance constitute central information that is drawn up and disseminated both nationally and locally. The Public Health Agency of Sweden is in charge of national monitoring of antibiotic resistance and antibiotic consumption. Together with the National Veterinary Institute, the Public Health Agency of Sweden publishes the annual SWEDRES/SVARM report, which provides an opportunity for more detailed studies and in-depth analyses of developments over time, but it is not sufficient to only publish data once a year. Current statistics are also needed continuously in the day-to-day work on rational use and to keep the question alive. The Public Health Agency of Sweden therefore also regularly publishes statistics on use and resistance on its website and in electronic newsletters

to provide fast feedback to laboratories, Strama groups, the healthcare services, decision-makers and the media.

Strama groups in the County Councils analyse and communicate local statistics on use and resistance to health and medical care staff and to decision-makers and the local media. Press releases have often been coordinated at national and local level, for example when annual consumption figures are published. The national media have reported on trends nationally while local media have reported on developments in the local County Council in relation to the country as a whole, with themes like "Children in Skåne are given the most antibiotics" and "Västerbotten prescribes the least antibiotics in the country".

Collaborative measures nationally and locally for communication of treatment recommendations

In order to achieve rational prescribing of antibiotics, care staff need research-based treatment recommendations (chap 5). The Medical Products Agency, Strama and the Public Health Agency of Sweden have drawn up treatment recommendations for infections in outpatient care, which give the prescribing physician support concerning when antibiotics are and are not to be used. For the treatment of infections in hospital care, national evidence-based care programmes have been drawn up by Infektionsläkarföreningen (the Swedish Society of Infectious Diseases).

The treatment recommendations for outpatient care are communicated through several channels, for example websites and material issued by the Medical Products Agency to all prescribers and to central organisations. New recommendations are usually also presented in articles in Läkartidningen intended for Swedish physicians. The articles are written by representatives of Strama/the Public Health Agency of Sweden and the Medical Products Agency.

National treatment recommendations for outpatient care are also summarised in presentations as supporting material for lectures at conferences and on courses. Furthermore, the recommendations have been printed in summarised form on pocket cards and in brochures intended for physicians and sent to health centres. Patient information about common infections, based on the treatment recommendations, has been drawn to facilitate communication between the patient and the physician or nurse. This national information is used by the Strama groups in their local work.

The local communication efforts carried on by among others Strama groups, and pharmaceutical committees are central to new recommendations having the intended impact in healthcare. It is here, through the Strama groups' direct discussions with prescribers, that Strama plays what is possibly its most important role. The meetings create prerequisites for a personal dialogue about attitudes, perceptions and treatment traditions at a workplace (chap 2). Local spokespersons who are well known and have high credibility are important for the recommendations to have the necessary impact. Based on the national recommendations, Strama groups and pharmaceutical commit-

tees often draw up and communicate local guidelines and memoranda adapted to local needs, traditions and information channels. Some local Strama groups have also used digital forms of communication and designed apps for smartphones with local treatment recommendations.

A central message in national treatment recommendations for outpatient care is to avoid treating viral respiratory tract infections and minor bacterial respiratory tract infections with antibiotics. This approach has also permeated the information given to the general public. But it is at the same time important to balance this message and that there is also information intended for healthcare staff in outpatient care about symptoms that may indicate more unusual serious infections. It is important that healthcare staff working in outpatient care and the telephone advisory service are aware of such symptoms so that patients are given the right care and treatment quickly regardless of any need for antibiotics. Patient information drawn up at the national level also describes what to be alert to.

The great challenge is not always to talk about what the recommendations contain but rather to get the staff to follow the recommendations that they already know about. This requires that the information is well-designed and that the Public Health Agency of Sweden produce knowledge base documents on how to change the behaviour of the staff at the health centres so that the decreasing trend in antibiotic consumption seen since the mid 1990's can be sustained.

Information for the general public

Information given to the general public have since Strama was formed in 1995 strived to increase awareness of antibiotic resistance and knowledge of common infections and antibiotics. The importance of good hygiene in reducing the spread of infection has also been emphasised. No major campaign directed at the general public has so far been implemented in Sweden, but this has been tried out in for example France and Belgium. Some County Councils have carried out local campaigns with general messages like "healthy without antibiotics" and "less antibiotics – more of your own defence".

A number of information material have through the years been drawn up at the local or national level directed at different population groups: patient information and posters at health centres, brochures about common infections aimed at the elderly and parents of small children, training parents of small children at children's health centres, school materials, short videos for the web and television and the website "antibiotics or not" and a web based training programme for physicians, "antibiotic smart"

National and local level have collaborated on information efforts for an education day for professional groups who work with pre-school children under the banner of "healthier children in pre-school". Strama planned the day together with the Swedish Institute for Communicable Disease Control/the Public Health Agency of Sweden, the National Board of Health and Welfare and the Swedish Association of Local Author-

ities and Regions and the local communicable disease control unit and the Strama group in the county of Örebro. Based on this concept and the material produced, the education day was then held by the local Strama groups and communicable disease control units in other places in Sweden. In the same way, training programmes have also been run aimed at professionals in eldercare and nurses who work with giving healthcare advice over the telephone.

In 2009 and 2011 an interview study was conducted by the European Commission's so called Eurobarometer in the EU's member states concerning knowledge of and attitudes towards antibiotics. The countries in northern Europe were among the best informed as regards the effects of antibiotics. Statements that the subjects were asked to respond to were: if antibiotics kill viruses, if antibiotics are effective against colds and influenza, if unnecessary use of antibiotics makes them ineffective, and if antibiotics can often have side-effects such as diarrhoea. People who stated that they had been given information about not taking antibiotics unnecessarily generally did better than those who stated that they had not been given any such information.

Press releases, press conferences, polemic articles and contact with national and local media have been important in disseminating information to the broader public and to decision-makers. Common topics in press releases include annual statistics on consumption and resistance and results from reports, studies and investigations.

News media have also covered the issue over the years and this has probably contributed to increase awareness of the problem of antibiotic resistance and over-prescription. In addition to the daily news media, other types of media directed at specific target groups have also run features on antibiotic resistance. In one of its 2011 issues, a magazine for parents of young children for example contained an article about "How to be antibiotics-smart in everyday life". The article brings up the problem of antibiotic resistance and tells readers when antibiotics are needed and when they are generally unnecessary and what parents should remember to ask about when visiting the doctor. Other features were run in radio programmes directed at young listeners, in TV and radio programmes on medical matters directed at the general public and in magazines for healthcare staff.

Rational use in focus during European Antibiotic Awareness Day

Sweden has participated every year in European Antibiotic Awareness Day, which since 2008 has been held on 18 November. The day is an initiative from the European Centre for Disease Prevention and Control (ECDC) to once a year call attention to the threatening development of antibiotic resistance and the importance of rational use of antibiotics. ECDC's website has instructive documents and campaign materials aimed at the general public, GPs and physicians at hospitals that have been developed to support national efforts. Specifically for the day, ECDC compiles statistics on the development of resistance in Europe that are presented in illustrative geographic maps together with a main message (section 3.2 on EARS-Net data).

In Sweden, seminars and meetings have been arranged for different target groups both on a national level and locally in conjunction with European Antibiotic Awareness Day. National and local press releases have taken up the problem of resistance in Europe and pointed out the need for action. In 2008, the day had a special focus on the importance of everyone ceasing to use antibiotics unnecessarily. One of the main messages from ECDC was "Cold? Flu? Take care not antibiotics". In Sweden, Strama used pictures of a hedgehog provided by ECDC in a brochure and on a poster with information about colds and coughs that were distributed to health centres.

In 2012, the focus in Sweden was on the need for collaboration between authorities and organisations in different sectors of society. The National Board of Health and Welfare and the Swedish Board of Agriculture were commissioned by the government to form a national intersectoral coordinating mechanism. This effort includes drawing up a general communication strategy to coordinate messages between actors in different sectors of society. This is needed in order to emphasise the work being done and disseminate knowledge about what antibiotic resistance in animals and humans may lead to. One central activity as regards the exchange of information within the framework of the new collaboration function is an antibiotics forum held in conjunction with European Antibiotic Awareness Day. The purpose of the forum is to give different stakeholders working to combat antibiotic resistance and healthcare-associated infections an opportunity to meet to forge contacts, collaborate and exchange information. These actors represent animal healthcare, food production, care companies, pharmaceutical companies, interest groups (for animals, the environment and care), professional associations, higher education, universities, research, national agencies and authorities, municipalities, county administrative boards and County Councils.

Having a large number of actors is a strength but demands coordinated messages

Sweden has several agencies, authorities, organisations and local stakeholders in health and medical care who in various ways communicate information about infections, antibiotics and antibiotic resistance to different target groups (chap 1). The fact that both national and local organisations contribute to communicate information to their respective target groups is a strength. But it means that messages between national and local actors and between local actors in a County Council must be coordinated. A person with questions concerning a sore throat, for example, should preferably receive similar information regardless of whether he or she receives it from a health centre, over the telephone, from the web-based healthcare advice service, or from printed information published by a national agency or authority.

The national treatment recommendations for infections in outpatient care aim to establish a standard for when antibiotics should be used. The recommendations then form the foundation for national and local information on antibiotics and common infections directed at both healthcare staff and the general public.

Physicians and nurses have access to producer-independent information on antibiotic treatment from both national agencies and authorities and local Strama groups. The general public can for example be given information in conjunction with contact with their health centres, children's healthcare, the healthcare advice service over the phone and on the web, pharmacies and school nurses and through information from local Strama groups or national agencies.

The spread of antibiotic resistance concerns many groups in society and collaboration is also needed between agencies and organisations operating in human medicine, veterinary medicine and food and environmental sectors. The intersectoral coordinating mechanism mentioned earlier has been in existence in Sweden since 2012 and has the important task of coordinating the communication of messages on antibiotics, resistance and the spread of infection. In 2014 the work for a renewed plan for the Swedish work against antibiotic resistance and hospital acquired infections, was appointed to the intersectoral coordinating mechanism.

Examples of information channels used nationally or by local Strama groups	Target groups	Application examples
Websites	Professional groups in communicable disease control, physicians, the general public, media	On its website the Public Health Agency of Sweden publishes statistics on antibiotic resistance and use of antibiotics, national knowledge bases and presentations from national meetings (www.folkhalsomyndigheten.se). The Strama website is an important meeting-point for publishing and exchanging local initiatives and informational efforts (www.strama.se) The Medical Products Agency publishes national treatment recommendations on its website (www.lakemedelsverket.se).
Newsletters	Occupational groups within communicable disease control, media	The Public Health Agency of Sweden's electronic newsletter regularly contains summaries of scientific articles in the area, descriptions of measures to check the spread of disease in the county councils, statistics and reports.
Press releases and press conferences	Media	Common topics in press releases include annual statistics on consumption and resistance and results from reports, studies and investigations.
The agency's own articles in the medical press	Physicians	National treatment recommendations for outpatient care have often been presented and discussed in articles for Läkartidningen written by representatives of the Medical Products Agency, Strama and the Public Health Agency of Sweden.
Polemical articles in printed news media	The general public and decision-makers	Polemical articles in the major dailies have among other things pointed to measures that are needed in health and medical care to handle antibiotic resistance and also what the general public can contribute. The various articles have among other things been written by representatives of Strama, the Public Health Agency of Sweden, the Swedish National Board of Health and Welfare, the Swedish Society of Infectious Diseases and the Swedish Association of Local Authorities and Regions.

Examples of information channels used nationally or by local Strama groups	Target groups	Application examples
E-mails	Physicians, County Council managers	Some Strama groups regularly mail statistics of antibiotic prescribing to clinics and decision-makers in the County Councils.
Conferences and courses	Physicians, nurses, decision-makers	Topics include presentations of treatment recommendations and panel discussions on antibiotic resistance.
Direct mailing to health centres and clinics	Physicians, nurses	The Medical Products Agency and Strama/the Public Health Agency of Sweden have sent pocket cards with summarised treatment recommendations to all health centres.
Meetings at health centres and clinics	Physicians	One of the Strama groups' core activities is discussions with physicians at health centres and clinics.

References

1. Zaidi AK, Huskins WC, Thaver D, Bhutta ZA, Abbas Z, Goldmann DA. Hospital-acquired neonatal infections in developing countries. Lancet. 2005 Mar 26-Apr 1;365(9465):1175–88. PubMed PMID: 15794973.

2. ECDC/EMEA. The bacterial challenge: time to react. A call to narrow the gap between multidrug-resistant bacteria in the EU and the development of new antibacterial agents. Stockholm: 2009.

3. Roberts RR, Hota B, Ahmad I, Scott RD, 2nd, Foster SD, Abbasi F, et al. Hospital and societal costs of antimicrobial-resistant infections in a Chicago teaching hospital: implications for antibiotic stewardship. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2009 Oct 15;49(8):1175–84. PubMed PMID: 19739972.

4. Klevens RM, Morrison MA, Nadle J, Petit S, Gershman K, Ray S, et al. Invasive methicillin-resistant Staphylococcus aureus infections in the United States. JAMA: the journal of the American Medical Association. 2007 Oct 17;298(15):1763–71. PubMed PMID: 17940231.

5. SCB. Utrikes födda 2012. Fortsatt ökning av utrikes födda i Sverige. Statistik från SCB. 2013;2013:55( ).

6. SCB. Medellivslängd 2013. Mäns medellivslängd för första gången över 80 år. Statistik från SCB. 2014.

7. Willner S. Svenska folkets hälsa i historiskt perspektiv, Statens Folkhälsoinstitut, 2005. Kapitel 2 Hälso- och samhällsutvecklingen i Sverige 1750–2000. 2005.

8. Socialstyrelsen. Sveriges officiella statistik. Statistik – Hälso- och Sjukvård. Dödsorsaker 2011. 2012. 2013 2013-8-6.

9. SCB. Kohortdödligheten i Sverige. Dödlighetsutvecklingen sedan 1861. 2010.

10. Socialstyrelsen. Hälso- och sjukvårdsrapport 2009, Socialstyrelsen. 2009.

11. Hälso- och sjukvårdslag (1982:763), (1982).

12. Anell A GA, Merkur S. Sweden: Health System review. Health Systems in Transition, 2012. WHO. The European Observatory on Health Systems and Policies, 2012.

13. OECD. Health at a Glance: Europe 2012: OECD Publishing.

14. Socialstyrelsen. Förslag till svensk handlingsplan mot antibiotikaresistens. 2000.

15. Socialdepartementet. Strategi för ett samordnat arbete mot antibiotikaresistens och vårdrelaterade sjukdomar. Regeringens proposition 2005/06:50. 2005.

16. Kommissionens Direktiv 2002/77/EG av den 16 september 2002 om konkurrens på marknaderna för elektroniska kommunikationsnät och kommunikationstjänster. Europeiska gemenskapernas officiella tidning. 2002.

17. SMI/SVA. SWEDRES-SVARM 2012. Use of antimicrobials and occurrence of antimicrobial resistance in Sweden. 2013.

18. Socialstyrelsen. Att förebygga vårdrelaterade infektioner – Ett kunskapsunderlag 2006.

19. Socialstyrelsens föreskrifter om basal hygien inom hälso- och sjukvården m.m. , (2007).

20. Ekdahl K, Hansson HB, Molstad S, Soderstrom M, Walder M, Persson K. Limiting the spread of penicillin-resistant Streptococcus pneumoniae: experiences from the South Swedish Pneumococcal Intervention Project. Microbial drug resistance. 1998 Summer;4(2):99–105. PubMed PMID: 9650995.

21. Molstad S, Cars O. Major change in the use of antibiotics following a national programme: Swedish Strategic Programme for the Rational Use of Antimicrobial Agents and Surveillance of Resistance (STRAMA). Scandinavian journal of infectious diseases. 1999;31(2):191-5. PubMed PMID: 10447331.

22. Molstad S, Cars O, Struwe J. Strama – a Swedish working model for containment of antibiotic resistance. Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin. 2008 Nov 13;13(46). PubMed PMID: 19021951.

23. Molstad S, Erntell M, Hanberger H, Melander E, Norman C, Skoog G, et al. Sustained reduction of antibiotic use and low bacterial resistance: 10-year follow-up of the Swedish Strama programme. The Lancet infectious diseases. 2008 Feb;8(2):125–32. PubMed PMID: 18222163.

24. Sandberg T, Skoog G, Hermansson AB, Kahlmeter G, Kuylenstierna N, Lannergard A, et al. Ciprofloxacin for 7 days versus 14 days in women with acute pyelonephritis: a randomised, open-label and double-blind, placebo-controlled, non-inferiority trial. Lancet. 2012 Aug 4;380(9840):484-90. PubMed PMID: 22726802.

25. Hanberger H, Nilsson LE, Swedish Study G. High frequency of antibiotic resistance among Gram-negative isolates in intensive care units at 10 Swedish hospitals. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 1997 Apr;3(2):208–15. PubMed PMID: 11864106.

26. Erlandsson CM, Hanberger H, Eliasson I, Hoffmann M, Isaksson B, Lindgren S, et al. Surveillance of antibiotic resistance in ICUs in southeastern Sweden. ICU Study Group of the South East of Sweden. Acta anaesthesiologica Scandinavica. 1999 Sep;43(8):815–20. PubMed PMID: 10492409.

27. Hanberger H, Diekema D, Fluit A, Jones R, Struelens M, Spencer R, et al. Surveillance of antibiotic resistance in European ICUs. The Journal of hospital infection. 2001 Jul;48(3):161–76. PubMed PMID: 11439002.

28. Walther SM, Erlandsson M, Burman LG, Cars O, Gill H, Hoffman M, et al. Antibiotic prescription practices, consumption and bacterial resistance in a cross section of Swedish intensive care units. Acta anaesthesiologica Scandinavica. 2002 Oct;46(9):1075–81. PubMed PMID: 12366501.

29. Hanberger H, Erlandsson M, Burman LG, Cars O, Gill H, Lindgren S, et al. High antibiotic susceptibility among bacterial pathogens in Swedish ICUs. Report from a nation-wide surveillance program using TA90 as a novel index of susceptibility. Scandinavian journal of infectious diseases. 2004;36(1):24–30. PubMed PMID: 15000555.

30. Lennell A, Kuhlmann-Berenzon S, Geli P, Hedin K, Petersson C, Cars O, et al. Alcohol-based hand-disinfection reduced children's absence from Swedish day care centers. Acta paediatrica. 2008 Dec;97(12):1672–80. PubMed PMID: 18945282.

31. Sundqvist M, Geli P, Andersson DI, Sjolund-Karlsson M, Runehagen A, Cars H, et al. Little evidence for reversibility of trimethoprim resistance after a drastic reduction in trimethoprim use. The Journal of antimicrobial chemotherapy. 2010 Feb;65(2):350–60. PubMed PMID: 19900952.

32. Ekdahl K, Cars O. Role of communicable disease control measures in affecting the spread of resistant pneumococci: the Swedish model. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 1999 Aug;5 Suppl 4:S48-S54. PubMed PMID: 11869284.

33. Socialstyrelsen. Pneumokocker med nedsatt känslighet för penicillin (PNSP) 2012.

34. Abelson Storby K, Osterlund A, Kahlmeter G. Antimicrobial resistance in Escherichia coli in urine samples from children and adults: a 12 year analysis. Acta paediatrica. 2004 Apr;93(4):487–91. PubMed PMID: 15188976.

35. Cars O SJ, Norman C, Sandberg T. Förkorta behandlingstiderna vid nedre urinvägsinfektion hos kvinnor och använd inte kinoloner! Läkartidningen. 2008;105:1114–5.

36. ECDC. Risk assessment on the spread of carbapenemase-producing Enterobacteriaceae (CPE) through patient transfer between healthcare facilities, with special emphasis on cross-border transfer. 2011.

37. CDC. Guidance for control of infections with carbapenem-resistant or carbapenemase-producing Enterobacteriaceae in acute care facilities. MMWR. 2009;58(2).

38. ECDC. Antimicrobial resistance surveillance in Europe 2012. Annual Report of the European Antimicrobial Resistance Surveillance Network (EARS-Net). 2013.

39. CMO SCD, Department of Health Annual Report of the Chief Medical Officer Volume Two, 2011. Infections and the rise of antimicrobial resistance. 2011.

40. Strama. ESBL-resistens hos tarmbakterier Förslag till åtgärdsprogram. Bakgrundsdokument. 2007.

41. Strama. ESBL-resistens hos tarmbakterier Förslag till åtgärdsprogram. 2007.

42. WHO. WHO Collaborating Centre for Drug Statistics Methodology. www.whocc.no.

43. Andre M, Vernby A, Odenholt I, Lundborg CS, Axelsson I, Eriksson M, et al. Diagnosis-prescribing surveys in 2000, 2002 and 2005 in Swedish general practice: consultations, diagnosis, diagnostics and treatment choices. Scandinavian journal of infectious diseases. 2008;40(8):648–54. PubMed PMID: 18979603.

44. Hanberger H, Arman D, Gill H, Jindrak V, Kalenic S, Kurcz A, et al. Surveillance of microbial resistance in European Intensive Care Units: a first report from the Care-ICU programme for improved infection control. Intensive care medicine. 2009 Jan;35(1):91–100. PubMed PMID: 18670757.

45. Wertheim HF, Chandna A, Vu PD, Pham CV, Nguyen PD, Lam YM, et al. Providing impetus, tools, and guidance to strengthen national capacity for antimicrobial stewardship in Viet Nam. PLoS medicine. 2013;10(5):e1001429. PubMed PMID: 23667342. Pubmed Central PMCID: 3646721.

46. Groth A, Enoksson F, Hermansson A, Hultcrantz M, Stalfors J, Stenfeldt K. Acute mastoiditis in children in Sweden 1993–2007 – no increase after new guidelines. International journal of pediatric otorhinolaryngology. 2011 Dec;75(12):1496-501. PubMed PMID: 21945244.

47. Spindler C, Stralin K, Eriksson L, Hjerdt-Goscinski G, Holmberg H, Lidman C, et al. Swedish guidelines on the management of community-acquired pneumonia in immunocompetent adults – Swedish Society of Infectious Diseases 2012. Scandinavian journal of infectious diseases. 2012 Dec;44(12):885-902. PubMed PMID: 22830356.

Annexes

The annexes can be downloaded from the Public Health Agency of Sweden's website www.folkhalsomyndigheten.se

Annex 1. Examples of studies

Annex 2. Examples of information material

Resistant bacteria pose a threat to the global health. Collaboration and exchange of experiences between countries are vital in the efforts to preserve effective antibiotic treatments also for future generations. Sweden has in an international perspective relatively low consumption of antibiotics and favourable resistance conditions. Sweden initiated long-term, structured measures early on, characterised by work on both local and national levels with the collaboration of many disciplines and sectors both nationally and locally, which is further described in the report.

The ambition is that the report or chosen chapters and examples can be seen and used as a "tool-box" and give inspiration to other organisations and countries that want to develop or further strengthen their work on rational antibiotic use and resistance surveillance within human medicine.

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