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Editorials

Turning the tide of antimicrobial resistance: Europe shows the way

D L Monnet (dominiquel.monet@ecdc.europa.eu)[1], K G Kristinsson[2]
1. Scientific Advice Unit, European Centre for Disease Prevention and Control, Stockholm, Sweden
2. Landspitali University Hospital and University of Iceland, Reykjavik, Iceland

Ten years ago, European officials, experts and other stakeholders met in Copenhagen, Denmark, at the invitation of the Danish Ministry of Health and the Danish Ministry of Food, Agriculture and Fisheries. This European conference on "The Microbial Threat" due to antimicrobial resistance resulted in the publication of "Copenhagen Recommendations" calling for action to limit the emerging problem of antimicrobial-resistant microorganisms [1]. Following the conference, the European Commission prepared a comprehensive Community strategy against antimicrobial resistance, which was published in 2001 [2] and presented in Eurosurveillance [3]. Later the same year, European Union (EU) Health Ministers adopted a Council Recommendation on the prudent use of antimicrobial agents in human medicine with a series of specific measures aimed at containing the spread of antimicrobial resistance by prudent use of antimicrobial agents [4].

A review article published in this journal in 2001 showed that only six European countries had a national action plan to contain antimicrobial resistance [5]. An evaluation of implementation of the Council Recommendation performed by the European Commission showed that, by 2003, 16 countries had developed a national strategy to contain antimicrobial resistance and nine countries had an action plan [6,7]. The European Commission is currently performing another evaluation of the implementation of the Council Recommendation and its results will be available in 2009.

Historically, Denmark was the first European country to report on the control of methicillin-resistant *Staphylococcus aureus* (MRSA), which took place at the end of the 1960s and in the 1970s. Although the interventions were never fully documented, this decrease in the percentage of MRSA in *S. aureus* blood isolates from more than 30% to less than 1% - a figure that still holds today - has been attributed to a more prudent use of antbiotics combined with increased awareness of hospital hygiene [8]. In Iceland, a public media campaign on the prudent use of antibiotics in children in the mid-1990s led to a change in parents' attitudes, to a reduction in antimicrobial use and, subsequently, to a decrease in the incidence of penicillin-non-susceptible *Streptococcus pneumoniae* which had increased rapidly at the beginning of the decade [9]. This issue of Eurosurveillance is the first of two special issues on antimicrobial resistance and focuses on the recent successes of several EU Member States in reverting trends in antimicrobial resistance or, for the Netherlands, in maintaining already low antimicrobial resistance rates.

Among the six countries reporting in this issue of Eurosurveillance, the French success is remarkable because this country, which had the highest outpatient antibiotic consumption per capita in the EU, has been able to reduce this consumption by 16% between 2000 and 2006 following repeated annual public awareness campaigns on the prudent use of antibiotics combined with interventions targeted at general practitioners, including academic detailing and promotion of rapid testing for *Streptococcus pyogenes* tonsillitis [10]. This decrease in antibiotic use combined with the introduction of the 7-valent protein conjugated pneumococcal vaccine for young children in 2002 resulted in reverting trends in penicillin resistance in *S. pneumoniae* [10]. Additionally, several data sources confirm a decrease in the incidence and the prevalence of MRSA. For example, data from the European Antimicrobial Resistance Surveillance System (EARSS) show a decrease in the proportion of MRSA in *S. aureus* from blood cultures from France, from 33% in 2001 to 26% in 2007 [11]. This decrease has been attributed to the gradual expansion of infection control structures as well as implementation of specific MRSA control measures in French hospitals [10]. In Belgium, national activities to contain antimicrobial resistance have been coordinated by the Belgian Antibiotic Policy Coordination Committee (BAPCOC) since 1999. Yearly public awareness campaigns on antibiotics since 2000 have resulted in a 32% decrease in antibiotic consumption when expressed in packages and a concomitant decrease in, e.g. macrolide resistance in *S. pneumoniae* and *S. pyogenes* [12]. However, France and Belgium remain among the European countries with the highest consumption of antibiotics per capita and have therefore decided to continue organising national public awareness campaigns each year to consolidate their progress towards prudent use of antibiotics.

Other European countries with much lower levels of antimicrobial consumption and resistance have shown success with their national actions on prudent use of antibiotics and infection control. Through repeated reports in the media and the introduction of rapid diagnostic tests, Slovenia was able to show a 20% decrease in antibiotic consumption in outpatients, although this decrease has so far not been followed by a concomitant decrease in resistance. In Slovenian healthcare facilities, the introduction of a comprehensive national strategy for MRSA control resulted in a decrease in the proportion of MRSA in *S. aureus* from blood cultures from 21% in 2000 to 8% in 2007 [13]. In the Czech Republic, an education programme targeted at primary care paediatricians, including repeated audits of

prescribing practices and feedback, was implemented in 2001 as a control measure following increasing antibiotic consumption and resistance in the community in the 1990s [14]. In Sweden, national activities are coordinated by the Swedish Strategic Programme Against Antibiotic Resistance (STRAMA) and relayed at county level by a network of local STRAMA groups. Regular collaboration with national and regional media combined with local activities resulted in a 22% decrease in outpatient antibiotic consumption between 1994 and 2004 [15]. Finally, the Netherlands still have the lowest outpatient antibiotic consumption per capita in the EU as reported by European Surveillance of Antimicrobial Consumption (ESAC) [16], with antimicrobial resistance proportions that are among the lowest registered by the EARSS [11]. A Dutch Working Party on Antibiotic Policy (SWAB) was created in 1996 to ensure that the low level of antimicrobial resistance is preserved while improving the quality of antimicrobial prescriptions through the development of guidelines education and surveillance [17].

These experiences from European countries are encouraging. They show that it is possible to turn the tide of antimicrobial resistance through prudent use of antibiotics, better infection control practices and use of vaccines. The challenge is now to get all European countries take similar action. On 10 June 2008, EU Health Ministers adopted the Council Conclusions on antimicrobial resistance that reiterated their call for action to contain antimicrobial resistance and called upon Member States "to ensure that structures and resources for the implementation of the Council recommendation on the prudent use of antimicrobial agents in human medicine are in place and to continue with the implementation of specific strategies targeted towards the containment of the antimicrobial resistance" [18]. The Council also called upon the Commission and Member States "to coordinate an annual European initiative to increase awareness of the general public and veterinary and healthcare professionals about antimicrobial resistance, the prudent use of antibiotics in humans and animals and infection control practices". On 18 November 2008, the first European Antibiotic Awareness Day will be launched at the European Parliament in Strasbourg and marked in 29 European countries. This European health initiative coordinated by the European Centre for Disease Prevention and Control will in 2008 focus on increasing awareness of the general public about prudent use of antibiotics, based on the experience of a number of pioneer Member States reporting in this issue of Eurosurveillance. More information about European Antibiotic Awareness Day can be found at: http://antibiotic.ecdc.europa.eu.

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Recent trends in antimicrobial resistance among *Streptococcus pneumoniae* and *Staphylococcus aureus* isolates: the French experience

Anonymous (b.coignard@invs.sante.fr)[1]
1. Contributors are listed at the end of the paper. The indicated corresponding author summarised the data and coordinated the editorial process.

In France, the overall proportion of penicillin-non-susceptible *Streptococcus pneumoniae* has decreased from 53% in 2002 to 38% in 2006, and the proportion of methicillin-resistant *Staphylococcus aureus* from 33% in 2001 to 26% in 2007. Although the rates remain very high compared to northern European countries, these trends suggest that the prevention efforts implemented since 2000 through two national programmes (the national plan for preserving the efficacy of antibiotics and the national infection control programme) and updated recommendations for pneumococcal vaccination are successful.

Introduction

Antimicrobial resistance is a multifaceted threat of global concern in the European Union. In this article, we illustrate results and efforts to counteract its spread in France through two microorganisms, *Streptococcus pneumoniae* and *Staphylococcus aureus*, that are frequently isolated from community-acquired or hospital-acquired infections, respectively*. The proportion of resistance in these species is a good indicator of the evolution of antimicrobial resistance in France and these bacteria are key targets of two national programmes: the national plan for preserving the efficacy of antibiotics [1] and the national programme for infection control [2]. Quantitative targets were included in these programmes in 2004 [3], aiming to reduce, by 2008, the proportion of penicillin-non-susceptible strains among *S. pneumoniae* isolates to under 30% and the proportion of methicillin-resistant (MRSA) strains among *S. aureus* isolates to under 25%.

Streptococcus pneumoniae resistance trends

Data sources

Antimicrobial susceptibility in *S. pneumoniae* is studied by a group of 22 regional laboratory networks (*Observatoires Régionaux du Pneumocoque*), covering the 22 French metropolitan regions (excluding overseas regions) and coordinated by the French national reference centre for *S. pneumoniae* (CNRP). The CNRP collects all blood or cerebrospinal fluid (CSF) isolates from children under the age of 15 years, all CSF isolates from adults, and a selection of strains isolated from adults with respiratory tract infections (respiratory or blood isolates) or from children with acute otitis media [4].

Since 2001, susceptibility testing results for invasive isolates (blood or CSF) have been submitted to the European Antimicrobial Resistance Surveillance System (EARSS; http://www.rivm.nl/earss/). All laboratories use agar dilution and recommendations from the Antibiogram Committee of the French Society for Microbiology (CA-SFM, http://www.sfm.asso.fr/) for antimicrobial susceptibility testing and breakpoints. However, yearly data submitted by France to EARSS only included the first six months of a given year due to time constraints in the European data collection process; the data presented in the following include all strains received annually by the CNRP.

Results

Participation of laboratories has been stable since 2001. In 2006, for instance, the CNRP collected 1,411 strains from 406 private or public microbiological laboratories that provide support for 444 healthcare facilities covering 61.4% of admissions to French medical wards. Among those strains, 857 (61%) were isolated from invasive infections (blood or CSF) and 554 (39%) were isolated from respiratory tract infections.

Overall, the proportion of penicillin-non-susceptible *S. pneumoniae* (PNSP) was negligible before 1987 and then increased regularly every year, up to 53% in 2002 (48% and 46% of blood and CSF isolates, respectively). Between 2003 and 2005, the proportion of PNSP decreased, and remained stable (38%) in 2006 (34% for blood and CSF isolates) (Figure 1) [4].

Among invasive *S. pneumoniae* isolates, the overall proportion of PNSP decreased from 47% in 2001 to 34% in 2006. This corresponded to a decrease from 51% to less than 32% in children under the age of 15 years, and from 45% to 35% in adults (Table 1). A sharp reduction was noted in the proportion of PNSP (from 67% to 27%) among CSF isolates from children under the age of two years. The change in blood isolates in the same age group was less pronounced, with the proportion of PSNP remaining at or above 40% throughout this period and even increasing in 2006.

Discussion: prevention and control activities

The observed decrease in PNSP started after the implementation in November 2001 by French public health authorities of the first national plan for preserving the efficacy of antibiotics (Figure 1). Two studies helped to define actions of this plan targeting the community: In 2000, a controlled, population-based trial was conducted in three French regions and demonstrated that intensive

educational strategies aimed at optimising antibiotic use could significantly reduce the rate of PNSP colonisation [5]. In 2002, a study conducted by the French National Insurance Fund for Salaried Workers (CNAMTS) showed that both physicians and patients had little knowledge on antibiotics, resulting in poor antibiotic practices.

A multifaceted programme was then initiated by CNAMTS to avoid inappropriate antibiotic use in outpatients. The "Antibiotics aren't automatic!" campaign (http://www.antibiotiquespasautomatiques.com/) aimed at increasing awareness of physicians as well as the public on good antibiotic practices. Using humoristic television commercials, it targeted specific populations likely to ask for antibiotics (young mothers, young workers, the elderly) and promoted prudent use of antibiotics. The campaign has been repeated every winter since 2002 and become widely known and popular, parents becoming more and more aware of the benefits and limits of antibiotics [6].

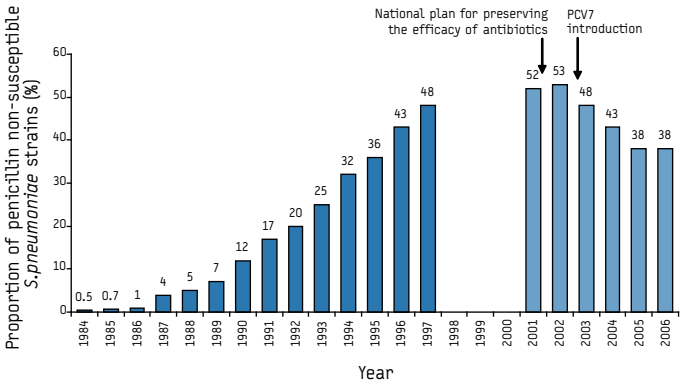
Other interventions since 2002 have been aimed at general practitioners, including academic detailing, peer-to-peer visits by health insurance delegates and the promotion of the streptococcal group A rapid diagnostic test for sore throat, that CNAMTS distributed to physicians free of charge. Data sent to the European surveillance of antimicrobial consumption (ESAC) network by the French Health Product Safety Agency (Afssaps) show that the overall antimicrobial consumption in ambulatory care in France has decreased from 33.0 defined daily doses per 1,000 inhabitants per day in 2001 to 27.9 in 2006, a reduction of 15%; the consumption of broad-spectrum penicillins (ATC4 code J01CA) has decreased by 20% and the consumption of macrolides (ATC4 code J01FA) by 39% (http://www.esac.ua.ac.be/). CNAMTS later demonstrated that its campaign was cost-effective [7].

In addition to reduced consumption of antibiotics, the introduction in March 2002 of the 7-valent protein conjugate vaccine (PCV7) for children under the age of two years [8] is likely to have contributed to the larger and faster decrease of PNSP rates among this age group than among adults. In 2002, serotypes covered by PCV7 (4, 6B, 9V, 14, 18C, 19F and 23F) accounted for 71% of invasive pneumococcal disease in France; most of them (68%) were PNSP, as compared to 44% for non-vaccine serotypes [4]. From 2004 to 2007, PCV7 vaccine coverage increased from 27% in six-month-old children to 56% in six- to 12-month-old children [9,10]. In children under the age of two years, the incidence between 2001/02 and 2006 of pneumococcal meningitis and bacteraemia decreased from 8.0 to 6.0 and from 21.8 to 17.5 cases per 100,000, respectively [11].

A partial replacement of vaccine serotypes by non-vaccine serotypes such as 19A, a serotype with a proportion of 85% PNSP in 2006, may explain why the decrease in the proportion of PNSP was not sustained in 2006 [12].

Figure 1

Proportion of penicillin non-susceptible *S. pneumoniae* among all strains studied by CNRP, France, 1984 to 2006 (n=50,300)



Note. no national figures from 1998 to 2000, as CNRP activities were interrupted. CNRP: national reference centre for *S. pneumoniae*; PCV7: 7-valent pneumococcal protein conjugate vaccine.

Table 1

Proportion of penicillin non-susceptible *S. pneumoniae* among invasive isolates, by age and type of isolate, France, 2001 to 2006

	2001		2002		2003		2004		2005		2006	
	N	%	N	%	N	%	N	%	N	%	N	%
Children												
<2 years												
Blood isolates	143	62.2	104	59.6	170	58.8	83	39.8	145	41.4	99	46.5
CSF isolates	87	66.7	69	62.3	99	44.4	72	50.0	76	39.5	67	26.9
2-15 years												
Blood isolates	150	30.7	87	37.9	183	33.9	123	31.7	206	23.8	133	23.3
CSF isolates	39	51.3	37	37.8	37	35.1	41	29.3	55	30.9	33	30.3
All isolates from children	419	50.8	297	51.2	489	44.8	319	37.6	482	32.4	332	31.6
Adults (>15 years)												
Blood isolates	828	46.0	678	46.0	635	41.6	232	44.8	461	36.2	308	34.1
CSF isolates	213	42.3	214	42.3	255	42.4	209	38.3	294	36.1	215	36.3
All isolates from adults	1,041	45.2	892	45.2	890	41.8	441	41.7	755	36.2	523	35.0
Total	1,460	46.8	1,189	47.5	1,379	42.9	760	40.0	1,237	34.7	855[1]	33.7

[1] age missing for two of the 857 strains reported in 2006.
N: strains tested for susceptibility; %: proportion of PNSP among tested strains.

Staphylococcus aureus resistance trends

Data sources

Data on methicillin resistance among *S. aureus* strains are issued from four different sources; all involved laboratories follow the recommendations from the Antibiogram Committee of the French Society for Microbiology (CA-SFM, http://www.sfm.asso.fr/) for antimicrobial susceptibility testing and breakpoints.

The first source is the data submitted each year since 2001 by France to EARSS (http://www.rivm.nl/earss/), collected by three microbiological networks that contribute to the *"Observatoire national de l'épidémiologie de la résistance bactérienne aux antibiotiques"* (Onerba). They include 19 teaching hospitals of the Azay-Resistance network, nine general hospitals of the Ile-de-France network, and, since 2004, 26 hospitals, mostly general hospitals, of the Reussir network (http://www.onerba.org/). These data allow calculating the proportion of methicillin-resistant *S. aureus* (MRSA) isolates among all *S. aureus* invasive isolates.

The second source is the national multidrug-resistant bacteria surveillance network (BMR-Raisin, http://www.invs.sante.fr/raisin/), which includes the five interregional infection control coordinating centres (CClin) and has been collecting data on MRSA isolates from all diagnostic specimens (excluding screening isolates) since 2002. More than 450 microbiological laboratories participate on a voluntary basis each year (between 478 in 2002 and 675 in 2006, when it accounted for 47% of all French hospital beds), making it possible to calculate the incidence density of MRSA infections in healthcare facilities per 1,000 patient days (pd) [13].

The third source is national prevalence surveys on nosocomial infections, which have been conducted every five years in French healthcare facilities since 1996. Antibiotic susceptibility profiles are recorded for selected pathogens (including *S. aureus*) that are recovered from any nosocomial infection, thus providing a measure of the prevalence of patients infected with MRSA [14].

The fourth and last source is a network of 39 teaching hospitals in the Paris area belonging to a single organisation, the *"Assistance publique - Hôpitaux de Paris"* (AP-HP); MRSA surveillance started there in 1993 and provides the longest continuous time series available on this topic in France.

Results

According to the latest EARSS report [15], France remained in 2006 one of the European countries with the highest proportion of MRSA among *S. aureus* isolates. However, while MRSA rates in most countries were increasing in 2006 (including those with the lowest rates), the report highlighted decreasing rates in two countries: France and Slovenia. In France, the MRSA proportion has decreased from 33% in 2001 to 26% in 2007. The additional 26 French laboratories enrolled in the EARSS data collection since 2004 actually slowed this downward trend, as they accounted for 38% of all *S. aureus* strains in 2006 and their MRSA proportions were higher than in other participating laboratories (Table 2).

The decreasing proportion of MRSA among *S. aureus*, as reported by EARSS, is confirmed by national incidence data collected through the BMR-Raisin network. Data from 227 laboratories that have participated in this network since 2003 (totalling more than 4,000,000 pd each year) point to a decreasing incidence density of MRSA infections in acute care wards, which fell from 0.89 MRSA infections per 1,000 pd in 2003 to 0.64 MRSA infections per 1,000 pd in 2007. This trend was even more pronounced in intensive care units, where the incidence density fell from 2.37 MRSA infections per 1,000 pd in 2003 to 1.59 MRSA infections per 1,000 pd in 2007 (Figure 2) [Raisin, unpublished data].

A decrease in MRSA rates was also noted in national prevalence surveys, through comparison of data from the 1,351 healthcare facilities having contributed to the surveys in 2001 and 2006 which included 550,637 patients (279,490 patients in 2001 and 271,147 in 2006). In these 1,351 healthcare facilities, the proportion of nosocomial infections with a microbiological diagnosis increased from 72% in 2001 to 78% in 2006, as did the proportion of *S. aureus* strains tested for antimicrobial susceptibility (93% in 2001 and 96% in 2006). The proportion of MRSA among *S. aureus* isolates decreased from 62% in 2001 to 50% in 2006. The prevalence of MRSA-infected patients decreased from 0.49% in 2001 to 0.29% in 2006, a reduction of 41%. This trend was

Table 2

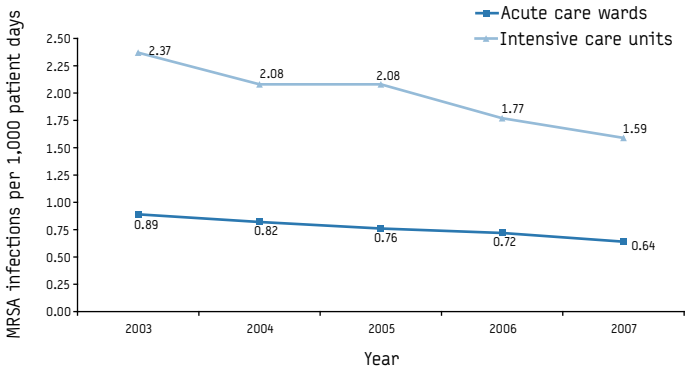
Proportion of methicillin-resistant *S. aureus* among strains isolated from invasive isolates, by network contributing to EARSS, France, 2001 to 2007

Year	Azay-Resistance		Ile-de-France		Reussir		Total	
	N	%	N	%	N	%	N	%
2001	1,459	32.8	248	35.5	-	-	1,707	33.2
2002	1,425	32.9	238	33.2	-	-	1,663	32.9
2003	1,419	28.3	285	31.9	-	-	1,704	28.9
2004	1,596	26.4	319	28.2	1,409	31.6	3,324	28.8
2005	1,905	24.9	204	30.9	1,343	29.9	3,452	27.2
2006	2,078	25.7	276	25.0	1,444	28.4	3,798	26.7
2007*	2,429	25.3	287	20.2	1,535	27.7	4,251	25.7

*preliminary data as of July 2008;
N: strains tested for susceptibility; %: proportion of MRSA among tested strains; EARSS: European Antimicrobial Resistance Surveillance System; MRSA: methicillin-resistant S. aureus;

Figure 2

Methicillin-resistant *S. aureus* incidence density in healthcare facilities that have participated since 2003 in the BMR-Raisin Network, by type of unit, France, 2003 to 2007 (n=227)



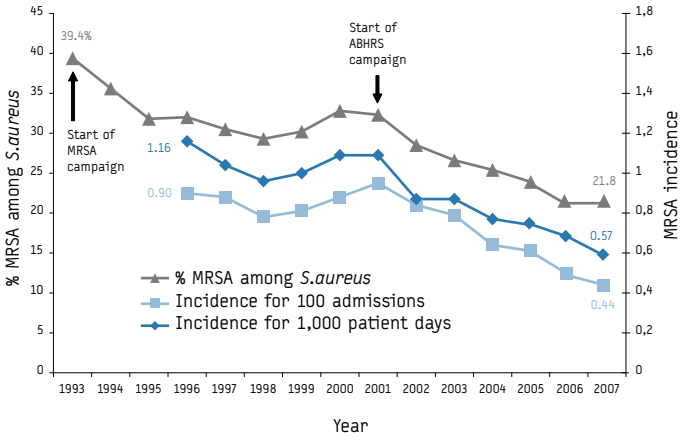
MRSA: methicillin-resistant *S. aureus*.

observed across all types of healthcare facility, from university hospitals to long-term care facilities, and across all subspecialties but obstetrics (Table 3); it remained significant after adjusting for the patients' case-mix in a multivariate analysis [14].

Finally, in the AP-HP group, the proportion of MRSA among *S. aureus* isolated from clinical specimens in acute care decreased from 39% in 1993 to 22% in 2007. At the same time, the incidence density of MRSA decreased from 1.16 MRSA infections per 1,000 pd in 1996 to 0.57 MRSA infections per 1,000 pd in 2007 (Figure 3) [AP-HP, unpublished data].

FIGURE 3

MRSA proportion among *S. aureus*, and MRSA incidence, 39 teaching hospitals of the Paris area, 1993 to 2007



Source: Assistance publique - Hôpitaux de Paris
MRSA: methicillin-resistant *S. aureus*. ABHRS: alcohol-based hand rub solutions

Discussion: prevention and control activities

Interventions that may account for the decrease in MRSA rates in France started in 1992, when the first European study on MRSA reported that the proportion of MRSA among *S. aureus* was 33.8% in France, the second highest proportion after Italy [16]. In 1995, a first multicenter survey in 43 hospitals showed that the median MRSA incidence in French intensive care units was 2.82 MRSA infections per 1,000 pd [17]. At that time, infection control teams were progressively implemented in French healthcare facilities, CClin had just been created, and antimicrobial resistance surveillance networks were being developed. A group of French intensive care specialists and microbiologists decided to start acting first in their own hospitals within the AP-HP group, and produced in 1993 (Figure 3) the first recommendations for prevention and control of multidrug-resistant bacteria [18].

The AP-HP recommendations provided the basis for the first national guidelines issued in 1999 by the French Ministry of Health and its Hospital Infection Control Advisory Committee [19]. They were disseminated to healthcare facilities and services through the CClin who coordinate regional networks of infection control teams and targeted diagnosis of multidrug-resistant bacteria, contact precautions, reinforcement of hand hygiene, isolation and cohorting, screening of patients, prudent antimicrobial use and evaluation through audits of practices and surveillance.

Interestingly, the fact that it is still necessary nowadays to include these key targets into national plans, shows that the fight against antimicrobial resistance is a long road. In addition, it takes time to provide the resources for adequate infection control nationwide – in 2006, 92% of French healthcare facilities had an infection control team, according to a yearly survey performed by the Ministry of Health [20] – and to integrate recommendations in the daily clinical practice – in 2001, a study assessing the implementation of recommendations in 395 French intensive care units found that 70% performed active surveillance cultures for MRSA and that 88% flagged and isolated carriers [21]. Even if there is still room for improvement, the situation appeared to be considerably better than the one in the United States, a country with very high MRSA

TABLE 3

Prevalence of methicillin-resistant *S. aureus* infected patients, by type of ward and year of survey; French national prevalence surveys, 2001 and 2006

Specialty	2001			2006			Δ (%)
	Patients	Infected		Patients	Infected		
	N	N	%	N	N	%	
Acute care	146,445	708	0.48	147,908	437	0.30	-39
- medicine	72,933	325	0.45	76,418	212	0.28	-38
- surgery	49,086	253	0.52	47,776	148	0.31	-40
- obstetrics	18,313	6	0.03	18,356	10	0.05	
- intensive care	6,113	124	2.03	5,358	67	1.25	-38
Rehabilitation	42,737	331	0.77	43,203	173	0.40	-48
Long term care	55,370	295	0.53	44,720	161	0.36	-32
Psychiatry	34,867	24	0.07	33,791	8	0.02	-66
Other	71	2	2.82	1,525	2	0.13	
Total	279,490	1 360	0.49	271,147	781	0.29	-41

Note: This analysis was restricted to nosocomial infections acquired in the 1,351 healthcare facilities that participated in both surveys.
Δ (%) = relative difference in prevalence between 2006 and 2001

rates, where only 18% of hospitals performed MRSA surveillance cultures in high risk units in 2003 [22].

More recently, MRSA control in France has been reinforced through the extensive promotion and use of alcohol-based hand rub solutions for hand hygiene. An intensive campaign to promote their use was launched within the AP-HP group (Figure 3), and the overall usage increased from 1 to 21 litres per 1,000 pd from 2000 to 2007 [AP-HP, unpublished data]. Similar campaigns were conducted in other hospitals and regions, e.g. in Western France where a survey recently reported that the usage of alcohol-based hand rub solutions has doubled in the period from 2002 to 2005 [23].

Other factors that possibly contributed to the decrease of MRSA in France may have been the strong and coordinated national infection control programme that allocates infection control resources and sets quantitative objectives through indicators, as well as patients' associations asking for more results and transparency. The benefits and pitfalls of public reporting of infection control indicators remain a matter of debate. Such indicators have been progressively implemented in France since 2006 by the Ministry of Health (http://www.icalin.sante.gouv.fr/). They include scores that rate nosocomial infection control organisation and activities in each hospital (ICALIN) and the overall consumption of alcohol-based hand rub products (ICSHA) [24]. Our experience suggests that they provide a strong incentive for healthcare facilities to develop infection control activities and may be a key element for a sustainable decrease in MRSA rates.

Conclusion

PNSP and MRSA rates remain very high in France compared to Northern Europe countries [15]. Although the recent trends are encouraging, it is difficult to relate them to specific actions, as the interventions were multifaceted and implemented simultaneously. However, they suggest that the prevention efforts implemented since 2000 were successful and the national targets set in 2004 for 2008 will hopefully be reached.

According to a modelling study published in 2006, it may take more than 10 years to lower MRSA rates in countries with high prevalence [25]. The trends observed in France confirm that the fight against antimicrobial resistance is a long and demanding challenge and suggest that the dissemination of recommendations for a rational use of antibiotics, infection control and vaccination should be actively pursued.

* Data on other multidrug-resistant bacteria in France are available through the InVS website at http://www.invs.sante.fr/ratb/ (French and English versions).

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Contributors in alphabetical order:

JM Azanowsky[1], C Brun-Buisson[2], A Carbonne[3], P Cavalié[4], B Coignard[3,5], T Demerens[6], JC Desenclos[5], D Guillemot[7], L Gutmann[8], V Jarlier[3,9], A Lepoutre[5], D Levy-Bruhl[5], S Maugat[3,5], L May-Michelangeli[2], P Parneix[3], B Schlemmer[1], JM Thiolet[3,5], E Varon[8]

1. Plan national pour préserver l'efficacité des antibiotiques (French national plan for preserving the efficacy of antibiotics), Health Ministry, Paris, France
2. Programme national de lutte contre les infections nosocomiales (French national infection control programme), Health Ministry, Paris, France
3. Réseau d'alerte, d'investigation et de surveillance des infections nosocomiales (Raisin, National nosocomial infection alert, investigation and surveillance network), Saint-Maurice, France
4. Agence française de sécurité sanitaire des produits de santé (Afssaps, French health products safety agency), Saint-Denis, France
5. Institut de veille Sanitaire (InVS, French institute for public health surveillance), Saint-Maurice, France
6. Caisse nationale d'assurance maladie des travailleurs salariés (CNAMTS, French National Insurance Fund for Salaried Workers), Paris, France
7. Institut Pasteur, Paris, France
8. Centre national de référence des pneumocoques (CNRP, French national reference centre for pneumococci), Paris, France
9. Observatoire national de l'épidémiologie de la résistance bactérienne aux antibiotiques (Onerba, French national observatory for epidemiology of the bacterial resistance to antimicrobials), Paris, France

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Achievements of the Belgian Antibiotic Policy Coordination Committee (BAPCOC)

H Goossens (herman.goossens@uza.be)[1], S Coenen[2], M Costers[3], S De Corte[3], A De Sutter[4], B Gordts[5], L Laurier[6], M. J. Struelens[7,8]
1. Laboratory of Medical Microbiology, Vaccine & Infectious Disease Institute, University of Antwerp, Antwerp, Belgium
2. Department of General Practice, Vaccine & Infectious Disease Institute, University of Antwerp, Antwerp, Belgium
3. Federal Public Service Health, Food Chain Safety and Environment, Brussels, Belgium
4. Department of General Practice, University of Ghent, Ghent, Belgium
5. Department of Microbiology and Infection Control, St. John's General Hospital, Bruges, Belgium
6. Federal Agency for Medicines and Health Products, Brussels, Belgium
7. Department of Microbiology, Hôpital Erasme, Brussels, Belgium
8. Infectious Diseases Epidemiology, School of Public Health, Université Libre de Bruxelles, Brussels, Belgium

A Belgian Antibiotic Policy Coordination Committee (BAPCOC) was officially established in 1999 by Royal Decree. The overall objective of BAPCOC is to promote judicious use of antibiotics in humans and animals and to promote infection control and hospital hygiene, with the overall aim to reduce antibiotic resistance. BAPCOC fostered strong and interdisciplinary public health, scientific and political leadership, which led to many evidence-based interventions such as multimedia campaigns to promote the prudent use of antibiotics in the community, national campaigns to promote hand hygiene in hospitals, publication of clinical practice guidelines, staffing and technical support for establishment of antibiotic management teams in all Belgian hospitals, surveillance programmes on antibiotic use and resistance in humans and animals and the promotion of research. These activities and interventions resulted in a measurable decrease in antibiotic use and resistance in the community and hospitals.

Introduction

Belgium is a small federal country with 10.5 million inhabitants living in three regions. In 1999, the Belgian Ministry of Health established by Royal Decree an official committee, called the Belgian Antibiotic Policy Coordination Committee (BAPCOC) [1].

The specific objectives of BAPCOC are to promote judicious use of antibiotics in humans and animals and enhance infection control and hospital hygiene, with the overall aim of reducing antibiotic resistance.

The specific tasks of BAPCOC are to:

- collect information on antibiotic use and resistance to antibiotics in humans and animals;
- publish reports on the evolution of antibiotic use and resistance;
- create awareness of the evolution of antibiotic resistance and the risks for public health;
- publish recommendations on the detection and surveillance of antibiotic resistance, on the appropriate use of antibiotics, on indications for prophylactic and therapeutic use of antibiotics, on the evaluation and the surveillance of antibiotic use in humans and animals, and on the implementation of international recommendations on the prudent use of antibiotics in humans and animals;
- and to publish recommendations on future research into the emergence, spread and control of antibiotic resistance.

Table

Key activities of the Belgian Antibiotic Policy Coordination Committee (BAPCOC)

Activity	Budget
Multimedia campaigns to promote the prudent use of antibiotics in the community	400,000 € per campaign
National campaigns to promote hand hygiene in hospitals	125,000 € per campaign
Staffing and technical support for establishment of antibiotic management teams in all Belgian hospitals	3.6 million € each year
Publication of clinical practice guidelines	25,000 € per guideline
Publication of guide to antibiotic prescribing in ambulatory care	100,000 € per guide
Surveillance programmes on antibiotic use and resistance in humans and animals	100,000 € each year
Promotion of research e.g. - prevalence of MRSA among nursing home residents - prevalence of MRSA ST398 in pigs and pig farmers	 100,000 € 150,000 €
Support infection control practices (better funding and clear organisation in hospitals)	3.4 million € additional funding in 2007

To address these specific tasks BAPCOC founded the following five multidisciplinary working groups: ambulatory care, hospital care, awareness campaigns, infection control and veterinary medicine. The working groups are composed of microbiologists, infectious diseases' and infection control specialists, epidemiologists, general practitioners (GPs), pharmacists, nurses, veterinarians, basic researchers, public health experts and health economists. The (scientific) secretariat, responsible for their day-to-day management, is hosted by the Federal Public Service Health, Food Chain Safety and Environment, Brussels, Belgium. A Steering Committee, composed of the presidents of the working groups, the chair and vice-chair of BAPCOC, meets monthly. The Steering Committee is responsible for the continuity, interaction and follow-up of initiatives and projects. At plenary meetings of BAPCOC, which are held every four months, the working groups report on their activities so that all stakeholders, including policy makers, scientific organisations, public health institutes are informed about the BAPCOC activities and results.

The key BAPCOC activities and corresponding budgets are listed in the Table. BAPCOC's annual budget in 2007 was 7.8 million EUR. Furthermore, BAPCOC participates in European projects, such as European Surveillance of Antimicrobial Consumption (ESAC; www.esac.ua.ac.be), European Antimicrobial Resistance Surveillance System (EARSS; www.rivm.nl/earss), ABS International (www.abs-international.eu), and e-bug (www.e-bug.eu).

This paper discusses selected examples of the activities and achievements of BAPCOC.

Public antibiotic awareness campaigns

The BAPCOC working group for public awareness campaigns set the following goals:

- to provide the general public with a better understanding of the natural course of minor and self-limiting infections, such as common cold, acute bronchitis, or influenza;
- to explain when the use of antibiotics is needed, i.e. in case of serious bacterial infections;
- to underline the consequences of emergence of resistance to antibiotics;
- and to facilitate a discussion between patients doctors and pharmacists on the need for appropriate antibiotic use.

No specific target for reductions in antibiotic sales was set.

In December 2000, BAPCOC launched a media campaign which ran over three consecutive winter seasons and concentrated on simple messages that were conveyed through booklets, handouts, posters, prime-time television and radio spots, and websites, like "Use antibiotics less frequently, but better", "Save antibiotics, they may save your life", and "Talk to your doctor, talk to your pharmacist" (www.red-antibiotica.org) [2,3]. The involvement of GPs, paediatricians, pneumologists, ear, nose and throat specialists as well as of retail pharmacists was sought through personalised letters accompanied by campaign materials for presentation to patients. In November 2004, a new media campaign was launched, using the slogan "Antibiotics are ineffective for the common cold, acute bronchitis and flu"; this ran until last winter season (www.antibiotics-info.be). On 18 November 2008, a new media campaign will be launched to mark the European Antibiotic Awareness Day.

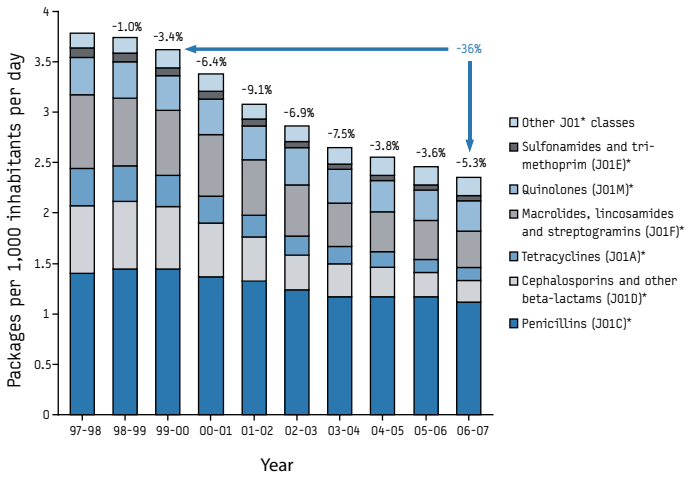
The impact of these activities has been evaluated through pre-and post-campaign face-to face interviews with the public, post-campaign surveys of the GPs, records of antibiotic sales and prescriptions in the retail pharmacies, and evolution of antibiotic resistance among pathogens frequently affecting the community. Outpatient antibiotic use, expressed by the number of reimbursed packages per 1,000 inhabitants per day, decreased by 36% between the winter season 1997-8 and 2006-7 in Belgium (Figure 1) [4]. Penicillin, tetracycline and macrolide resistance in *Streptococcus pneumoniae* increased up to the year 2000, after which it decreased substantially (Figure 2). Similarly, macrolide resistance in *Streptococcus pyogenes* decreased dramatically from 17% in 2001 to 2% in 2007 (Figure 3).

National hand hygiene campaigns

BAPCOC has organised two countrywide campaigns – in 2005 and in 2007 – for the prevention of nosocomial infections by improving

Figure 1

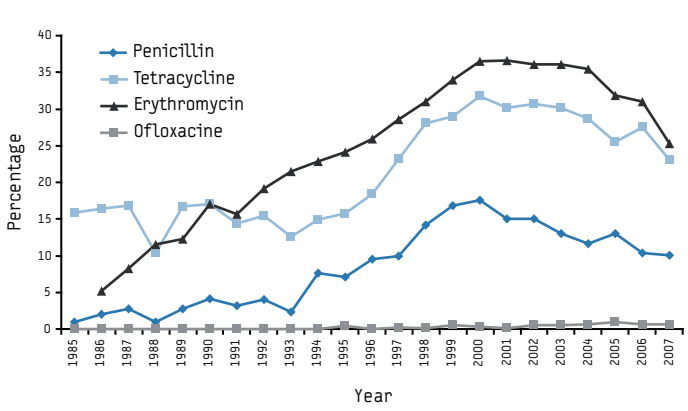
Outpatient antibiotic use in packages per 1,000 inhabitants per day, Belgium, July 1997 to June 2007



*Anatomical Therapeutic Chemical (ATC) classification code

Figure 2

Penicillin, tetracycline, macrolide (erythromycin) and ofloxacine resistance in *Streptococcus pneumoniae*, Belgium, 1985-2007



Number of strains tested varied between 1,218 in 2002 and 1,744 in 2005.
Source: National Reference Centre *S. pneumoniae* (University of Leuven)

hand hygiene compliance in Belgian hospitals. Key components of these campaigns were audit with performance feedback, reminders (posters), educational sessions for healthcare workers, promotion of alcohol-based hand rubs, and patient awareness (folders). Participation, on a voluntary basis, was excellent for both campaigns: 97% for acute care hospitals, 66% for long-term care hospitals and 63% for psychiatric hospitals. Overall compliance with hand hygiene (measured by direct observation) increased significantly from 49% to 69% for the first campaign and from 53% to 69% for the second campaign. The third campaign will be held in December of 2008.

Antibiotic Management Teams in hospitals

Since the 1990s, there has been a move in Belgian hospitals to establish multidisciplinary antibiotic management teams (AMT) to contain antibiotic resistance and improve antibiotic prescribing. The BAPCOC working group on hospital care developed an implementation plan for this strategy by mobilising federal funding for AMTs and antibiotic managers. In 2002, a pilot project started with a yearly budget of 0.93 million euros for hiring trained antibiotic managers in 37 hospitals, selected from 69 candidate hospitals for their expertise and experience with a local antibiotic stewardship programme. Based on successful activity reports of these pilot hospitals [5], the project was extended to 61 hospitals in 2006 by doubling the financial support to 1.83 million euros and since July 2007 to all acute care hospitals with an annual budget of 3.61 million euros. The AMTs will remain in the BAPCOC programme and their tasks have been defined by Royal Decree. BAPCOC provides scientific support to the participating hospitals by means of a dedicated training course, national study days, standardised evaluation of local progress reports and national surveillance of antibiotic consumption in hospitals. In the years 2002-7, over 600 hospital pharmacists and physicians participated in BAPCOC-supported interuniversity teaching courses in antibiotic management. National workshops were held twice to share good practices between hospital AMTs. Analysis of the recent reports of the 61 pilot phase hospitals clearly demonstrates general adoption of well- established quality improvement interventions, such as an antibiotic formulary, guidelines for prophylactic and therapeutic antibiotic use, regular analysis of local antibiotic consumption and resistance profiles, and increasing conductance of clinical audits and drug use evaluations. In a recent international survey of structural indicators of antibiotic stewardship programmes, Belgian hospitals scored high on average (3.75/5). The survey showed that 90% of hospitals had key structural resources and tools in place for effective antibiotic management and infection control [6].

The impact of these activities in hospital infection control and antibiotic stewardship is monitored through a newly developed surveillance of hospital-anti-infective drug consumption as well as by several longstanding surveillance schemes of nosocomial infection and multidrug resistant pathogens coordinated by the Scientific Institute of Public Health. These include methicillin-resistant *Staphylococcus aureus* (MRSA), extended spectrum beta-lactamase (ESBL)-producing *Enterobacteriaceae* and pathogenic *Clostridium difficile*. An example of encouraging results is the 35 % relative reduction since 2004 in the incidence of nosocomial acquisition of MRSA among patients admitted to acute care hospitals [7].

Publication of guidelines and a guide for appropriate use of antibiotics

BAPCOC, in collaboration with scientific experts and organisations, produced evidence-based guidelines for the appropriate use of antibiotics in hospitals and ambulatory care for important infectious disease syndromes such as acute sore throat, otitis media, sinusitis, community-acquired pneumonia, uncomplicated and complicated urinary tract infections. All BAPCOC guidelines were disseminated free of charge to all relevant physicians (GPs and/or specialists) in Belgium. The guideline recommendations for ambulatory care were supplemented by conclusions of systematic literature reviews. BAPCOC also produced a booklet in 2004 on antibiotic treatment of community-acquired infectious diseases. All Belgian GPs received a copy of this first antibiotic booklet in 2004. A copy of the second edition of this antibiotic guide will be distributed among all primary care physicians in November 2008. The impact of this antibiotic guide for outpatients is monitored based on antibiotic prescribing in the community by indication, age and class of antibiotics.

Surveillance programmes on antibiotic use and resistance in humans and animals

BAPCOC provides support and additional funding for surveillance of MRSA, vancomycin-resistant enterococci (VRE), ESBL-producing *Enterobacteriaceae*, *S. pneumoniae* and *S. pyogenes*. BAPCOC also supports surveillance programmes on antibiotic use in hospitals, such as point prevalence surveys. The results of these surveillance programmes are published in an annual report, published by the Public Health Institute in Brussels.

Research projects funded by BAPCOC

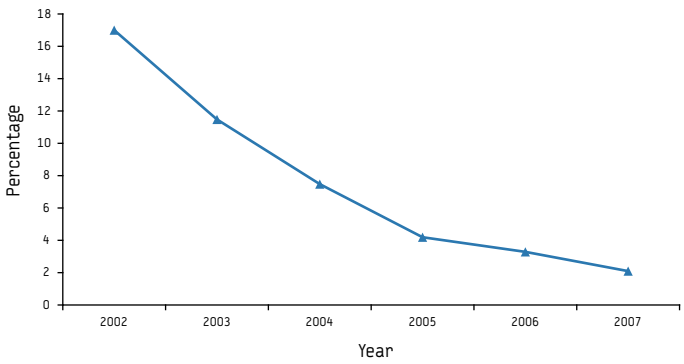
BAPCOC funded a number of research projects to provide scientific evidence for national policies and guidelines of which examples are given below.

National survey of prevalence of MRSA carriage among residents of nursing homes

BAPCOC funded the first national survey of prevalence of MRSA carriage among residents of nursing homes in Belgium. The objectives of this survey were to study the national prevalence of MRSA colonisation in Belgian nursing home residents, to identify risk factors for MRSA carriage among nursing home residents, in respect of both the individual resident and of the nursing home

Figure 3

Macrolide (erythromycin) resistance in *Streptococcus pyogenes*, Belgium, 2002 to 2007



Number of strains tested varied between 1298 in 2002 and 934 in 2007.
Source: National Reference Centre *Streptococcus pyogenes* (University of Antwerp)

facility, and to study the molecular epidemiology and susceptibility of MRSA strains isolated from residents living in these facilities. Based on a representative sample of 3,000 residents in 60 institutions, a prevalence of 19% carriage was noted (unpublished data). Importantly, 90% of MRSA carriers found in the survey were not identified as such by the nursing and medical personnel in spite of routine MRSA screening on transfer from hospitals and a discharge letter being sent by the hospital, in the majority of cases, to the participating nursing homes at the time of patient referral. A better understanding of the MRSA reservoir in nursing homes and analysis of risk factors permitted the adaptation of an MRSA control policy. National guidelines to prevent the spread of MRSA in nursing homes have been developed and the impact of these guidelines on the evolution of MRSA carriage in nursing homes will be evaluated by a new prevalence survey in the near future.

Prevalence survey of MRSA in swine farmers in Belgium

BAPCOC funded a survey on MRSA in swine farmers and their household contacts, to determine if MRSA strains in those farmers are related to those in swine, to characterise and compare phenotypes and genotypes of MRSA strains from humans and swine, and to study risk factors for MRSA colonisation and assess levels of personal hygiene in farm workers. Extensive colonisation with two subtypes of the livestock-associated ST398 MRSA strain was found in swine (44% carriers from 68% of farms) and farmers (38%) in contact with swine and other animals. Reported use of personal protection equipment and decontamination showed no difference in the rates of colonisation [8]. As a result of this survey, a National MRSA Med Vet Task Force was established to coordinate further investigation of the epidemiology of MRSA in animals and persons in contact with animals and to develop guidelines for risk management.

National investigation on the infection control practices in surgery

BAPCOC funded and supported a national investigation on infection control practices in operating rooms. More than half of all acute care hospitals participated in a national inventory evaluating the extent to which internationally suggested infection prevention precautions are defined, carried out and followed-up. A list of essential precautions was grouped into different categories: architecture and structure, environmental cleaning, peri-operative procedures, sterilisation, logistic activities and surveillance of postoperative wound infections.

For each essential item, participants reported the estimated degree of compliance in their institution, the existence of a standard operating procedure (SOP) for the performance for this precaution, and finally whether the respective items are written down in institutional guidelines or procedures. The investigation clearly demonstrated the extensive variability in infection control practices in Belgian operating rooms, with respect to standards described in institutional operating procedures as well as to actual compliance with local and/or (inter)national precaution measures. The results are detailed in an advisory document reported to the authorities, stating the necessity of quality control standards implementation and official follow-up of procedures regarding peri-operative infection control.

Conclusions

Our experience demonstrates that strong joint and interdisciplinary public health, scientific and political engagement in Belgium led to many evidence-based interventions, aimed at both the general public and healthcare professionals and those interventions in return resulted in a decrease in antibiotic use and resistance in the community and hospitals. They also show that creating awareness for the factors driving antimicrobial resistance and providing a knowledge base for physicians, public health experts and scientists is crucial in containing antibiotic resistance. A number of scientific conferences and public health workshops organised by BAPCOC were helpful in this respect.

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Experiences in prevention and control of antibiotic resistance in Slovenia

M Čižman (milan.cizman@mf.uni-lj.si)[1]
1. Department of Infectious Diseases, University Medical Center Ljubljana, Slovenia

During 1991-1999 a significant increase of consumption of macrolides and fluoroquinolones was observed in Slovenia, and this was associated with significant increase of resistance of *Streptococcus pneumoniae* and *Streptococcus pyogenes* to macrolides and *Escherichia coli* to fluoroquinolones, respectively. Between 1999 and 2007 the prevalence of *S. pneumoniae* resistant to erythromycin increased from 3.7% to 16.8% even though the use of macrolides in the same period decreased from 3.81 to 2.43 defined daily doses (DDD) per 1,000 inhabitants and per day. The co-resistance and the spread of resistant clones were the reason for constant increase in macrolide resistance. Slovenia is one of the few European countries with decreasing prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) in hospital care during the last years. As a result of control measures introduced in 1999, the MRSA prevalence rates decreased from 21.4% in 2000 to 8.3% in 2007.

Background

Slovenia is a small central European country with over two million inhabitants [1]. The country has a centralised compulsory Bismarck-style* health insurance system, which is administered by the Health Insurance Institute of Slovenia and includes almost all inhabitants (>99%). However, approximately 1.4 million residents also have supplementary health insurance provided by three private insurance providers. Prescription is needed for every antibiotic purchase, and in human medicine antibiotics may only be prescribed by physicians. The consumption of antibiotics in ambulatory care has been monitored in Slovenia since 1974, and the consumption of antibiotics in hospital care has been monitored since 1985. Since 2000 Slovenia has participated in EARSS (European Antibiotic Resistance Surveillance System) and since 2001 in ESAC (European Surveillance of Antibiotic Consumption) projects.

Resistance to antibiotics is a global public health problem. Selective antibiotic pressure and transferable resistance (clonal spread or horizontal resistance genes transfer) are major determinants of resistance development. It is irrefutable that the use of antibiotics promotes resistance. In this paper we describe the experiences in prevention and control of antibiotic resistance in ambulatory care, focusing on methicillin-resistant *Staphylococcus aureus* (MRSA) in hospital care.

Ambulatory care

In Slovenia the increased use of antibiotics in ambulatory care during the 1990s was associated with increased resistance of some respiratory infection pathogens. An increase in macrolide prescriptions by 3.5 between 1991 and 1996 was associated with significant increase in macrolide resistance in *Streptococcus pyogenes* and non-invasive *Streptococcus pneumoniae* between 1994 and 1997 [2]. Between 1994 and 1999, the macrolide consumption increased twofold, from 1.89 to 3.84 defined daily doses (DDD) per 1,000 inhabitants and per day, and at the same time the macrolide resistance in *S. pyogenes* increased from 0 to 7.4% and of non-invasive strains of *S. pneumoniae* from 0 to 9% [3]. The outpatient consumption of fluoroquinolones increased by 2.5, from 0.59 DDD per 1,000 inhabitants and per day in 1992 to 1.50 DDD per 1,000 inhabitants and per day in 1999 and this was paralleled by an increase of resistance of *Escherichia coli* to ciprofloxacin in adult patients from 3.6% in 1996 to 9.2% in 1999 [4].

Seeing that the resistance of some pathogens (*S. pneumoniae*, *S. pyogenes*, *E. coli*) had been increasing constantly, interventions were introduced to decrease their prevalence in the community. In June 2000, based on suggestions from infectious disease specialists, the Health Insurance Institute of Slovenia introduced administrative restrictive measures for the prescription of amoxicillin and clavulanic acid (co-amoxiclav) and fluoroquinolones [5]. Co-amoxiclav could no longer be prescribed for patients with *S. pyogenes* infections diagnosed clinically or documented microbiologically. Fluoroquinolones could only be prescribed as an alternative treatment for therapy of acute respiratory and urinary tract infections after clinical failure of first-choice antibiotics, or on the basis of tests showing susceptibility to fluoroquinolones and resistance to first-choice antibiotics [5]. In May 2004, the prescription of respiratory fluoroquinolones (moxifloxacin, levofloxacin) was modified. They could be prescribed in an unrestrictive manner only for severe community-acquired pneumonia and chronic obstructive pulmonary disease and when respiratory infection with resistant pathogens was expected. The staff of Health Insurance Institute of Slovenia checked the implementation of restrictive interventions by controlling individual prescriptions of physicians.

In Slovenia the overall consumption of antibiotics in outpatients decreased during the period between 2000 and 2007 by 20.32% [unpublished data]. However a greater decrease was observed for restricted than for non-restricted antibiotics (27.7% vs. 16.1%) [unpublished data]. This result shows that restrictive intervention can be efficient. To date a focused campaign directed at public and health care professionals has not been organised.

A detailed analysis of the causes and consequences of decreased antibiotic consumption over five years (1999-2003) showed a positive correlation between antibiotic consumption and repeated media reports and a negative correlation with the number of rapid diagnostic tests (C-reactive protein test (CRP), streptococcal antigen tests) [5]. Professional communication (scientific articles) and media reports for general public (lay articles) showed small negative correlation with antibiotic consumption. No increase in mastoiditis cases was observed in spite of reduced antibiotic consumption [5]. Reduced antibiotic consumption was paralleled by a decrease in penicillin resistance among invasive pneumococci and lower costs of antibacterials for systemic use. In contrast, reduced macrolide resistance rates of *S. pneumoniae* and *S. pyogenes* was not observed despite the 21.3% decline of total macrolide use during the period 1999 – 2004 [6].

A recent analysis showed that the prevalence of erythromycin resistance among invasive *S. pneumoniae* isolates increased from 3.7% in 1999 to 16.8% in 2007 in spite of a decrease of consumption of macrolides by 36.3% in the same period (from 3.81 to 2.43 DDD per 1,000 inhabitants and per day) [7]. The resistance increased almost eightfold among isolates from children (from 3.1% in 1999 to 24.6% in 2007). The most likely explanation for the continuous increase in macrolide resistance was co-resistance and the spread of resistant clones. The most frequent co-resistance pattern in the erythromycin-resistant strains of invasive *S. pneumoniae* isolates with erm(B) gene was resistance to penicillin, tetracycline and trimethoprim-sulfametoxazole.

To decrease the resistance of respiratory infection pathogens to macrolides, measures to reduce the use of macrolides especially new ones (by educational and/or restrictive interventions) and/or the introduction of conjugated pneumococcal vaccine are being discussed.

In addition, according to EARSS data the prevalence of resistance of *E. coli* to quinolones doubled (from 8.5% to 17.4%) between 2001 and 2007 in spite of reduced (15%) use of fluoroquinolones in the community (from 1.3 to 1.11 DDD per 1,000 inhabitants and per day) [8]. This data shows the complex correlation between antibiotic use and antibiotic resistance and indicates that the reduction of antibiotic use alone does not guarantee that lower prevalence of resistance can be achieved.

Hospital care

In 2008 Slovenia has 29 hospitals including two teaching hospitals, 10 general hospitals and 14 specialised hospitals providing orthopedic (1), pulmonary (2), gynecological (2), psychiatric (5), nursing (1), rehabilitation (2) and oncology (1) care, and three hospitals providing diagnostic or surgical procedures. All but three hospitals providing diagnostic or surgical procedures are state owned. In this section we focus exclusively on MRSA as an example to control antibiotic resistant bacteria. Slovenia is one of the few European countries which succeeded to reduce the prevalence of MRSA. In the period from 2000 to 2007 the prevalence decreased from 21.4% to 8.3% (by 61.3%).

In 1997 and 2001 two point prevalence studies showed high (75% and 60%) prevalence of MRSA in the adult intensive care units (ICU) in Slovenia [9]. Also a national point prevalence study of hospital-acquired infections in acute care hospitals in 2001 showed high (61.8%) prevalence of MRSA [10]. After the high prevalence of MRSA in Slovenia had been recognised two studies showed that with the comprehensive infection control program the number of MRSA cases could be decreased. In the first study the proportion of MRSA cases acquired in the hospital decreased from 50% to 6.1% during 1999 – 2002, and in the second the incidence of ICU-acquired MRSA decreased from 7.8% to 1.9% [11,12]. The legislation and regulation of the infection control program in health care institutions published in 1999 and the audit of infection control implementations in health care institutions published in 2006 also had an impact on the decline of the prevalence of MRSA in Slovenia [13,14].

Currently, the components of Slovenian strategy for MRSA control are:

- active surveillance – selective screening for MRSA in patients at risk of carrying MRSA on admission;
- contact isolation of patients with MRSA (not always possible because of single bedroom shortage);
- promotion of hand hygiene – use of alcohol-based hand rub;
- selective decolonisation;
- improved communication (reporting) about patients with MRSA within and between health care facilities;
- continuous education of health care workers (HCW) on appropriate hygiene procedures in health care institutions (hospitals, nursing homes);
- use of hospital computer system to record MRSA carriers;
- education of professionals (postgraduate educational courses have been organised by the Medical Faculty in Ljubljana since 1984 (162 physicians and 290 nurses have participated till 2008), national scientific meetings;
- education of patients (newspapers, magazines, TV, leaflets);
- spread of information to media and politicians.

The greatest obstacle for a further decrease in the prevalence of MRSA is the shortage of single-bed rooms and staff.

Notwithstanding the success in decreasing the prevalence of MRSA, a new resistant pathogen has emerged recently, the vancomycin-resistant enterococcus (VRE). Before the year 2005 according to EARSS data all invasive strains of *Enterococcus faecium* isolates had been susceptible to vancomycin [8]. In 2006, 6% and in 2007, 4.6 % of *E. faecium* invasive isolates were found to be resistant to vancomycin. The main source of resistant isolates are patients hospitalised in one haematological department in a tertiary care centre. In this department not enough single- or double-bed rooms are available, so the contact precautions are not possible to be provided.

In recent years higher use of linezolid was followed by the emergence of linezolid resistant enterococci (LRE) [unpublished data].

Conclusion

In Slovenia, antibiotic resistance is a problem in outpatient as well as hospital settings [8]. In order to combat antibiotic resistance, antibiotic policy and infection control are needed. Despite reduced use of all antibiotics including macrolides and fluoroquinolones in outpatient care, resistance of *S. pneumoniae* to macrolides and *E. coli* to fluoroquinolones is still increasing. Hospital consumption of antibiotics in Slovenia is moderate and stable and we have observed a decrease in MRSA prevalence probably due to better infection control [8,15]. However the emergence of VRE isolates has become an increasing problem in the last three years. Reducing prevalence of resistance is a difficult task; apart from prudent antibiotic use and better infection control it requires many other sustained interventions.

Acknowledgements

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*Note: Bismarck model healthcare systems are systems based on social insurance, where there is a multitude of insurance organisations (e.g. Krankenkassen) that are organisationally independent of healthcare providers.

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Improvements in antibiotic prescribing by community paediatricians in the Czech Republic

V Jindrák (vlastimil.jindrak@homolka.cz)[1], J Marek[2], V Vaniš[1], P Urbaskova[3], J Vlček[4], L Janiga[5], V Marešová[6]
1. Antibiotic Centre, Na Homolce Hospital, Prague, Czech Republic
2. Society for Primary Care Paediatricians, Czech Medical Association of J. E. Purkyně, Prague, Czech Republic
3. National Reference Laboratory for Antibiotics, National Institute of Public Health, Prague, Czech Republic
4. Department of Social and Clinical Pharmacy, Faculty of Pharmacy, Charles University, Hradec Králové, Czech Republic
5. Janiga Labs Information Technology (IT) Company, Prague, Czech Republic
6. 1st Department of Infectious Diseases, 2nd Faculty of Medicine, Charles University, Prague, Czech Republic

Repeated surveys among primary care paediatricians were performed annually from 1998 to 2002 in the Czech Republic. The task was to assess the prescription of antibiotics in treatment of respiratory infections in children. The results were evaluated in the light of existing guidelines and conclusions were used in a number of interventions aimed at reducing the inadequate use of antibiotics and hence preventing the potential increase of the antibiotic-resistant bacteria. In addition, data on overall consumption of antibiotics in outpatient care and trends in the prevalence of resistant strains of *Streptococcus pneumoniae* and *Streptococcus pyogenes* are discussed.

Introduction

The centrally regulated healthcare system with limited financial resources, existing in the former communist Czechoslovakia, resulted in a low level of antibiotic consumption and rare occurrence of antimicrobial resistance. Despite the obvious defects of the system, some remarkable activities established during this period have proved beneficial from the long-term perspective. One of these was the establishment of "antibiotic centres" in the 1970s which contributed to promoting the prudent use of antibiotics. These organisational units were incorporated into the clinical microbiology departments and made responsible for local surveillance of antimicrobial resistance and supervision of the use of restricted antimicrobials. The network of antibiotic centres has remained active until the present time and currently represents a local structure ready to use for the organisation of systematic interventions.

A significant shift in antibiotic consumption was observed in the early 1990s, after the political changes. The most significant change was documented from 1992 to 1994, when the privatisation of primary and outpatient care took place, and sophisticated marketing of pharmaceutical industry was introduced as a new phenomenon. In this period, the total ambulatory consumption of antibiotics increased from 14 to 20 defined daily doses (DDD) per 1,000 inhabitants and per day, and at the same time also the proportion of second-line antibiotics increased significantly although prescribing of these costly drugs was not appropriate in the existing epidemiological context [1]. The first warning signs of growing antimicrobial resistance among pathogens in the community were recorded a few years later. The earliest signal was associated with the rapidly increasing resistance of *Streptococcus pyogenes* to macrolides [2], which was probably due to changes in prescribing habits in primary paediatric care.

In these changed conditions, the application of new methods and innovative tools to prevent antibiotic resistance was needed. We describe a series of multicentre interventions, including annual surveys, aimed at identifying the diagnostic and prescribing habits and promoting the prudent use of antibiotics among participating paediatricians. In addition, we present data on overall ambulatory antibiotic consumption and antimicrobial resistance available from other sources.

Methods

Survey of antibiotic prescriptions in paediatric care

Annual surveys on outpatient antibiotic prescriptions in the treatment of respiratory infections in children were conducted among primary care paediatricians between 1998 and 2002. The surveys were organised every year during four weeks in November, with one week of follow up. The surveys in 1998, 1999 and 2000 were held in two Prague districts. The surveys in 2001 and 2002 were multicentre and involved 13 different districts across the Czech Republic. Participation in the survey was voluntary. Paediatricians were invited through regional coordinators of the Czech Society of Primary Care Paediatricians. Training sessions for participants were held before each annual survey: first centrally organised "training of trainers" later followed by local training seminars for participants in all regions. Two coordinators of the survey were established in every region including one expert from the antibiotic centre and one experienced paediatrician.

The questionnaire used in the survey focused on diagnostic and therapeutic approaches to the management of acute respiratory infections in children. The case definitions, criteria of appropriateness of antibiotic use and definitions of second-line antibiotics were adopted according to the national guidelines for antibiotic therapy in primary and ambulatory care issued, updated and disseminated by the Subcommittee on Antibiotic Policies of the Czech Medical Association [4]. Participating paediatricians were asked to fill in one questionnaire for each patient presenting with acute respiratory illness, irrespective of the prescription of antibiotics. Requested information included diagnostic approaches,

such as indication of laboratory or other diagnostic tests (e.g. throat swab culture, C-reactive protein test, X-ray examination). Aetiology of particular case of respiratory illness was presumed on the basis of clinical diagnosis. Computer software tools were developed for processing of questionnaires and validation and analysis of the data. The survey results were processed and communicated as individual, local and aggregated.

Interventions, educational activities

Feedback based on the results of the repeated surveys was the most important intervention tool used to promote good prescribing habits among participating doctors. This was accomplished by dissemination of printed survey results to individual doctors. In addition, a final conference and local seminars in regions were organised for participants to explain the obtained prescribing parameters. A comparison of individual approaches with a defined good practice was made.

Information obtained from the surveys was also used in educational activities organised by the Society for Primary Care Paediatricians, postgraduate training courses for all medical professionals and press conferences aimed at the general public.

Surveillance of ambulatory antibiotic consumption

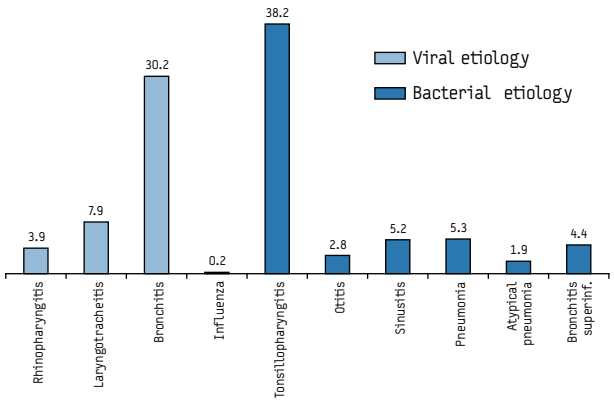
We used data on ambulatory antibiotic consumption that is reported yearly to the European Surveillance of Antimicrobial Consumption (ESAC). It is calculated on the basis of information obtained from health insurance system. Data obtained from this source are processed by the national ESAC co-ordinator according to the methods agreed by the WHO Collaborating Centre for Drug Statistics Methodology and ESAC [3]. Only aggregated data on the overall ambulatory consumption of antibiotics are available. Detailed sorting of the data according to a geographical area or medical specialisation is not possible.

Surveillance of antimicrobial resistance in community

Monitoring of the resistance of bacterial pathogens causing respiratory infections in the community has been organised by the National Reference Laboratory for Antibiotics since 1996. About 50 antibiotic centres are involved in this periodic surveillance every year. It takes place during the last quarter of the year and in 2007 covered a catchment population of about 80%. Every centre provides susceptibility data of 100 consecutive isolates of *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Streptococcus pyogenes* from clinically relevant samples.

FIGURE 1

The proportion of antibiotic prescriptions in treatment of community-acquired respiratory tract infections in children, by clinical diagnosis. Output of multicentre survey of antibiotic use in primary paediatric care in the Czech Republic in 2001



Results

Survey of antibiotic prescriptions in paediatric care

The repeated surveys identified the respiratory infections most frequently diagnosed as the cause of patients' visits to primary care paediatricians and revealed the doctors' prescribing habits in the context of particular clinical diagnosis [5,6]. The number of participating doctors varied from year to year: 13 took part in 1998, 23 in 1999, 28 in 2000, 114 in 2001 and 57 in 2002. The numbers of registered visits/cases of acute respiratory illnesses were the following: 3,707/3,006 (1999), 4,230/3,273 (2000), 31,077/19,013 (2001), 14,801/9,373 (2002). The numbers of visits per practitioner were comparable.

In the first survey in 1998 only information on cases in which antibiotics were prescribed was collected. In the following surveys (1999-2002) all cases of acute respiratory infections were documented including those in which no antibiotics were administered.

Here we present the results of the largest and most representative multicentre survey performed in 2001, but similar output was obtained in other survey years as well. In the 2001 survey, 19,013 acute respiratory illness cases were registered by the participating paediatricians with the following clinical diagnoses: rhinopharyngitis (56.3% of the cases), laryngotracheitis (13.8%), bronchitis (16.8%), influenza (1.9%), tonsillopharyngitis (18.3%), otitis (2.2%), sinusitis (2.4%), pneumonia (1.9%), atypical pneumonia (0.7%), bronchitis-bacterial superinfection (1.5%). Several visits with different diagnoses could be linked to one case which is why the sum of these percentages exceeds 100%. We estimated that in 42.2% of the cases in which antibiotics were prescribed, the prescriptions were issued inappropriately for an inadequate treatment of predominantly viral illnesses. Prescribing preferences according to clinical diagnosis are described in Figure 1. Acute bronchitis and laryngotracheitis represented 38.1% of all indications for antibiotic treatment. This percentage indicates a large proportion of overuse and the opportunity for improvement. The treatment was initiated using second-line and more expensive drug in 47.2% of all cases in which antibiotics were prescribed while the first choice and mostly cheaper antibiotic recommended in an official guideline was not used.

Interventions, educational activities

Taking part in the survey and receiving feedback seems to have positively influenced the prescribing habits of participating physicians. The 57 doctors who participated in the survey in both 2001 and 2002 and reported a significant number of cases of acute bronchitis and laryngotracheitis, had changed their prescribing habits and considerably reduced the use of antibiotics in inadequate indications (Figure 2). A rapid improvement of prescribing preferences in the treatment of acute tonsillopharyngitis of 10 doctors participating in surveys in 1998, 1999 and 2000 is shown in Figure 3 as another example of the interventional effect.

Based on the results of the surveys, half-day seminars focused on prudent use of antibiotics in paediatrics were organised in all

regions of the Czech Republic during 2002, in the framework of official educational activities of the Society for Primary Care Paediatricians. The information obtained from the surveys was disseminated via this multicentre educational event to all interested paediatricians. Easy to understand messages explaining the priorities for improvement and ways to reach better prescribing practices were communicated.

In addition, since 2002, interdisciplinary training courses on the use of antibiotics have been regularly organised by the Institute for Postgraduate Medical Education.

No specific financial resources were available for the preparation of systematic public campaigns. Nevertheless two press conferences specifically focused on the overuse of antibiotics and on the threat of antimicrobial resistance were held in 2002 and 2003.

Trends in ambulatory antibiotic consumption

The quantitative trends in outpatient consumption of antibiotics in the Czech Republic are shown in Figure 4. In the early 1990s, the total antibiotic consumption was approximately 14 DDD per 1,000 inhabitants and per day, with penicillins predominating. An increase of consumption to 20 DDD per 1,000 inhabitants and per day occurred during 1994, and remained at that level till 2002.

A qualitative change was observed from 1990 to 1994: the proportion of penicillins decreased giving way to macrolides (increase from 0.33 to 1.75 DDD per 1,000 inhabitants and per day), aminopenicillins with beta-lactamase inhibitors (0.01 to 1.4 DDD per 1,000 inhabitants and per day) and cephalosporines (0.16 to 1.04 DDD per 1,000 inhabitants and per day). Subsequently, in

FIGURE 2

The proportion of antibiotic prescriptions in treatment of predominantly viral respiratory tract infections in children. Comparison of results of repeated surveys including 57 primary care paediatricians in the Czech Republic in 2001 and 2002

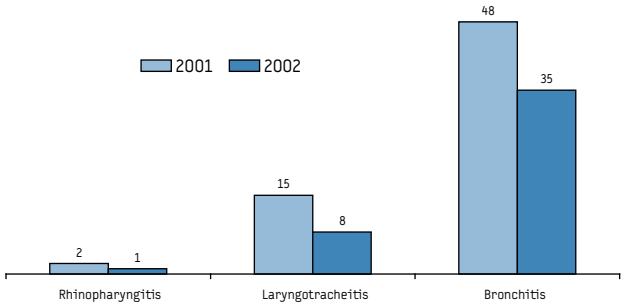


FIGURE 3

The proportion of various classes of antibiotics prescribed in treatment of acute tonsillopharyngitis in children. Comparison of results of repeated surveys including 10 primary care paediatricians, in the Czech Republic in 1998, 1999 and 2000

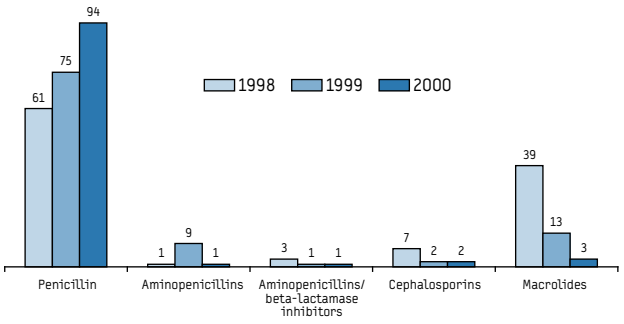
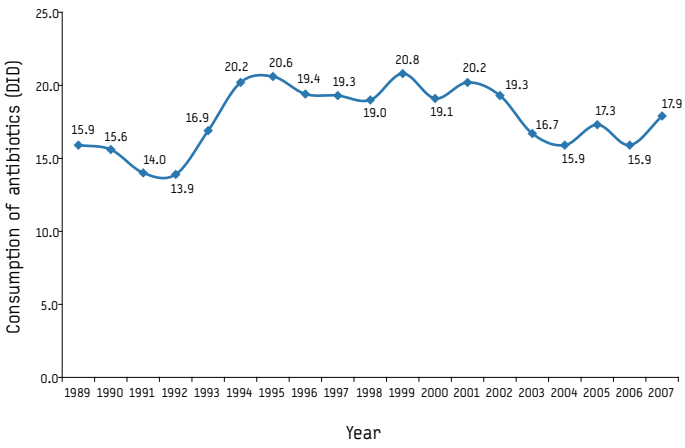


FIGURE 4

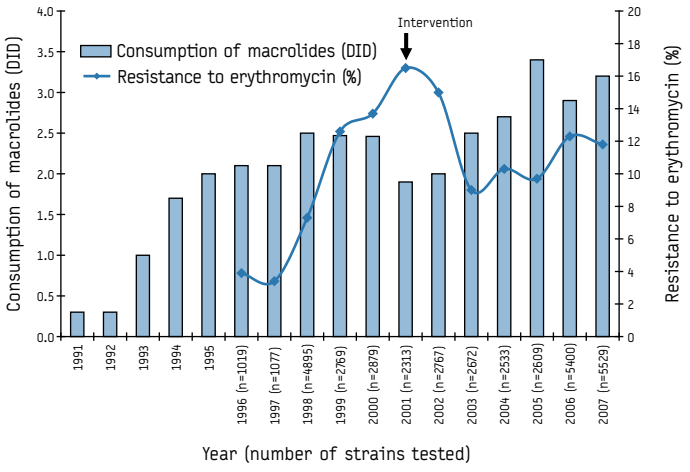
Trends in ambulatory antibiotic consumption, Czech Republic, 1989 - 2007



Source of data: 1989-2002 [1], 2003-2006 [3], 2007 - preliminary data
DID - Defined daily doses per 1,000 inhabitants and per day

FIGURE 5

Total consumption of macrolides in the community and resistance of *Streptococcus pyogenes* to erythromycin, Czech Republic, 1991-2007



Note: The arrow indicates the beginning of official educational activities in prudent use of antibiotics in paediatric care organised by the Czech Medical Association
Source of data on consumption: 1989-2002 [1], 2003-2006 [3], 2007 - preliminary data.
DID - Defined daily doses per 1,000 inhabitants and per day

2003, a significant decrease of the overall antibiotic consumption was observed, however its qualitative structure remained inappropriate (high consumption of aminopenicillins with beta-lactamase inhibitors, macrolides and fluoroquinolones) [1,3].

Trends in antimicrobial resistance in community

The resistance of some bacterial pathogens causing community acquired respiratory infections has remained low in the past years. This is namely true for *Streptococcus pneumoniae*. The strains causing invasive infections [7], as well as respiratory isolates are mostly fully susceptible to penicillin, intermediate susceptibility is present only in 4-5% of the isolates, and a high-level resistance is extremely rare. The resistance of invasive isolates to erythromycin is one of the lowest in Europe [7]. The situation is different for *Streptococcus pyogenes*. A rapid increase of resistance to erythromycin from 3% to more than 16% was observed between 1996 and 2000. This dangerous trend was interrupted and the rates fell back to 9% in 2002-2003 [2]. A decrease in macrolide consumption during 2001-2002 was probably in the background of this phenomenon. However, from 2003, the consumption has been rapidly growing again, which is likely to cause increase in resistance.

Discussion

The fact that more than half of the patients' visits to paediatricians are due to common cold (56% reported in 2001 survey) was surprising. At the same time, antibiotic prescription for common cold was rare. Nevertheless it is important to note that frequent visits due to this self-limited illness induce unnecessary overloading of paediatricians, when time and resources could be used to address more serious problems, including careful explanation of non-antibiotic management of viral illnesses to the patients and the parents.

In the surveys, the overuse of antibiotics for viral respiratory illnesses was especially marked in case of febrile, coughing children with diagnosis of acute bronchitis or laryngotracheitis. This clinical picture has a strong psychological impact influencing the decisions of doctors as well as treatment expectations of parents. Meta-analyses arguing in favour of non-antibiotic management of these diseases were available already during the 1990s but the traditional approach previously recommended antibiotic treatment.

The differentiation between bacterial and viral aetiology of acute tonsillopharyngitis and otitis media was not done in the surveys described here. However, an important fraction of these illnesses is caused by viruses and this fact represents another chance for improvement of diagnostics and antibiotic prescribing.

Our results clearly identified priorities for systematic interventions with a potential to eliminate about 40% of total antibiotic prescriptions in primary paediatric care. The influence of the repeated surveying showed good example of real improvement.

The limited availability of structured ambulatory consumption data makes it impossible to carry out a detailed analysis of antibiotic usage for particular medical specialities (primary care paediatricians, general practitioners for adults, outpatient specialists), for smaller geographical areas (regions, districts), and for the routine evaluation of prescribing patterns of individual doctors. Consequently, the impact of interventions is difficult to analyse, and the basis for routine performing of systematic activities are incomplete. This barrier seems to be an important obstacle in persuading health insurance companies to organise nationwide interventions.

No change in the healthcare reimbursement system was made which could have contributed to the decrease of antibiotic consumption observed from 2003. The change from "fee for service" to "per capita" payment was carried out for primary care in 1997, surprisingly without any influence on high ambulatory consumption of antibiotics during the late nineties. No significant differences in the occurrence of acute respiratory illnesses were observed in association with decreasing antibiotic consumption before or after 2003.

The decrease in the resistance of *Streptococcus pyogenes* to erythromycin seems to be in correlation with a time-limited decrease in macrolide consumption which may be at least partially attributed to the performed surveys and interventions (Figure 5). Nevertheless, more detailed analyses are needed to identify the reasons behind these resistance trends. Only a short interruption of the increasing macrolide consumption (2001-2002) indicates a limited sustainability of the outcome of performed interventions, which should be long lasting and nationwide. Otherwise, drug marketing can easily overcome its effectiveness.

The echo of press conferences has remained quite long lasting. There are more opportunities to address the general public in the media, including radio and television, in comparison with the previous period. The journalists seem to be still interested in this topic which facilitates the organisation of the first European Antibiotic Awareness Day this year.

Conclusions and further developments

The results of limited interventions performed in connection with the annual voluntary surveys among paediatricians in the Czech Republic provided good background for the planning of systematic nationwide activities focused on the prudent use of antibiotics and control of antimicrobial resistance in the community. The expectations regarding potential savings of the budget of the public health insurance system are fully justified. A specialised training of regional coordinators supporting good prescribing practice has been running since 2005 and a pool of competent professionals has been constantly growing. However, we are now at a starting point for further developments when routine operations of the existing know-how require regular support from the government and health insurance companies.

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Strama - a Swedish working model for containment of antibiotic resistance

S Mölstad[1,2], O Cars[3], Johan Struwe (johan.struwe@smi.ki.se)[3]
1. Unit of Research and Development in Primary Care, Jönköping, Sweden
2. Department of Medical and Health Sciences, Linköping University, Linköping, Sweden
3. The Swedish Strategic Programme against Antibiotic Resistance - Strama, Solna, Sweden

The overall aim of Strama (The Swedish Strategic Programme Against Antibiotic Resistance) is to preserve the effectiveness of antibiotics in humans and animals. Strama is organised at two levels: a network of independent local multidisciplinary groups in each county that provide prescribers with feedback on antibiotic use and resistance and implement guidelines; and a national executive working group funded by the government. To gain an insight into antibiotic use, Strama has conducted several large diagnosis-prescribing surveys in primary care, in the hospital settings and in nursing homes. National antibiotic susceptibility data for Sweden and mandatory notification show that in recent years the proportion of *Streptococcus pneumoniae* with decreased sensitivity to penicillin V has stabilised (around 6 %), but the number of notified cases of meticillin-resistant *Staphylococcus aureus* (MRSA) has increased and ESBL-producing *Enterobacteraceae* have turned into an endemic situation. Still, Sweden is among the countries with the lowest rates of MRSA (<1 %), *S. pneumoniae* can still be treated with penicillin V and the rate of *Escherichia coli*-producing ESBLs is below 5 %. Strama´s activities have contributed to a steady decrease in antibiotic use from the mid 1990s until 2004 (when total use slowly started to increase again) without measurable negative consequences. Regular collaboration with national and regional news media has been one of the key strategies.

Background

Increasing use of antibiotics and spread of penicillin-resistant pneumococcal clones in the beginning of the 1990s alarmed the medical profession and authorities in Sweden. Strama (The Swedish Strategic Programme against Antibiotic Resistance) started as an informal network between experts and authorities in 1994. In 2000, Strama, in close cooperation with the National Board of Health and Welfare, prepared a proposal for a national action plan to contain antibiotic resistance [1]. This proposal was later developed into a governmental bill "Strategy to prevent antibiotic resistance and health-care associated infections" [2], which was passed in 2006. Since then Strama has been institutionalised as an independent governmental body with an annual budget of 10 million Swedish crowns from the Ministry of Health and Social Affairs. Recently, a corresponding Strama VL (Veterinary and Food) coordinated by the National Veterinary Institute has been inaugurated.

The overall aim of Strama's activities is to preserve the effectiveness of antibiotics in humans and animals. Strama is organised at two levels: local groups in each county and a national executive working group funded by the government. Detailed overviews of the efforts to contain antibiotic resistance in Sweden and of the systems for the surveillance of antibiotic consumption and antibiotic resistance have been published [3-5].

Local Strama groups

Strama developed as a network with nodes of independent local groups coordinated by each county department for communicable disease control. The local groups are the drivers of Strama activities. These local groups usually comprise specialists in communicable diseases, infectious diseases, clinical microbiology, infection control, general practice and pharmacy. Paediatricians as well as ear, nose and throat specialists are common additional members. In most counties there is a close link to the local drug and therapeutics committee.

The guiding principle underlying local Strama activities is to promote the rational use of antibiotics by providing prescribers with feedback on local or individual data on prescription for comparison with other prescribers and prevailing therapy recommendations. Local data on antibiotic resistance is provided by the clinical microbiology laboratory. Other important activities are to develop local therapeutic guidelines and to organise courses and lectures for local physicians and other health-care workers at different levels of training. While initially focussing on general practice, parallel groups targeting hospital care were recently developed in an increasing number of counties and regions.

There is no formal reporting on either activities or on budgets from the local groups to the national level. Data from local projects are shared and discussed at national meetings at least once annually. A problem is that many of the local activities rely on personal commitment from devoted physicians and that a formal mandate and financial support from the county council is still missing in many counties. However, the awareness of a need for such targeted and mandated activities to contain antibiotic resistance is slowly increasing and a growing number of Strama groups (or equivalent bodies) are now supported.

Strama at national level

While the local groups coordinate activities targeting local prescribers, the national executive working group is responsible for national coordination of information and meetings, initiating studies in areas where knowledge gaps have been identified, disseminating Strama´s results and acting as a node for international collaboration. The executive working group is supported by a secretariat.

Strama has a formal regulatory instruction from the Swedish government. The chairman is appointed by the government and reports directly to the Ministry of Health and Social affairs. The Strama governance board has members from the Swedish Institute for Infectious Disease Control, the National Board of Health and Welfare, the National Veterinary Institute, the Medical Products Agency, the Swedish Corporation of Pharmacies (Apoteket AB), the Swedish Association of Local Authorities and Regions, the Swedish Reference Group for Antibiotics and the professional societies for infectious diseases, infection control and communicable diseases. The executive working group has a broad multisectorial composition including several clinicians and meets at least bimonthly to outline working-directions and priorities and to define areas needing further studies.

Although penicillin resistance in *S. pneumoniae* in the community was the first target of Strama, national activities have continuously expanded and today include many additional fields e.g. hospital care, intensive care ("ICU-Strama") [6-7], nursing homes, day-care centers and clinical trials. ICU-Strama has developed a close collaboration with the Swedish Intensive Care Registry (SIR) and is now integrated as a part of its national quality registry. Experiences from ICU-Strama have been incorporated into the European network care-ICU [8].

Strama has co-organised several workshops yielding national recommendations for the treatment of various diagnoses common in general practice such as acute otitis media, acute pharyngotonsillitis, impetigo, acute sinusitis, urinary tract infections and lower respiratory tract infections.

The national office supports the local groups, coordinates different activities, supplies national data and manages a national website (www.strama.se). A national meeting with annual updates on scientific and medical aspects of antibiotic resistance, statistics on antibiotic use and resistance as well as results and analysis of performed studies, interventions and educational programmes is held for the members of the local Strama groups and other interested parties. Abstracts and/or presentations are distributed via the website for further dissemination as a rule. News, regional and national data on antibiotic use and resistance are regularly updated as well as treatment guidelines and results from Strama-funded projects. A physician is contracted who regularly distributes relevant news in the field from the medical press and other sources and "Strama News" containing summaries of relevant recent scientific publications is distributed by email to listed subscribers about eight times a year.

Occasionally, a more acute situation unfolds and calls for more extensive actions. This was the case when it became evident that *Enterobacteriaceae* producing extended-spectrum beta-lactamases (ESBLs) rapidly became increasingly prevalent and caused outbreaks. This prompted Strama to organise a workshop whose findings were then translated into a proposal for a national action plan [9].

Antibiotic utilisation

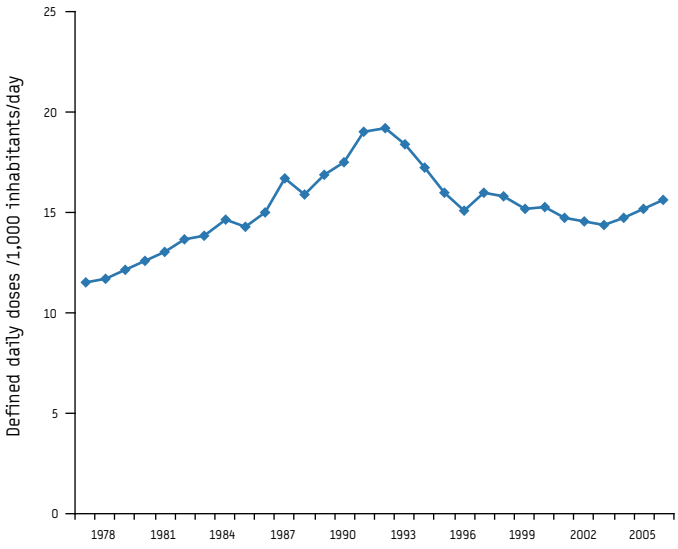
Strama has taken the responsibility for the regular analysis of antibiotic consumption at national level. A detailed description and analysis of antibiotic consumption and resistance: "SWEDRES - A report on Swedish antimicrobial utilisation and resistance in human medicine" is published yearly in collaboration with Swedish Institute for Infectious Disease Control (SMI) and is co-produced and packaged with the corresponding veterinary report SVARM [5]. Following the increased awareness and the inception of the Strama programme, the total antibiotic sales in general practice in Sweden continuously decreased in the 1990s until 2004. In contrast, the other Nordic countries have either remained at a comparatively higher level of antibiotic use (Iceland and Finland) or experienced an uninterrupted increasing trend. According to official figures from the respective medicine agencies in the Nordic countries, Sweden has had the lowest antibiotic use since 2003. However, since 2004 a slow rise, mainly attributable to increased prescription of penicillin to children, has been seen again (Figure 1).

Drug-prescribing surveys and other studies

To learn more about compliance with guidelines in general practice and about antibiotic use in the hospital setting, Strama has initiated and coordinated several large diagnosis- prescribing surveys. The use of antibiotics in primary care and compliance with the recommendations from the workshops and the quality indicators defined by the General Practitioners Association (SFAM) have been studied in diagnosis-prescribing surveys conducted in 2000, 2002 and 2005 [10-15]. These studies comprised altogether 15,371 patients with infectious symptoms treated by around 600 general practitioners (GPs). The studies showed high antibiotic prescribing in acute otitis media, acute pharyngotonsillitis and acute bronchitis, indicating that the current treatment guidelines for these conditions had not been not fully implemented. For the treatment of uncomplicated urinary tract infections a shift from the use of trimethoprim and fluoroquinolones to pivmecillinam and nitrofurantoin is recommended. A restricted use of fluoroquinolones was advocated already in 1996, [16] leading to a decreasing trend as clearly documented in the surveys.

FIGURE 1

Antibiotic use in outpatients, methenamine excluded, in defined daily doses (DDD) per 1,000 inhabitants and per day, Sweden, 1978-2007



Source: Apoteket AB

To address antibiotic use in the hospital setting Strama initiated and coordinated nationwide point prevalence studies in 2003, 2004 and 2006. The number of participating hospitals was 54, 49 and 64 and the number of covered hospitalised patients (proportion of all hospitalised patients in somatic clinics in the respective years) was 13,536 (60 %), 11,348 (50%) and 17,113 (80 %), respectively [17]. Data in these studies were reported by a web-based system and results were likewise available for the participating Strama groups. The studies showed that approximately every third hospitalised patient on a given day received antibiotics. While almost 10 % were given antibiotics to treat a health-care associated infection, 6-7 % were given surgical or medical prophylaxis and the remaining 17-19 % treatment for a community acquired infection. The method and protocols used formed the basis for a pan-European study coordinated by ESAC [18].

Increasing antibiotic use in the elderly population prompted a separate study in 2004 on indications for antibiotic prescribing in 58 nursing homes [19].

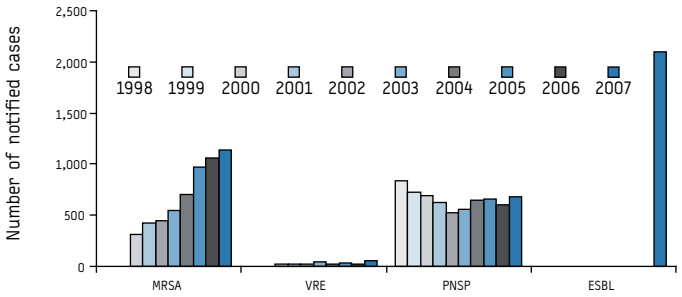
It is important that as a result of the efforts to improve antibiotic use, the reduction in prescriptions does not cause unwanted negative effects. A survey of hospital admissions recorded in the national registry of diagnosis in hospital care, showed no increase in the number of patients with acute sinusitis, quinsy and acute mastoiditis despite the reduction in antibiotic prescriptions for children between 1987 and 2003 [20]. Continuous systems for such monitoring need to be implemented. Another important task for Strama is to encourage studies aimed at preserving the efficacy of existing drugs e.g. through modified dosing regimens or drug combinations.

Antibiotic resistance

A comparatively widespread practice of culturing clinical specimens in combination with well-functioning diagnostic laboratories using harmonised methods (www.srga.org) have formed the basis for the surveillance of antibiotic resistance in Sweden. Surveillance mainly relies on two major sources: notification of any resistance according to the Swedish Communicable Diseases Act and since 2002 a combined surveillance and quality control programme (RSQC surveys) that was further developed into the web-based ResNet (http://130.237.97.245/ResNet/index.jsp). National antibiotic susceptibility data are presented regularly on the internet. Figure 2 illustrates reporting according to the Swedish Communicable Diseases Act. While the proportion of *S. pneumoniae* with decreased sensitivity to penicillin V has stabilised, the number of notified cases of methicillin-resistant *Staphylococcus aureus* (MRSA) has increased, ESBL-producing Enterobacteracaeae have turned into an endemic situation and, most recently, the hitherto largest outbreaks of vancomycin-resistant enterococci (VRE) is ongoing in the Stockholm region. Still, Sweden is among the countries with the lowest rates of MRSA (still below 1 %), *S. pneumoniae* can still be treated with penicillin V and the rate of *Escherichia coli*-producing ESBLs is below 5 %.

Figure 2

Notifications of infections or colonisation with antibiotic-resistant pathogens notifiable by the Swedish Communicable Disease Act, 1998-2007



MRSA: methicillin-resistant *S. aureus* since year 2000
VRE: vancomycin-resistant *E. feacalis* and *E. feacium* since year 2000
PNSP: penicillin-nonsusceptible *Streptococcus pneumoniae* (minimum inhibitory concentration (MIC) for penicillin G ≥ 0.5 mg/L, since 1996)
ESBL: extended spectrum beta-lactamase-producing Enterobacteriaceae, since 2007.

Conclusions

Strama's multidisciplinary and multisectorial programme has developed into a coordinated national effort that has contributed to a decrease in antibiotic use without measurable negative consequences. Furthermore, resistance levels are still comparatively low in Sweden. Some factors that have paved the way for this success have been the utilisation and early involvement of pre-existing structures and resources such as the communicable disease officers, the multi-disciplinary approach, the collaboration with the local drug and therapeutics committees and microbiology laboratories and the political support at national level. The most suitable structure for such local nodes will no doubt differ from one country to the next and may take some extra resources to identify and put in place. Particular difficulties can be expected when trying to collect local data sent to different (remote) microbiology laboratories and to develop mechanisms to aggregate prescriptions from individual prescribers or health-care facilities. Not least, regular collaboration with national and regional news media has been one of the key strategies.

Recently, however, antibiotic sales seem to have started to rise again and resistance is increasing in several species. This must be met by intensified information and education campaigns, aimed at doctors as well as the general public, on the rational use of antibiotics and the promotion of compliance with basic hygiene in the health-care sector. Examples of areas which call for further attention are antibiotic use in long-term care facilities, among private health-care providers, to treat sexually transmitted diseases (STIs) and for some chronic conditions such as acne, chronic obstructive pulmonary disease and diabetic foot infections. To achieve this goal, all local groups should be formally supported with a defined mission incorporated in the patient safety and quality work by 2010.

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Experiences with the Dutch Working Party on Antibiotic Policy (SWAB)

J M Prins (j.m.prins@amc.nl)[1], J E Degener[2], A J de Neeling[3], I C Gyssens[4,5], the SWAB board

1. Academic Medical Center, Department of Internal Medicine, Division of Infectious Diseases, Tropical Medicine and AIDS, Amsterdam, the Netherlands
2. Department of Medical Microbiology, University Medical Centre Groningen, Groningen, the Netherlands
3. Laboratory for Infectious Diseases and Perinatal Screening (LIS), National Institute for Public Health and the Environment (RIVM), Bilthoven, the Netherlands
4. Infectious Diseases Section, Department of Medicine, Nijmegen University Center for Infectious Diseases (NUCI), Radboud University Nijmegen, Nijmegen, the Netherlands
5. Department of Medical Microbiology and Infectious Diseases Canisius Wilhelmina Hospital, Nijmegen, the Netherlands

The Dutch Working Party on Antibiotic Policy (Stichting Werkgroep AntibioticaBeleid, SWAB) was founded in 1996 as an initiative of the Society for Infectious Diseases, the Dutch Society for Medical Microbiology, and the Dutch Association of Hospital Pharmacists. Its primary goal is to contribute to the containment of antimicrobial resistance and the expanding costs incurred for the use of antibiotics. SWAB is the Intersectoral Coordinating Mechanism (ICM) for the Netherlands, and it is at present the National Antimicrobial Resistance (AMR) Focal Point. It coordinates the national surveillance of antibiotic resistance, in collaboration with the National Institute for Public Health and the Environment (RIVM), coordinates the surveillance of the use of antibiotics, and runs a guideline development programme. Information about consumption of antimicrobial agents and antimicrobial resistance among medically important bacteria is presented annually in NethMap. Over the past decade, outpatient consumption of antibiotics has risen only slightly, but in the hospital setting there was an overall significant increase in antibiotic use, due mainly to the steady reduction in the average length of patient hospital stays. In 2006 we introduced our electronic national antibiotic guide 'SWAB-ID' for the antibiotic treatment and prophylaxis of common infectious diseases in hospitals.

Background

The Dutch Working Party on Antibiotic Policy (Stichting Werkgroep Antibiotica Beleid, SWAB) was founded in 1996 as an initiative of the Society for Infectious Diseases (VIZ), the Dutch Society for Medical Microbiology (NVMM), and the Dutch Association of Hospital Pharmacists (NVZA). Its primary goal is to contribute to the containment of antimicrobial resistance and the expanding costs incurred for the use of antibiotics. This was to be achieved by optimising the use of antibiotics through guideline development, education, and surveillance of antibiotic use and resistance. Following advice by the Dutch Advisory Council on Health Research in 2000 on the containment of Antibiotic Resistance, in 2001 SWAB was appointed by the Dutch Ministry of Health, Welfare and Sports to coordinate the national surveillance of antibiotic resistance, in collaboration with the National Institute for Public Health and the Environment (RIVM) (currently: the Centre for Infectious Disease Control Netherlands, CiB), and to coordinate the surveillance of the use of antibiotics. Structural funds were provided, also for the guideline development programme. Finally, a platform with the Veterinary Antibiotic Usage and Resistance Surveillance Working Group (VANTURES) was created. When the "Council Recommendation on the prudent use of antimicrobial agents in human medicine" (2002/77/EC) [1] was issued, SWAB became the Intersectoral Coordinating Mechanism (ICM) for the Netherlands, and it is at present the National AMR Focal Point.

NethMap – the annual report on antimicrobial use and resistance

NethMap 2003 was the first epidemiological report with information about consumption of antimicrobial agents and antimicrobial resistance among medically important bacteria in the Netherlands. It was presented in April 2003 during the SWAB symposium 2003 [2]. NethMap was named after a similar yearly report from Denmark (DANMAP). In contrast to the DANMAP report, veterinary data in the Netherlands are published in separate reports, called MARAN (http://www.cvi.wur.nl/NL/publicaties/rapporten/maranrapportage/).

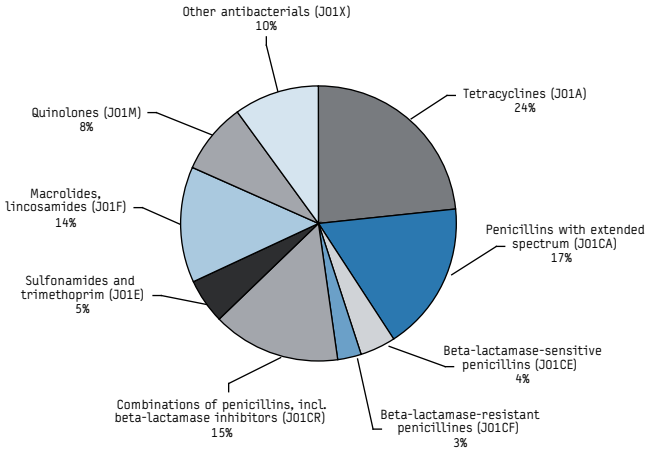
From 2003 through 2008 NethMap has been updated annually, and can be downloaded from http://www.swab.nl >professional>NethMap. NethMap is published by SWAB in collaboration with the RIVM. Data on delivery of antimicrobials from hospital pharmacies are collected by SWAB (Figure 1), and data from 90% of all community pharmacies are provided by the Foundation for Pharmaceutical Statistics (Figure 2). Data on antimicrobial resistance in hospitals are collected from local laboratories by RIVM. The susceptibility of strains collected from outpatients and hospital departments (Urology, Pulmonology and Intensive Care) is determined quantitatively by the Laboratory of Medical Microbiology of Maastricht University. The population coverage for the resistance surveillance programmes is approximately 30%.

Over the past decade, outpatient consumption of antibiotics has risen only slightly, from 9.9 to 11.1 defined daily doses

(DDD)/1,000 inhabitants/day. In hospitals overall antibiotic use increased significantly from 47.8 to 62.2 DDD per 100 patient-days, but this increase was due to the steady reduction in the average length of patient hospital stays. Overall antibiotic use per 100 admitted patients remained constant. Outside hospitals, co-amoxiclav gradually replaced amoxicillin (Figure 3) and, according to revised guidelines for general practitioners (GPs) for the treatment of cystitis, more nitrofurantoin was used at the expense of trimethoprim. The percentage of *Streptococcus pneumoniae* which was of intermediate susceptibility or resistant to penicillin and the percentage of *Staphylococcus aureus* resistant to oxacillin (MRSA) remained lower than 3%, but resistance of *S. pneumoniae* and *S. aureus* to macrolides has increased to nearly 10% of the investigated isolates. *Escherichia coli* resistance to ciprofloxacin among hospitalised patients increased to 9% in 2007 (Figure 4). Occasionally, hospital epidemics of *Klebsiella pneumoniae* resistant to third-generation cephalosporins occurred, but the overall percentage of such strains remained low at 3-6%. In contrast, the ciprofloxacin resistance in *Neisseria gonorrhoeae* from sexually transmitted diseases' (STD) clinics has increased to such a high level (44%) that fluoroquinolones cannot be advised anymore for first-line treatment. The Dutch guidelines for treating gonorrhoea have been adapted accordingly.

Figure 1

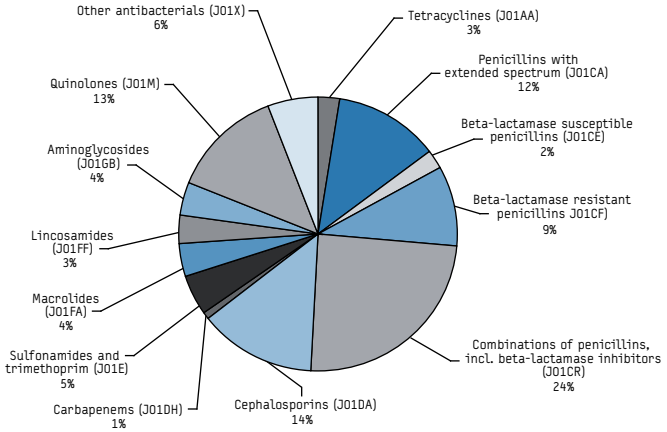
Distribution of antibiotics administered for systemic use* (defined daily doses (DDD)/1,000 inhabitants/day) in primary health care, the Netherlands 2007



Source: Stichting Farmaceutische Kengetallen - SFK.
* Anatomical Therapeutic Chemical (ATC) Classification System J01

Figure 2

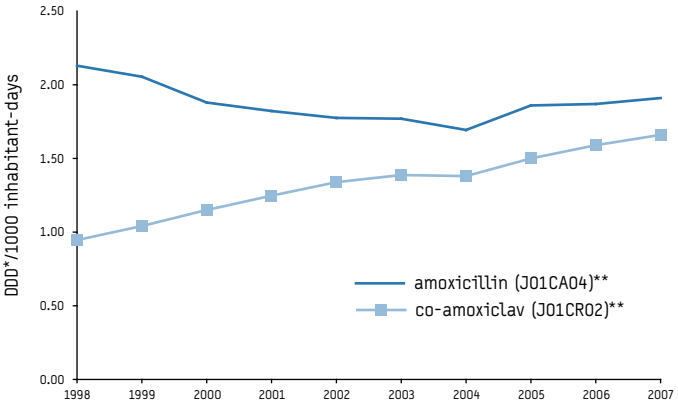
Distribution of antibiotics administered for systemic use* (Defined Daily Doses (DDD)/100 patient-days) in hospitals, the Netherlands, 2006



Source: Dutch Working Party on Antibiotic Policy - SWAB.
* Anatomical Therapeutic Chemical (ATC) Classification System J01

Figure 3

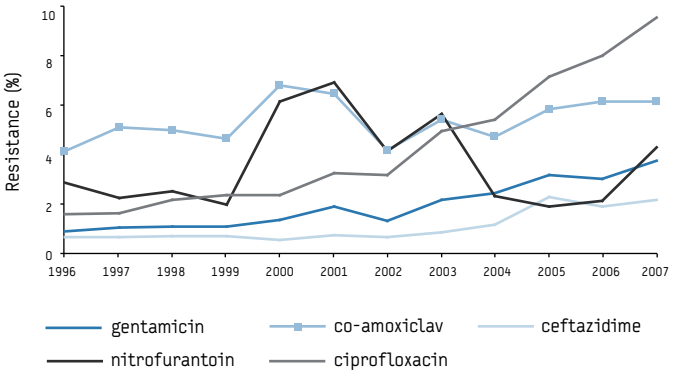
Use of amoxicillin and co-amoxiclav in primary health care, the Netherlands 1998 – 2007



Source: Stichting Farmaceutische Kengetallen – SFK.
* Defined Daily Doses
** Anatomical Therapeutic Chemical (ATC) classification code

Figure 4

Trends in resistance to antibiotics among *Escherichia coli* from unselected hospital departments, the Netherlands, 1996-2007



Guideline development in the Netherlands

Since the late 1980s, the Dutch College for General Practitioners has been running a guideline programme. Guidelines have been developed for e.g. otitis media in children, sinusitis, sore throat and pneumonia. These guidelines are regularly updated. In addition, the GPs have in place a "peer review group" system: a nationwide structure of general practitioners' peer review groups, with collaborating pharmacists, which aims to promote rational prescribing through audit and feedback [3].

Since its conception, SWAB has developed national guidelines for the use of antibiotics, which are aimed at the hospitalised adult patient. Initially, the draft guidelines were prepared by a writing committee, selected by SWAB, consisting of five to ten experts: medical microbiologists, infectious diseases' specialists, hospital pharmacists and medical specialists relevant to the specific topic. After review by another 25 experts, the guidelines were finalised and published. Guidelines were published in the major national Dutch medical journal (Nederlands Tijdschrift voor Geneeskunde) [4].

In 2001, a survey among hospital antibiotic policy committees revealed that the majority of respondents were aware of SWAB guidelines, but it was suggested that the draft guidelines should be made more broadly available, e.g. on the internet, and with a clearer method for grading the strength of the evidence on which the guideline was based. A particular feature of infectious diseases' guidelines is that local epidemiology and resistance data must be taken into account, and NethMap has provided this information since 2003. As a result of our survey and following the principles of evidence-based guideline development [5] we revised the procedures for the development of SWAB guidelines in 2005 [6,7]. The new procedure includes the consultation of the concerned professional societies for delegating experts to the writing committee, and all their members are given an opportunity to comment on draft guidelines. There are now also GPs on the writing committee to ensure that there is consistency between the guidelines for ambulatory care and hospitals. After final approval by the board, SWAB guidelines are posted on the SWAB website (www.swab.nl). For most of the guidelines English versions are freely available from the internet. Implementation of the guidelines in hospitals is studied by government-funded research projects [8].

The national electronic antibiotic guide 'SWAB-ID' for use in hospitals

The survey (unpublished data) among Dutch hospital antibiotic policy committees also revealed their wish to compile a comprehensive, national antibiotic treatment guide. SWAB took up this challenge, and in 2006 we introduced our electronic national antibiotic guide 'SWAB-ID' for the antibiotic treatment and prophylaxis of common infectious diseases in hospitals [9]. This guide also contains a formulary for all antimicrobial drugs available in the Netherlands. Treatment choices and dose regimens are based on existing national evidence-based guidelines, where available. Where no guideline is available, the advice is based on an inventory of the antibiotic policies of the 12 Dutch centres with an infectious diseases' or medical microbiology training programme. The national antibiotic guide can be accessed through the SWAB website (http://customid.duhs.duke.edu/NL/Main/Start.asp) and can also be downloaded on PDA/PocketPC, free of charge. The guide is updated regularly, for instance when new guidelines are issued or new antimicrobial agents become available.

Every hospital antibiotic policy committee in the Netherlands is offered the opportunity to edit the national version for local use. For a relatively small fee, SWAB provides a copy of the national version, in which adaptations can be made if local circumstances so demand, and this local version is again accessible through the internet, and downloadable on PDA. So far, six out of eight university hospitals, and ten non-academic hospitals / hospital groups are now using a local version of the national SWAB guide.

SWAB, Europe, and the First European Antibiotic Awareness Day

SWAB assisted Croatia in implementing EU directives and recommendations in the field of antimicrobial resistance and the sound use of antibiotics within a framework project launched by the Dutch Ministry of Foreign Affairs in 2006 [10]. Although antibiotic use and resistance rates in the Netherlands are relatively low compared to almost any other country [11], the NethMap surveillance 2008 report shows that figures are rising slowly. The reasons for this are not fully understood. Up to now, SWAB initiatives to maintain prudent antibiotic use have addressed healthcare professionals only. The Council document [1] included recommendations to make consumers aware of the risks posed by antimicrobial resistance. In the spirit of the first European Antibiotic Awareness Day that will take place across Europe on 18 November 2008 [12], SWAB will soon develop activities to increase awareness among the general public of the importance of consolidating the prudent use of antibiotics.

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