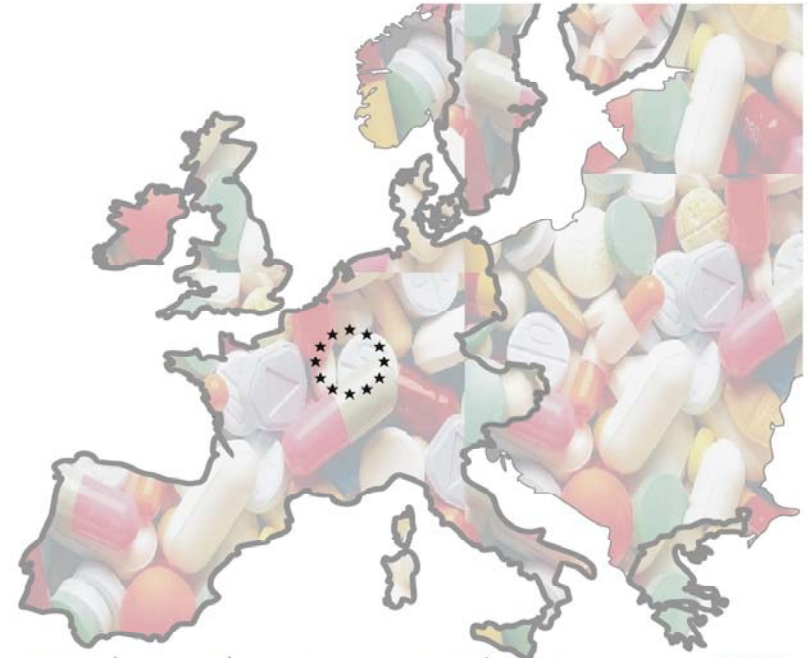
PROGRAMME OF COMMUNITY ACTION ON THE PREVENTION OF AIDS AND CERTAIN OTHER COMMUNICABLE DISEASES

Project Reference Number: 2001/SID/136
Agreement : N°SI2.325736 (2001CVG4-016)

FINAL IMPLEMENTATION REPORT



ESAC European Surveillance of Antimicrobial Consumption

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FINAL IMPLEMENTATION REPORT

November 2001

-

January 2004

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MISSION STATEMENT

European Surveillance of Antimicrobial Consumption

ESAC

granted by DG/SANCO of the EC Commission,
is an international network of surveillance systems,
aiming to collect
comparable and reliable antibiotic use data
in all European Countries

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1. INTRODUCTION

ESAC, granted by DG/SANCO of the European Commission (project number: 2001/SID/136), is an international network of national surveillance systems, collecting comparable and reliable antibiotic use data.

During the period November 2001 – January 2004, actions to harmonise the registration of antimicrobial consumption in all European Countries were taken.

A data collection system has been developed allowing producing comprehensive national data on volume of antibiotic consumption, in ambulatory and in hospital care.

Standardised national data were assembled in a European database for sub regional comparison of antibiotic use in relation to antibiotic resistance patterns and socio-economic and general health parameters.

These data were presented orally and as posters at scientific meetings and are also presented on the ESAC website (www.ESAC.ua.ac.be) to disseminate the results to a broader public.

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2. PARTNERS – ORGANISATIONS - COUNTRIES INVOLVED

2.1 ESAC Management team

2.1.1. Members of the ESAC Management Team

The following persons contributed to the ESAC Management Team (MT). As there was an amendment to the original protocol, tasks within the MT were reassigned whenever needed or necessary.

ESAC MANAGEMENT TEAM				
FUNCTION	NAME	E-MAIL	WORKLOAD	
			Months	%
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2.1.2 Tasks of the members of the ESAC MT

According to the ESAC protocol, the members of the ESAC MT carried the following tasks to enable them to fulfil the central coordination of the project, and to assure feedback to the participating countries (by means of their National ESAC Representatives) and the collaborating institutes (by means of their representatives appointed).

- Project leader (10%)
    - Co-ordination of the project
    - External representative of the project
- Data manager (100%)
    - Support to the representatives of the participating countries
    - Operate and maintain the central databank
    - Write algorithms for automated checking, linking and analysis
- Scientist (100%)
    - Support to the representatives of the participating countries
    - Work out the questionnaires
    - Assistance in the interpretation of data at the central level, trouble shooting, analysis of data
    - Writing of the final report
- Webmaster / Network Development (50%)
    - Development of the website
    - Adaptation of the data generated by the data manager to the web site
    - Development and maintenance of access mechanisms to the central data base and web site
- Senior Co-ordinator (40%)
    - Lead the ESAC network building process
- Junior Research Assistant (100%)
    - Act as a facilitator: gathering information on the feasibility of establishing a national ESAC project and at the same time making an inventory of expected problems
- Administrator (100% for 4m; 50% for 23m; 40% for 12m)
    - Organisation of the different meetings (preparatory, kick off, evaluation meeting and final conference)
    - Correspondence: send invitations, documents etc.

2.2 ESAC National Representatives

2.2.1. List of ESAC National Representatives (NR)

The list with all ESAC NR's is presented in table format (see following pages). The participating countries are listed in alphabetical order with the particulars of each NR mentioned below.

2.2.2 Tasks of the ESAC NR

The following tasks were appointed to the ESAC NR's.

- The collection of antibiotic consumption data for the period 1997 – 2002 within their country
- The delivery of a comprehensive list of antibiotics available on the national market, in order to create national registers of antibiotics
- To inform the ESAC MT about ongoing projects and intervention actions in the field of antibiotic consumption in their country and about national policies for data collection on antibiotic consumption
- To attend to regional ESAC-meetings
- To set up and maintain a national ESAC-network

The objectives of installing a national ESAC-network were the following.

- To establish a close collaboration between
    - The ESAC NR
    - The National Task Force for the Microbial Threat
    - The National Surveillance Institute of Infectious Diseases
    - Regulatory Authorities
    - Health Insurers
    - Health Professional Organisations
    - Pharmaceutical Industry
    - Universities and Scientific Organisations
- To compile a national register of available antibiotics according to European standards (linked to the ATC/DDD classification, offered by the WHO Centre in Oslo)
- To install Standard Operating Procedures (SOPs) for the maintenance of this register and to assure its future sustainability
- To prospectively collect drug utilisation data from 2002 on a continuous basis in compliance with European quality criteria of data collection

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2.3 Collaborating Institutions and Representatives

The following institutions or projects collaborated with the ESAC project. They are also listed alphabetically with the particulars of their representatives for ESAC mentioned below.

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3. OBJECTIVES OF THE ESAC PROJECT

3.1 Short term objectives

The main objective of the ESAC project was to collect consumption data on human antimicrobial consumption in hospitals and communities of all Member States of the European Community, in countries signatories to the Agreement on the European Economic Area and in associated countries of Central and Eastern Europe.

Furthermore monitoring systems for consumption of antimicrobials were identified, their method(s) of data collection analysed and their accuracy and comparability evaluated.

Quantity and quality of use of antimicrobials was analysed as well.
A checklist of possible sources of bias was used to check the validity of consumption data. Feedback on problems with the data set was given to the NR, after which scoring of the corrected data set with the checklist was possible and resulted into 3 categories of data. These preliminary results and validity scores were then discussed with the NR's and the scientific community

Information on prescription patterns in term of their appropriateness was provided to the NR's.

An agreement on definitions of measurement units of antimicrobial consumption adapted to the European situation was established.

A national ESAC network was set up to bring together all partners involved, to ensure regular delivery of administrative data, to facilitate collaboration with the National Surveillance Institute installed by the Community Network for Epidemiological Surveillance and Control of Communicable Diseases, to facilitate the co-operation of the applicant countries and countries from the European Economic Area and to construct communication channels with other networks in the field of antibiotic surveillance programs

Tools to distribute the information on consumption of antimicrobials in a meaningful manner were developed.

3.2 Long-term objectives

The most important objectives of the ESAC project are the long-term objectives, which go beyond the boundaries of the project and can serve the whole of the Community and possible beyond those boundaries as well, in terms of the improvement of health and health related issues and policies.

More specifically they aim to promote "Good Antibiotic Practice". A standardised and validated data set of outpatient antibiotic use in Europe is to be made publicly available, which might facilitate the establishment of indicators of antimicrobial consumption, and the auditing of antibiotic prescribing, monitoring of interventions, and evaluation of the implementation of guidelines and public health policies.

As they were developed, integrated, used, evaluated, adjusted and refined, tools and methods can be recommended in order to refine and enhance future data collection concerning antimicrobial consumption in European countries and possibly future data collection of other health related topics as well.

Within the project the implementation of a standardised system for the exchange of antimicrobial consumption data between countries was necessary. Therefore a "network of networks" was created between the different Member States of the European Community, countries signatories to the Agreement on the European Economic Area and associated countries of Central and Eastern Europe in order to facilitate communication and collaboration. This network approach can allow future communication and collaboration between all countries and might even deepen if other health related topics might be found suitable to be addressed in the same international way.
It might furthermore contribute to a reduction of antimicrobial resistance in the Member States of the European Community, in countries signatories to the Agreement on the European Economic Area and in associated countries of Central and Eastern Europe. For instance, the ESAC antibiotic use data were correlated with published data on resistance among *S. pneumoniae*, *S. pyogenes* and *E. coli*, three pathogens causing massive antibiotic prescribing in primary care. Although ecological studies have to be interpreted cautiously, these results support the hypothesis that differences in selection pressure account for geographic variation of resistance.

Analysis and evaluation of changes in the prevalence of antimicrobial resistance in function of trends in antimicrobial consumption might result in the recommendation of methods and tools of integration for existing surveillance systems of antimicrobial use and resistance.

4. METHODOLOGICAL APPROACH

In order to meet the objectives of the ESAC project a 'network of networks' approach was taken -as mentioned before- and all the member states of the EU and all the applicant member states, as well as other countries of the wider European region were invited to participate.

A central multidisciplinary management team co-ordinated a network of national representatives, liasing with national data providers and bodies responsible for antibiotic policy, and in close co-operation with all the interested parties at national level, to build viable national data collection networks in each country.

The following common goals were addressed: to collect data on the consumption of systemic antibiotics for human use, to collect quarterly data and to collect data for ambulatory and hospital care separately, pertaining to the period 1997 through 2002.

4.1. Data collection

Data collection was expected to be aggregated at the level of the active substance (not at brand level), using the taxonomy of the Anatomical Therapeutic Chemical (ATC) classification system, as recommended by the World Health Organisation (Guidelines for ATC classification and DDD assignment. Oslo: WHO Collaborating Centre for Drug Statistics Methodology; 2003) and limited to the ATC class J01, excluding antifungals, antibacterials for tuberculosis, antitumoral antibiotics, as well as topical antibiotics.

Consumption was to be expressed in defined daily doses (DDD) (Guidelines for ATC classification and DDD assignment. Oslo: WHO Collaborating Centre for Drug Statistics Methodology; 2003), the assumed average maintenance dose per day for a drug used for its main indication in adults. It is a unit of measurement and does not reflect precisely the recommended or prescribed daily dose. As the ATC/DDD system is a dynamic system which is updated annually, data collected on the basis of previous versions were reformatted into the 2003 version (ATC Index with DDDs. WHO Collaborating Centre for Drug Statistics Methodology, Oslo, Norway, January 2003; Rønning M, Blix HS, Harbø BT, Strøm H. Different versions of the anatomical therapeutic chemical classification system and the defined daily dose--are drug utilisation data comparable? Eur J Clin Pharmacol 2000;56:723-7).

Through a questionnaire filled out by the national representatives, information was gathered regarding the nature of the ATC/DDD assignment process (the

authors of the link between consumption data and the ATC/DDD classification; the version used; the handling of missing ATC codes and DDD values, etc.).

Additional information was collected on the characteristics of the data providers and data sources (separately for ambulatory and hospital care) and specific details were requested for antibiotic consumption in nursing homes, in dental care and in specialist care to outpatients, in order to establish how the split was made between ambulatory care and hospital care in each country.

Finally, information on the midyear population of the country for ambulatory care, and on the number of bed days for hospital care was collected to calculate population-based measures of antibiotic exposure.

Prior to the interpretation of the consumption data, the MT focused on detection bias in sample and census data and evaluated whether the data covered less than 90% of the national population (sample or incomplete census data) or 90% and more (census data), and, if applicable, the method of data extrapolation or weighting to estimate the consumption of antibiotics in the total population.

The validity of the consumption data provided was also evaluated by means of a checklist including possible sources of bias, developed during the project as experience with methodological problems grew.

CHECKLIST FOR THE EVALUATION OF THE VALIDITY OF DATA
1. Problems with population coverage
1.1. Sample bias in samples of less than 90 % of the population, not or incorrectly extrapolated.
1.2. Census bias in census data, covering less than 90% not or incorrectly extrapolated
1.3. Census bias in census data, covering at least 90% but less than 100%: with significant differences in consumption between rest of population and population covered, not properly weighted.
1.4. Under detection bias in countries where the reimbursement system does not cover substantial segments of the population (in data collection systems based on reimbursement data).
1.5. Under detection or over detection bias by parallel import and export (in data collection systems based on distribution data).
2. Problems with drug coverage
2.1. Under detection bias by over-the-counter (OTC) sales (in data collection systems based on reimbursement data).
2.2. Under detection bias in countries where specific classes of antibiotics are excluded from reimbursement (in data collection systems based on reimbursement data).
2.3. Measurement bias by problems with ATC/DDD assignment.
3. Problems with ambulatory care/hospital care mix
3.1. Assignment of data from nursing homes, day care centres and dental care to one of both settings (AC or HC).
3.2. Assignment of specialist prescribing (prescribing by specialists based in ambulatory care; prescribing by hospital-based specialists to outpatients; dispensing by hospital pharmacists to outpatients).

Furthermore the MT focused on errors in assigning medicinal product packages to the ATC; errors in calculations of DDD per package; bias by over-the-counter (OTC) sales and parallel trade; and bias in ambulatory care (AC) / hospital care (HC) mix.

Data sets were corrected after national feedback, and classified into 3 categories: valid data; data considered valid but with minor biases not invalidating the estimate of exposure; invalid data with major biases invalidating the estimate of exposure.

Posters with preliminary results and validity scores per country were first discussed at an internal meeting of all the national representatives in Bath, UK, in November 2002, and later presented at the 13th Meeting of the European Society of Clinical Microbiology and Infectious Diseases in Glasgow, Scotland, in May 2003.

4.2. Data sources and providers

4.2.1 Data providers

Thirty-two countries participated in the ESAC data collection. All 15 countries of the European Union, 12 of the 13 applicant countries (not Cyprus), and 5 other countries joined the project (Croatia, Iceland, Norway, Russia and Switzerland). Three countries were not able to deliver data (Romania, Switzerland, and Russia).

Twenty-two countries delivered both ambulatory care and hospital care data separately. Among the remaining 7 countries, Iceland could only deliver aggregated total data; Bulgaria only total and hospital care data; Austria, Ireland, Turkey and UK (limited to England only) only ambulatory care data; and Malta only hospital care data.

Antibiotic consumption data was provided by a wide range of reliable providers, described per country (Table 4.2.1). These included health insurers, regulatory authorities, scientific institutions, and professional associations of health care providers (pharmacists). Data from Turkey and Croatia were obtained from private market research organisations.

Table 4.2.1 – Specific providers of data on antibiotic consumption per country.

COUNTRY	DATA SOURCES AND PROVIDERS
Austria	Social Insurance Companies provided reimbursement data (100% coverage).
Belgium	Reimbursement data (90.5% of population covered) is available by law from the community and hospital pharmacies, which transmit to the health insurers and the National Institute for Health Insurance.
Bulgaria	Sales data for 1999 and 2000 was provided by the Bulgarian Drug Agency. Consumption data of one hospital (the main multipurpose hospital in Sofia) was available, covering a period of 5 years.
Croatia	Sales data was collected by a market research company and provided in collaboration with the National Institute of Public Health and National Institute for Statistics, with almost 100% coverage for ambulatory and hospital care.
Czech Republic	The Institute for Health Information and Statistics (Ministry of Health) delivered reimbursement data provided by the health insurers, covering nearly 100% of the insured population, but without guarantee of comprehensiveness. In hospital care, only one hospital has provided data up to now.
Denmark	Sales data was collected from the community pharmacies and hospital pharmacies, and is provided by the Danish Medicines Agency.
Estonia	Complete sales data was provided by the National Agency for Medicines, for ambulatory care as well as hospital care.
Finland	Complete sales data was provided by the National Agency for Medicines, for ambulatory care as well as hospital care.
France	Sales data was provided by the French Health Products Safety Agency and collected on the basis of mandatory annual reporting by pharmaceutical companies.
Germany	Ambulatory care data was provided by the WIdO (scientific institute of the AOK health insurance company) using a 0.4% sample for the years before 2000, and a total compulsory health insurance prescription database for the year 2001. Hospital care data was estimated from the SARI project covering 35 intensive care units located in 17 different regions, and from the MABUSE programme covering the medical and surgical services of 8 university hospitals.
Greece	Sales data was provided by the National Organization for Medicines and collected on the basis of mandatory reporting by the pharmaceutical companies.
Hungary	Complete reimbursement data for the period 1998-2001 was provided by the National Health Insurance for ambulatory care. For hospital care, complete sales data (only for 2001) was delivered by the same data provider.
Iceland	Total sales data from pharmaceutical companies was provided by the Ministry of Health. No differentiation between ambulatory and hospital care use could be made.
Ireland	Reimbursement data was provided by the GMS (General Medical Services). The data covers 32% of the population and approximately 75% of the overall drug consumption. The GMS Payments Board receives copies of all prescriptions written for GMS patients as part of pharmacists' claims for payments.
Italy	Sales data per year for the period 1999-2001, covering 90% of the population, was provided by the Ministry of Health. Prescribed, non-reimbursed and OTC antibiotics were all included. For hospital care, data was collected from one hospital for the period 1997-2000 and from 6 hospitals for 2001.
Latvia	The State Medicinal Agency only provided 2001 sales data from wholesalers, separately for ambulatory and hospital care. Validation of the use of the ATC-methodology, comprehensiveness of the data, and details on the split between ambulatory and hospital care could not be assessed.

Lithuania	Ambulatory care data – provided by the State Patient Fund – is not comprehensive, because of the complex nature of the reimbursement status of antibiotics (only a limited number of antibiotics are reimbursed, only for special categories of patients and certain diseases). Hospital care data stems from a sample of 5 hospitals, which cover up to 15% of the total patient days.
Luxemburg	Reimbursement data for ambulatory care was provided by the National Health Insurance Company. Hospital care data was collected by hospital pharmacists.
Malta	No ambulatory care data is available. For hospital care, comprehensive data is collected by the Government Pharmaceutical Services, covering all public hospitals and 97% of the private hospitals.
The Netherlands	Ambulatory care data was collected and analysed by the Foundation of Pharmaceutical Statistics and provided by the SWAB (Stichting Werkgroep Antibioticabeleid); data from a sample of 88% of community pharmacies was weighted and extrapolated. For hospital care, SWAB requested data from all Dutch hospital pharmacists; 60 hospitals responded (62% bed days) and the results were extrapolated.
Norway	Total sales data were provided by the National Institute of Public Health. For 1998 and 2001, separate hospital care data was available and the differentiation between ambulatory care and hospital care could be made by subtracting hospital care use from the total use.
Poland	Sales data was provided by the National Institute for Public Health, for ambulatory care as well as hospital care. Data was derived from 200 out of 400 wholesalers (covering about 60% of the market) and was extrapolated for coverage of the complete population.
Portugal	Reimbursement data for ambulatory care, covering 75% of the population, was provided by the Ministry of Health. For hospital care, only data for 1998 could be delivered.
Slovakia	Wholesaler data was provided by the Slovak Institute for Drug Control. Since 1999 data has been split between ambulatory and hospital care delivered on a monthly basis.
Slovenia	Data was provided by the Institute of Public Health with 100% coverage for ambulatory care. In hospital care, hospital pharmacists provided the data. The coverage of bed days between 1998 and 2001 was, 85%, 89%, 98% and 100%, respectively.
Spain	Reimbursement data for ambulatory care was provided by the Spanish Drug Agency and obtained from the ECOM (Especialidades Consumo de Medicamentos) database of the Ministry of Health; Hospital care data was provided by the Society of Hospital Pharmacists, and includes 15% of hospitals (predominantly large hospitals).
Sweden	Sales/prescription data was provided by the National Corporation of Swedish Pharmacies (Apoteket AB).
Turkey	Only incomplete sales data expressed in units was available from a market research company for ambulatory care. The ATC-DDD methodology was not used: data was expressed in units per 1000 inhabitants per day, which did not allow direct comparison with other countries.
UK / England	Reimbursement data with >95% coverage for ambulatory care was provided by the Department of Health based on the PCA (Prescription Cost Analysis) database, which covers all prescriptions which are dispensed in the community in England. No data was available for hospital care.

4.2.2 Data sources

Data on antibiotic consumption was collected from either distribution or reimbursement systems. Distribution or sales data was based on reports from the pharmaceutical companies, wholesalers, pharmacies or market research companies. Reimbursement data was collected by the third party payer on the basis of financial claims from legitimate beneficiaries, from prescribers or from dispensing pharmacies (community or hospital).

4.2.2.1 Data collection performance in ambulatory care

Ambulatory care data was available from 26 countries, originating from the distribution chain in 14 countries and the reimbursement systems in 12 countries (Table 4.2.2). Twenty-one of the 26 countries delivered census data of 90% or more, 3 delivered incomplete census data (30-78%) and 2 delivered sample data (25-60%). Seventeen countries were able to provide ambulatory data on a quarterly basis in at least one year of the study period.

4.2.2.2 Data collection performance in hospital care

Hospital care data was available from 24 countries. As hospitals are budgeted in most countries, hospital care data was distribution data in all countries but Belgium. Census data covering at least 90% of the population was provided in 15 countries (Table 4.2.2). Sample data was collected in 9 countries, ranging from 5 to 62% population coverage. Eight countries were able to provide quarterly data in at least one year of the study period.

Table 4.2.2 – Source and coverage (%) of data on antibiotic consumption in ambulatory and hospital care per country.

COUNTRY	AMBULATORY CARE		HOSPITAL CARE	
	Type of data*	Coverage of data (%)	Type of data*	Coverage of data (%)
Austria	R	90-100	no data available	
Belgium	R	90	R	95
Bulgaria	Separate AC data not available		D3	>10 (sample data)
Croatia	D4	>95	D4	>95
Czech Republic	R	30-100	D3	<5 (sample data)
Denmark	D3	100	D3	100
Estonia	D2	100	D2	100
Finland	D2	100	D2	100
France	D1	100	D1	100
Germany	R	90	D3	<10 (sample data)
Greece	D1	100	D1	100
Hungary	R	100	D3	100
Iceland	Separate AC data not available		Separate HC data not available	
Ireland	R	35 (incomplete census)	no data available	
Italy	R	90	D3	<50 (sample data)
Latvia	D2	90	D2	90
Lithuania	R	20-40 (incompl.census)	D3	<15 (sample data)
Luxemburg	R	96	D3	90
Malta	no data available		D3	97
The Netherlands	D	90	D3	62 (sample data)
Norway	D2	100	D3	100
Poland	D2	60 (sample data)	D2	60 (sample data)
Portugal	R	78 (incomplete census)	D3	>50 (sample data)
Slovakia	D2	100	D2	100
Slovenia	D2	100	D3	85-100
Spain	R	100	D3	15 (sample data)
Sweden	D3	100	D3	100
Turkey	D4	<25 (sample data)	no data available	
UK / England	R	100	no data available	

*Legend of data sources:

D = Distribution
R = Reimbursement

1. Manufacturers
2. Wholesalers
3. Pharmacies
4. Marketing research companies

4.2.2.3 Evaluation of the validity of the data set

Detailed information per year and per country regarding the availability and the validity of antibiotic consumption data in Europe for the period 1997 to 2002 is given in Table 4.2.2.3.

For ambulatory care, the estimate of exposure was valid (or only slightly biased) for international comparison in 22 countries (14 for all 5 years). Of these, 17 countries provided data on a quarterly basis for at least one year (10 for all five years).

For hospital care, 15 countries were able to deliver valid data (9 for all 5 years).

A valid estimate of the total exposure of national populations to human antibiotic consumption could be made in 18 countries.

Table 4.2.2.3 – Availability of data on volume of utilisation of antibiotics (ATC J01) in Europe within the ESAC project.

Year	1997			1998			1999			2000			2001			2002		
	AC	HC	TC	AC	HC	TC	AC	HC	TC	AC	HC	TC	AC	HC	TC	AC	HC	TC
EUROPEAN UNION COUNTRIES																		
Austria	·	·	·	O	·	·	O	·	·	O	·	·	O	·	·	O		
Belgium	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	
Denmark	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Estonia	·	·	·	·	·	·	·	·	·	·	·	·	·	·	·	●	O	●
Finland	●	O	●	●	O	●	●	O	●	●	O	●	●	O	●	●	O	●
France	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Germany	●	·	·	●	○	○	●	○	○	●	○	○	●	·	·	●	·	·
Greece	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O
Ireland	●	·	·	●	·	·	●	·	·	●	·	·	●	·	·	·	·	·
Italy	·	○	·	·	○	·	●	○	○	●	·	·	●	·	·			
Luxemburg	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●			
Netherlands	O	O	O	O	O	O	O	O	O	O	O	O	O	·	·	O	·	·
Portugal	●	·	·	●	○	○	●	·	·	●	·	·	●	·	·	●	·	·
Spain	O	○	○	O	○	○	O	○	○	O	○	○	O	○	○	O	○	○
Sweden	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
UK / Engl.	●	·	·	●	·	·	●	·	·	●	·	·	●	·	·	●	·	·
APPLICANT COUNTRIES (FIRST AND SECOND WAVE)																		
Bulgaria	·	○	·	·	○	·	·	○	O	·	○	O	·	○	O		○	O
Cyprus	Country not yet participating in ESAC																	
Czech Rep.	·	·	O	●	·	O	●	·	O	●	·	O	●	○	O	●	○	O
Estonia	·	·	·	·	·	·	·	·	·	·	·	·	·	·	·	●	●	●
Hungary	·	·	·	●	·	·	●	·	·	●	·	·	●	●	●	●	●	●
Latvia	·	·	·	·	·	·	·	·	·	·	·	·	○	○	O	○	○	O
Lithuania	·	·	·	·	·	·	·	·	·	○	·	·	○	○	○	·	O	·
Malta	·	●	·	·	●	·	·	●	·	·	●	·	·	●	·	·	●	·
Poland	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O	O
Romania	*Participant not yet able to provide data*																	
Slovakia	·	·	●	·	·	●	●	●	●	●	●	●	●	●	●	●	●	●
Slovenia	●	○	○	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
OTHER EUROPEAN COUNTRIES																		
Croatia	·	·	·	·	·	·	·	·	·	●	●	●	●	●	●	●	●	●
Iceland	·	·	●	·	·	●	·	·	●	·	·	●	·	·	●	·	·	●
Norway	·	·	●	O	O	●	·	·	●	·	·	●	O	O	●	●	●	●
Russia	*Participant not yet able to provide data*																	
Switzerland	*Participant not yet able to provide data*																	
Turkey	○	·	·	○	·	·	○	·	·	○	·	·	○	·	·	○	·	·

Legend:
AC = ambulatory care; HC = hospital care; TC = total care;

· = no data provided
○ = data with major bias, invalidating exposure estimation;
O = data available in DDD, but with minor bias, not invalidating exposure estimation;
● = valid data available in DDD

4.3. Approach to methodological problems encountered

4.3.1 Problems with population coverage

In a number of countries, data stemmed from samples that covered less than 90% of the population. In ambulatory care, 2 of the 25 data sets were samples that did not allow valid extrapolation (Lithuania, Turkey). Valid extrapolation was possible in 2 countries (Poland, The Netherlands). In hospital care, of the 24 data sets, valid extrapolation was impossible in 7 countries (Bulgaria, Czech Republic, Germany, Italy, Lithuania, Portugal and Spain); in 2 samples (the Netherlands and Poland) a credible extrapolation was made, based on stratification of the participating hospitals.
Even in data collection systems where at least 90% but less than 100% of the population is covered census bias may still exist. It may be caused by slight variations in the exact number of insured persons. Some countries extrapolated to the whole population, others did not, based on the assumption that the consumption of non-insured patients was channelled to the insured patients and was paid for by insured patients. There may be substantial differences in the small segment of the non-insured population (the very poor in some countries and the very rich in other countries), but none of the countries had a procedure for weighting for these differences. In the Netherlands, a small part of the population is served by dispensing general practitioners in rural areas.
In many European countries, the reimbursement system is universal and covers (almost) the entire population. Countries where this is not the case, have switched to collecting distribution data, to provide a better estimate of population exposure. Lithuania was only able to provide reimbursement data for a limited (and underprivileged) segment of their population (40%).
In countries with data collection based on distribution data and with substantial parallel export, the validity of the population exposure estimate may be distorted (e.g. Greece up to 10% overestimation of consumption).

4.3.2 Problems with drug coverage

In countries with data collection systems based on reimbursement data and with substantial OTC sales, significant under detection bias is possible. This was documented in Spain (about 10% underestimation of consumption) and suspected in Italy and Portugal.
Data sets based on distribution data are less vulnerable to this source of bias, as they cover the sales of all prescribed OTC antibiotics, whether or not they are reimbursed.
In many European countries, all antibiotics are at least partially reimbursed and, therefore, data collection based on reimbursement data will not be biased. However, in some countries several antibiotics are excluded from the

reimbursement list, either because they are too expensive, too inexpensive or considered inappropriate (Denmark) or because their reimbursement is limited to certain diagnoses or population groups (Lithuania). In some countries, part of initial antibiotic usage is not reimbursed when it forms part of a deductible sum that has to be paid in full by the patient (Denmark, Iceland, Ireland, Sweden). These particularities of the reimbursement system do not hamper data collection when the countries concerned collect distribution data (Denmark, Iceland, Sweden). Additionally, reimbursement in some countries might not include antibiotics when they are cheaper than a fixed fee for prescription (Austria, Germany, UK), but the potential effect on data collection in these countries was considered minute. Only in Lithuania and Ireland was the validity of data collection seriously hampered by the limitations of the reimbursement system, as in those two countries no alternatives to reimbursement data were publicly available.

Compliance with the ATC/DDD classification has been a major issue in the ESAC pilot project. All countries (except Turkey) were able to aggregate their consumption data in terms of the ATC Classification. All countries stated that they had used the ATC/DDD 2003 version for the retrospective period of 1997-2002, but several adjustments were necessary (e.g. in some countries data on urinary antiseptics was not recalculated after the switch in 1999 from G04 to J01MB, J01XE and J01X and consumption for these products was initially not recorded before 2000). Local ad-hoc assignments of DDDs, deviating from the official DDD (e.g. higher ad hoc DDDs for amoxi-clav in several countries) were observed and corrected. For 23 older antibiotics (e.g. benzathine benzylpenicillin and benzathine phenoxymethylpenicillin) and 19 antibiotic combinations (e.g. sulfametrole plus trimethoprim), an official DDD has not yet been assigned by the WHO Collaborating Centre in Oslo. Their consumption remained either undetected or was misclassified. For example, in Croatia, no DDD was assigned to benzathine phenoxymethylpenicillin, a narrow spectrum penicillin used extensively in this country. Because of the absence of DDD assignment, the consumption of this substance was not recorded, leading to a substantial underestimation of consumption in this class.

4.3.3 Problems with ambulatory care/hospital care mix

The last source of potential bias concerned the proper determination of the mix between ambulatory and hospital care. In Iceland and Bulgaria, it was not possible to split the total data originating from wholesalers. In other countries, substantial variation was observed between the methods used to separate ambulatory and hospital care data. Most problematic here was the status of nursing homes. Antibiotic consumption in these institutions might be substantial in a number of countries. In 14 countries, consumption data from nursing homes was allocated completely to ambulatory care, in 5 countries it was partly allocated

to ambulatory care, in 2 countries it was completely allocated to hospital care and in 4 countries the allocation of antibiotic use data was unknown. Similarly, caution is to be exercised with the attribution of consumption in day care centres and with prescriptions written by dentists. Attribution of specialist prescribing is another tricky issue. In some countries, the health care system allows for private specialists working in primary care outside the hospital, and their prescriptions are attributed to primary care, while in other countries this kind of services do not exist. In some countries, prescriptions by hospital-based specialists to outpatients (polyclinic prescribing) are dispensed in the community pharmacy, in other countries in the hospital pharmacy. In some countries, the hospital consumption of a limited number of small private hospitals may be attributed to ambulatory care (the Netherlands, Greece). Finally, hospital pharmacies in some countries are allowed to dispense a limited number of pharmaceuticals (e.g. AIDS or anti-tumour medication) to outpatients (e.g. Belgium). In most countries, these problems with determining the mix between ambulatory and hospital care probably caused only minor biases. In Finland and Latvia, however, the split between ambulatory care and hospital care was considerably distorted.

A final methodological aspect was the denominator problem. It was easy to find data on the midyear population of each of the countries from traditional databases providing statistical data. It proved to be more difficult to find reliable data on hospital bed days. Definitions and calculation methods for bed days differ from country to country. Data on bed days at the national level is difficult to access in many countries, since it is often only available on a yearly basis and with considerable delay. In international databases (at the WHO or the Organization for Economic Co-operation and Development) inexplicable discrepancies were found among data on bed days. Moreover, in many countries no reliable and timely data on the apportionment of acute, chronic and psychiatric beds is available. For the ESAC project, trying to express hospital consumption in terms of DDD per 100 bed days was considered impractical, unreliable and not useful. For this reason, hospital care consumption data was expressed in DDD per 1000 inhabitants per day, as there seems to be a strong correlation between the midyear population and the number of bed days in European countries (Monnet DL. Quality of antibiotic consumption data and opportunities for benchmarking. [Abstract S128] 13th European Congress of Clinical Microbiology and Infectious Diseases, Glasgow (Scotland, 10-13 May 2003).).

4.4. Relationship between antibiotic use and resistance

Within the ESAC project the relationship between antibiotic use and resistance was also studied. Therefore an ecologic study design was used to measure the effect of antibiotic (total and ATC groups) exposure on antibiotic resistance according to the mechanism of resistance.

We searched surveillance studies from countries for which antibiotic resistance data of *S. pneumoniae*, *S. pyogenes* and *E. coli* was available. A time lag of 1 to 2 years was used between antibiotic use and strain isolation. Non-susceptibility to penicillin included both intermediate and high-level resistance.

Correlations between antibiotic resistance and use were calculated using two-tailed Spearman's coefficient (r) for non-parametric correlations, considering a p-value of less than 0.05 as significant and a p-value between 0.05 and 0.1 as a trend towards significance.

5. RESULTS

The results presented in this section represent not a comprehensive overview of the findings made within the project. They however give an important overview of the results obtained and show a selection of the possible ways of looking into the consumption data by using the created ESAC database.

More results are available attached to this report, presented as the ESAC country posters as designed for the 2003 ECCMID meeting in Glasgow.
(ESAC – Results of the Retrospective Data Collection, 1997-2001, Posters presented at ECCMID, Glasgow, 2003).

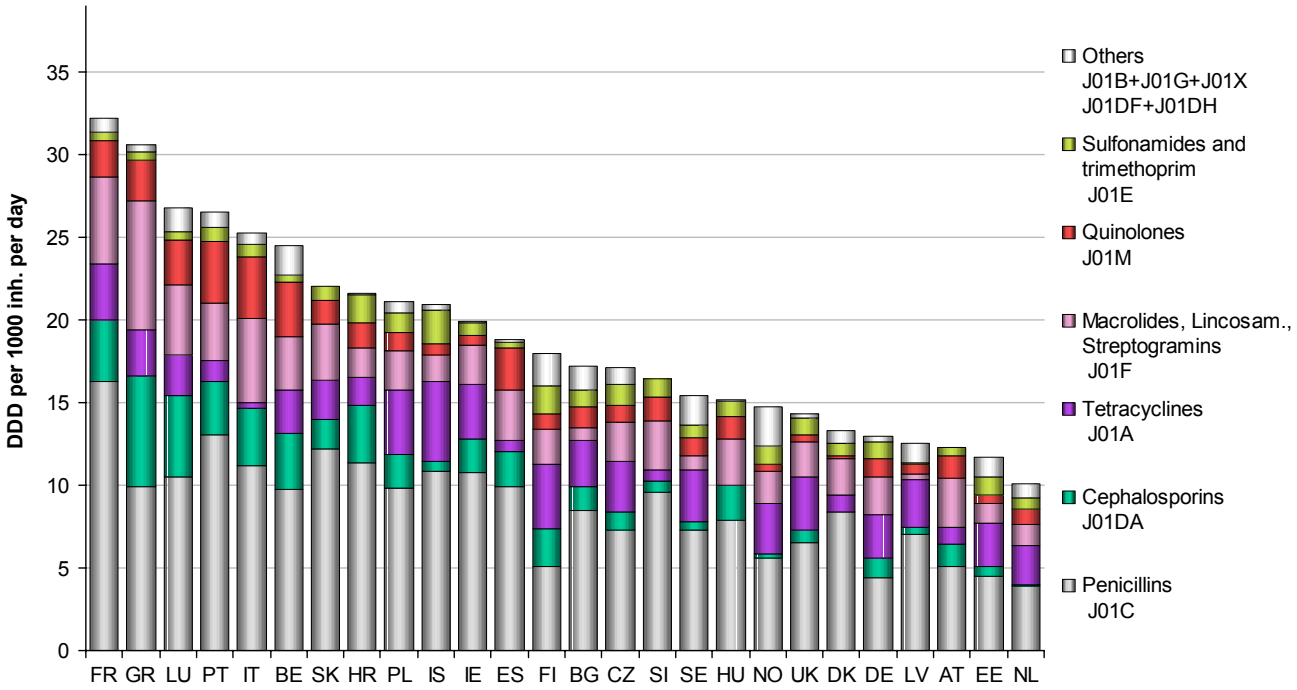
Results can also be obtained from the ESAC website (http://www.ua.ac.be/esac/) where general data is accessible for everyone and specific data can be obtained on request, after protocol submission.

Within the figures presented next, country abbreviations may be found.
The list of abbreviations is presented in the following table.

LIST OF ABBREVIATIONS OF COUNTRIES			
Austria	AT	Lithuania	LT
Belgium	BE	Luxemburg	LU
Bulgaria	BG	Malta	MT
Croatia	HR	The Netherlands	NL
Czech Republic	CZ	Norway	NO
Denmark	DK	Poland	PL
Estonia	EE	Portugal	PT
Finland	FI	Romania	RO
France	FR	Russia	RU
Germany	DE	Slovakia	SK
Greece	GR	Slovenia	SI
Hungary	HU	Spain	ES
Iceland	IS	Sweden	SE
Ireland	IE	Switzerland	CH
Italy	IT	Turkey	TU
Latvia	LV	United Kingdom	UK

5.1. Outpatient consumption data

5.1.1 Total outpatient antibiotic use in Europe in 26 European countries in 2002

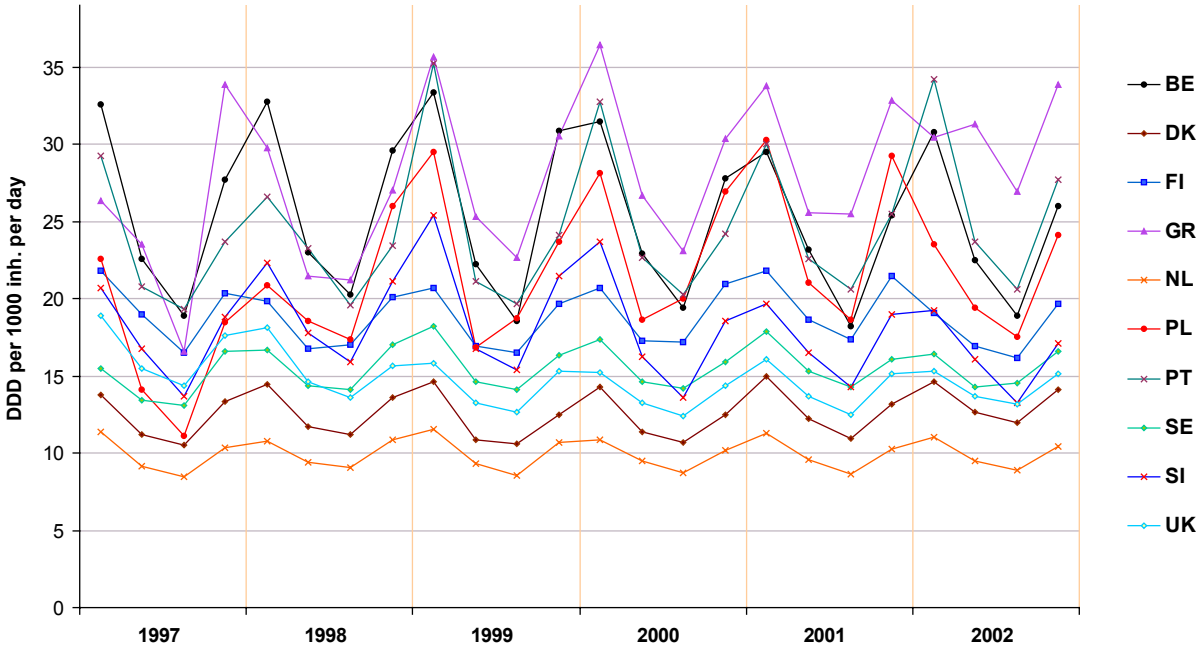


This figure shows total outpatient antibiotic use in 26 European countries for 2002, including one country (Ireland) where the most recent data was from 2001 and two countries (Bulgaria and Iceland) with total use data, expressed in DDD per 1000 inhabitants per day (DID).

This figure also depicts the use for major antibiotic groups, the tetracyclines (J01A), penicillins (J01C), cephalosporins (J01DA), sulfonamides and trimethoprim (J01E), macrolides, lincosamides and streptogramins (J01F), and quinolones (J01M), according to the ATC classification.

Outpatient antibiotic use varied with a factor of 3.2 between the country with the highest (32.2 DID in France) and lowest (10.0 DID in the Netherlands) use.

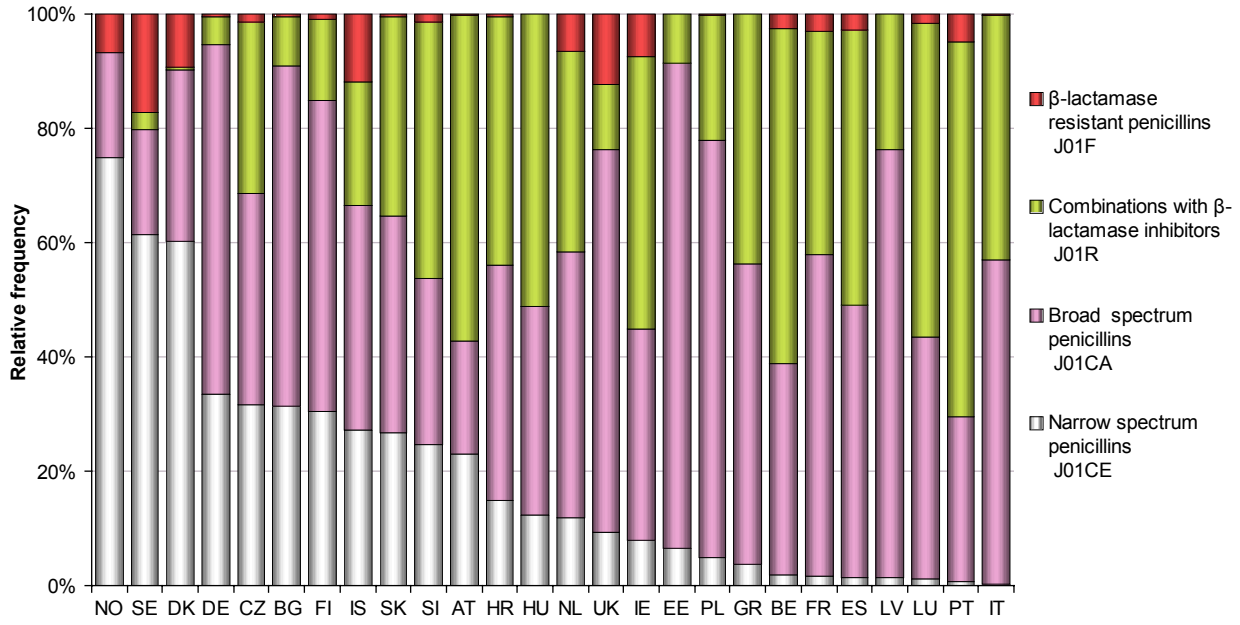
5.1.2 Seasonal variation of total outpatient antibiotic use in 10 European countries



This figure shows the seasonal fluctuation of outpatient antibiotic use in 10 European countries, which provided quarterly data for the whole period 1997-2002.

High seasonal fluctuations (mean increase more than 30% in the first and fourth quarter compared to the second and third quarter) were observed in Southern and Eastern European countries, while in Northern European countries the increase in antibiotic use during winter was limited to less than 25%.

5.1.3 Outpatient use of penicillins (J01C) in 26 European countries in 2002 in descending order of narrow spectrum penicillins

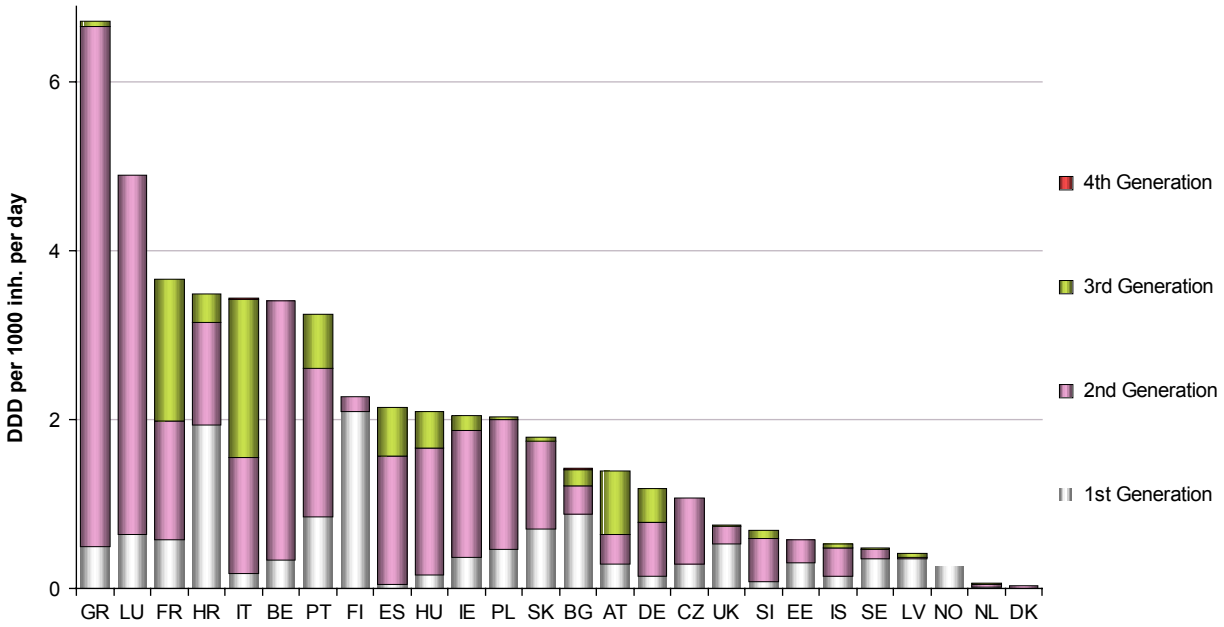


Total outpatient penicillin (ATC group J01C) use in 2002 varied with a factor of 4.2 between the country with the highest (16.3 DID in France) and lowest (3.9 DID in the Netherlands) penicillin use.

The proportion of use of the 4 different types of penicillins according to the ATC classification (J01CE, beta-lactamase-sensitive or so-called narrow spectrum penicillins; J01CA, broad-spectrum penicillins; J01CR, combinations of penicillins with beta-lactamase inhibitor; J01CF, beta-lactamase resistant penicillins) for 2002 is shown in the figure above.

We observed that in 3 countries (Norway, Sweden and Denmark) the narrow spectrum penicillins (J01CE) still represented more than 60% of penicillin use, whereas in 7 countries (Belgium, France, Italy, Latvia, Luxemburg, Portugal, and Spain) these drugs represented less than 2% of the total outpatient penicillin use.
In most other countries, the broad-spectrum penicillins (J01CA, mainly amoxicillin) have become the most popular penicillins; however, in 5 countries (Austria, Belgium, Hungary, Luxemburg, and Portugal), combinations of penicillins with beta-lactamase inhibitors (J01CR, mainly amoxicillin/clavulanic acid) represented more than 50% penicillin use.

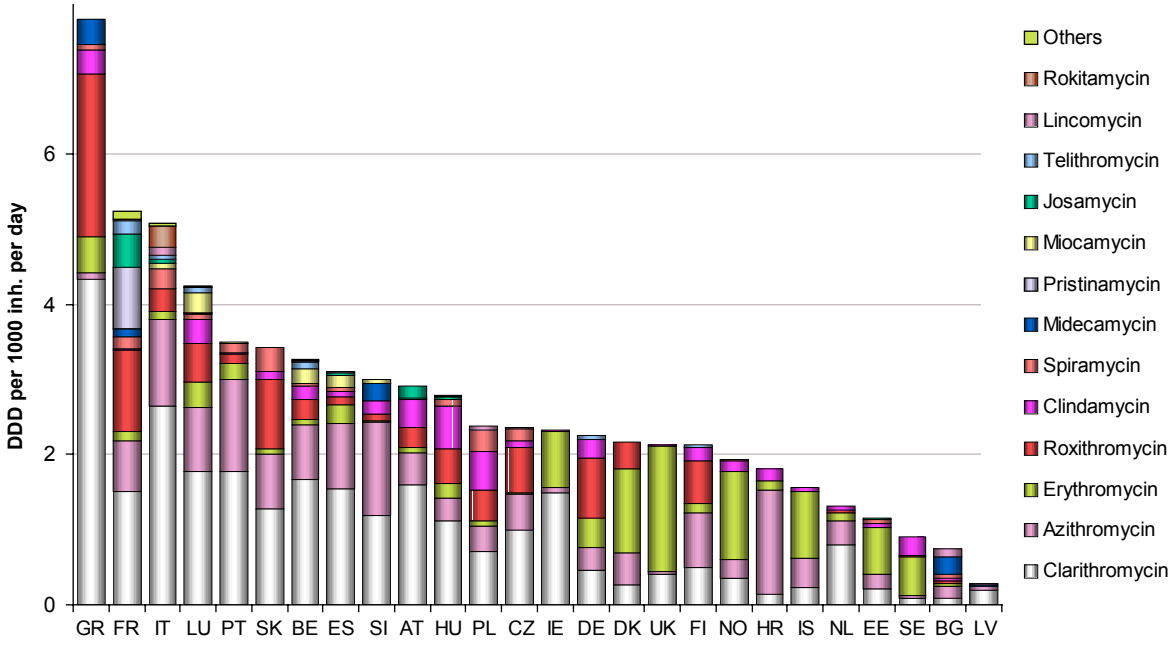
5.1.4 Outpatient use of cephalosporins (J01DA) in 26 European countries in 2002



Total outpatient cephalosporin (ATC group J01DA) use in 2002 varied with a factor of 256.2 between the country with the highest (6.7 DID in Greece) and lowest (0.03 DID in Denmark) cephalosporin use. The figure above shows the outpatient use of cephalosporins (J01DA) in 2002 aggregated by generations (we further divided the cephalosporins in 4 generations based on their spectrum of activity; see also www.whocc.no).

In Greece, the high cephalosporin use observed in 2002 was due to a shift from first to second generation cephalosporins, mainly cefuroxime, with strong seasonal variations, over the period 1997 to 2002 (data not shown). In France and Italy, the high cephalosporin use was due to the markedly high use of third generation cephalosporins, representing about one third of cephalosporin use in these countries, i.e. of the injectable (ceftriaxone in Italy) and oral (ceftibuten and cefixime in Italy; cefpodoxime and cefixime in France) cephalosporins. Remarkably, the third generation cephalosporins also represented about 50% of cephalosporin use in Austria. Italy is the only country where we observed an outpatient use of the new 4th generation cephalosporins (mainly cefepime). On the other hand, the old first generation cephalosporins still represented more than 50% of the total outpatient cephalosporin use in 8 countries (Norway, 100% of cephalosporin use; Finland, 91.7%; Latvia, 81.8%; Sweden, 73.7%; the United Kingdom, 70.9%; Bulgaria, 62.0%, Croatia, 55.4% and Estonia, 53.8%).

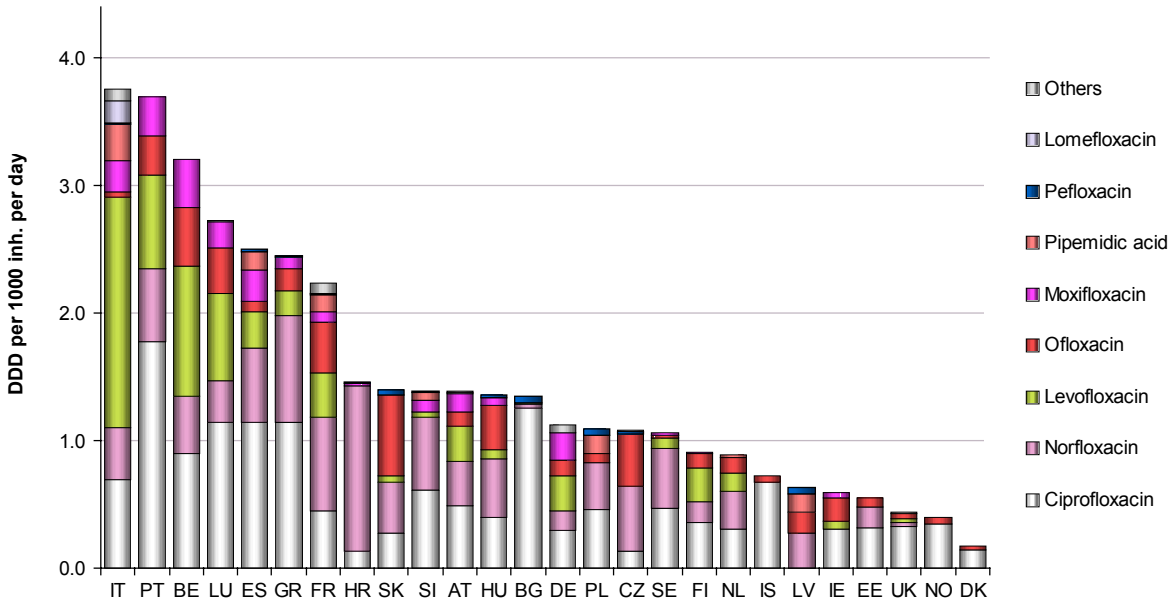
5.1.5 Outpatient use of macrolides, lincosamides and streptogramins (J01F) in 26 European countries in 2002



Total outpatient use of the J01F ATC group, including macrolides (J01FA), lincosamides (J01FF) and streptogramins (J01FG) (the so-called MLS group of antibiotics) in 2002 varied with a factor of 26.9 between the country with the highest (7.8 DID in Greece) and the country with the lowest (0.3 DID in Latvia) J01F use.

The figure above shows the outpatient use of this MLS group of antibiotics at the fifth level of active substance. Erythromycin still represented the most widely prescribed MLS antibiotic in 2002 in the United Kingdom (78.4% of the ATC group J01F), Norway (61.2%), Sweden (58.3%), Iceland (56.8%), Estonia (54.0%) and Denmark (51.1%). Clarithromycin was the most prescribed MLS antibiotic in all other countries in 2002, except in Croatia, Finland and Slovenia (azithromycin most prescribed MLS antibiotic), in Germany (roxithromycin most prescribed MLS antibiotic) and in Bulgaria (midecamycin most prescribed MLS antibiotic). Finally, France, Luxemburg and Belgium are the only countries where pristinamycin is used for outpatient care, representing 15.6, 0.5% and 0.01% of the ATC group J01F in 2002, respectively.

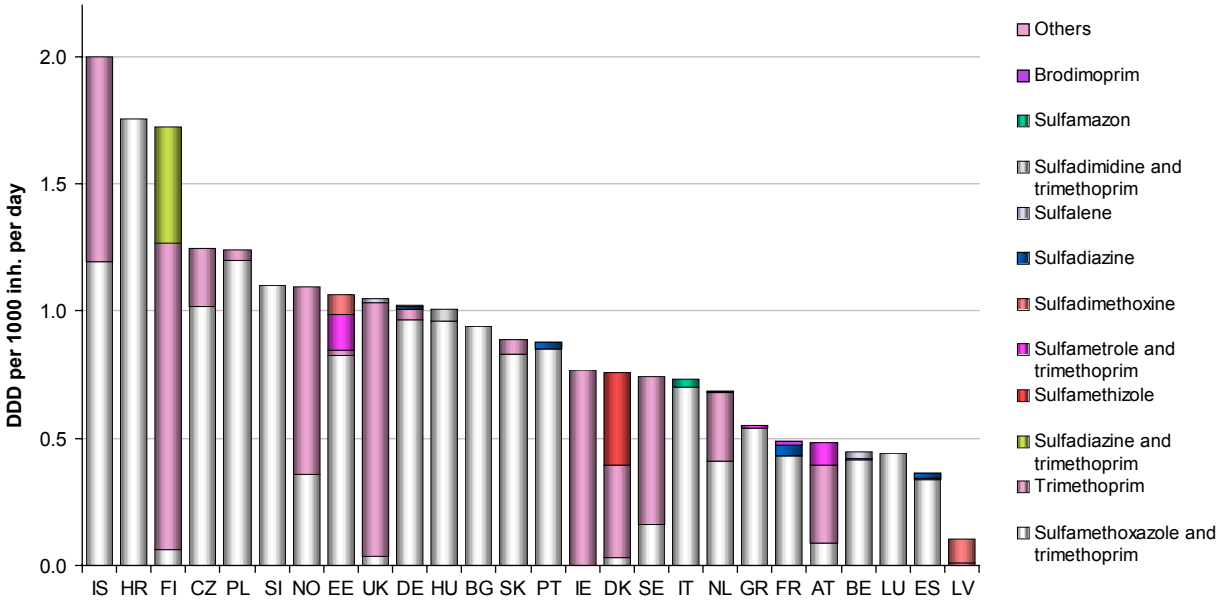
5.1.6 Outpatient use of quinolones (J01M) in 26 European countries in 2002



Total outpatient quinolone (ATC group J01M) use in 2002 varied with a factor of 21.2 between the country with the highest (3.76 DID in Italy) and the country with the lowest (0.17 DID in Denmark) quinolone use.

The figure above shows the outpatient use of these quinolones at the fifth ATC level of an active substance.
Norfloxacin, one of the oldest quinolones, still represented the most widely prescribed quinolone in 2002 in Croatia (89.0% of the ATC group J01M), Czech Republic (46.9%), Sweden (44.4%), Slovenia (46.0%), Latvia (43.6%), Hungary (33.8%), and France (33.2%).
In all other countries, ciprofloxacin was the most widely prescribed quinolone in 2002, except in Italy and Belgium (levofloxacin most prescribed quinolone) and in Slovakia (ofloxacin most prescribed quinolone).

5.1.7 Outpatient use of sulfonamides and trimethoprim (J01E) in 26 European countries in 2002

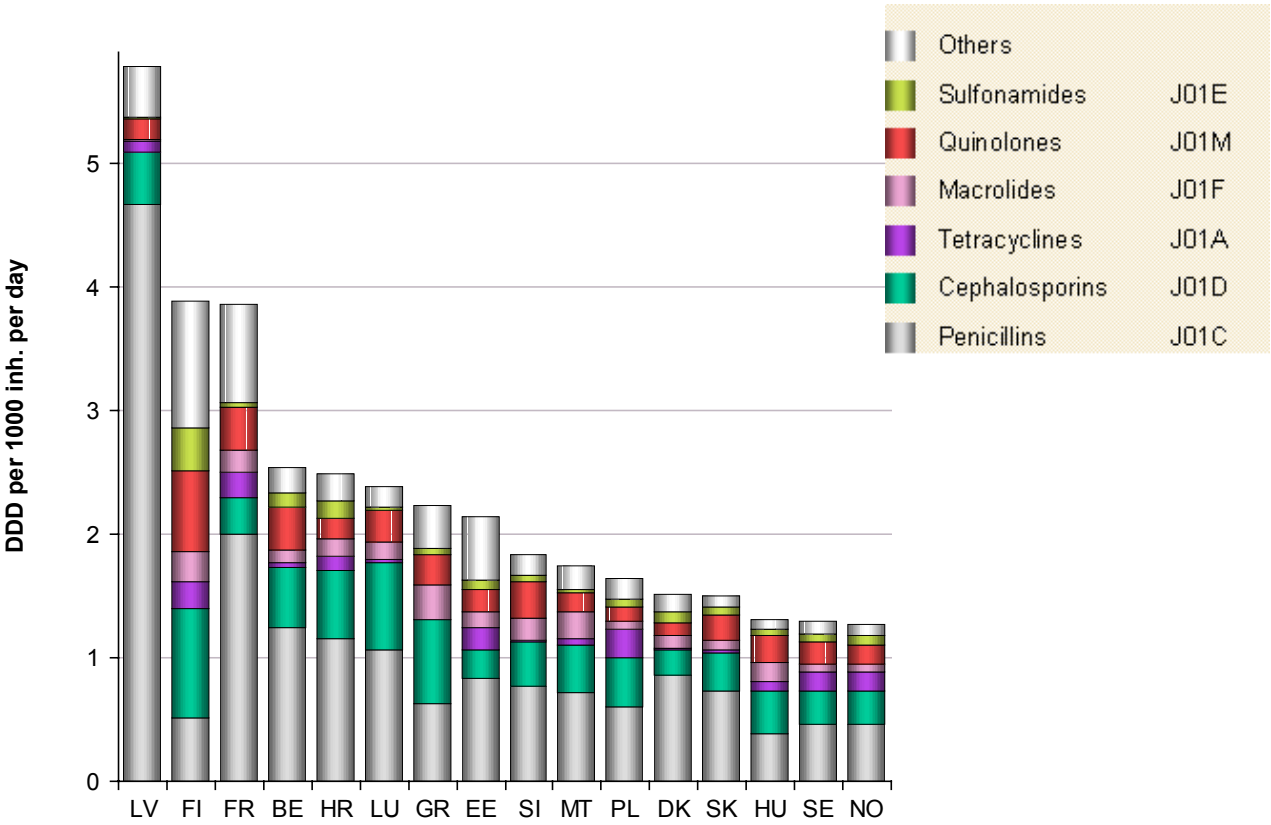


Total outpatient sulfonamides and trimethoprim (ATC group J01E) use in 2002 varied with a factor of 19.5 between the country with the highest (2.0 DID in Iceland) and the country with the lowest (0.1 DID in Latvia) sulfonamide and trimethoprim use.

The figure above shows the outpatient use of these sulfonamides and trimethoprim at the fifth level of active substance.

5.2. Hospital consumption data

5.2.1 Antibiotic Consumption in Hospital Care in 2002 - Absolute numbers in 16 countries

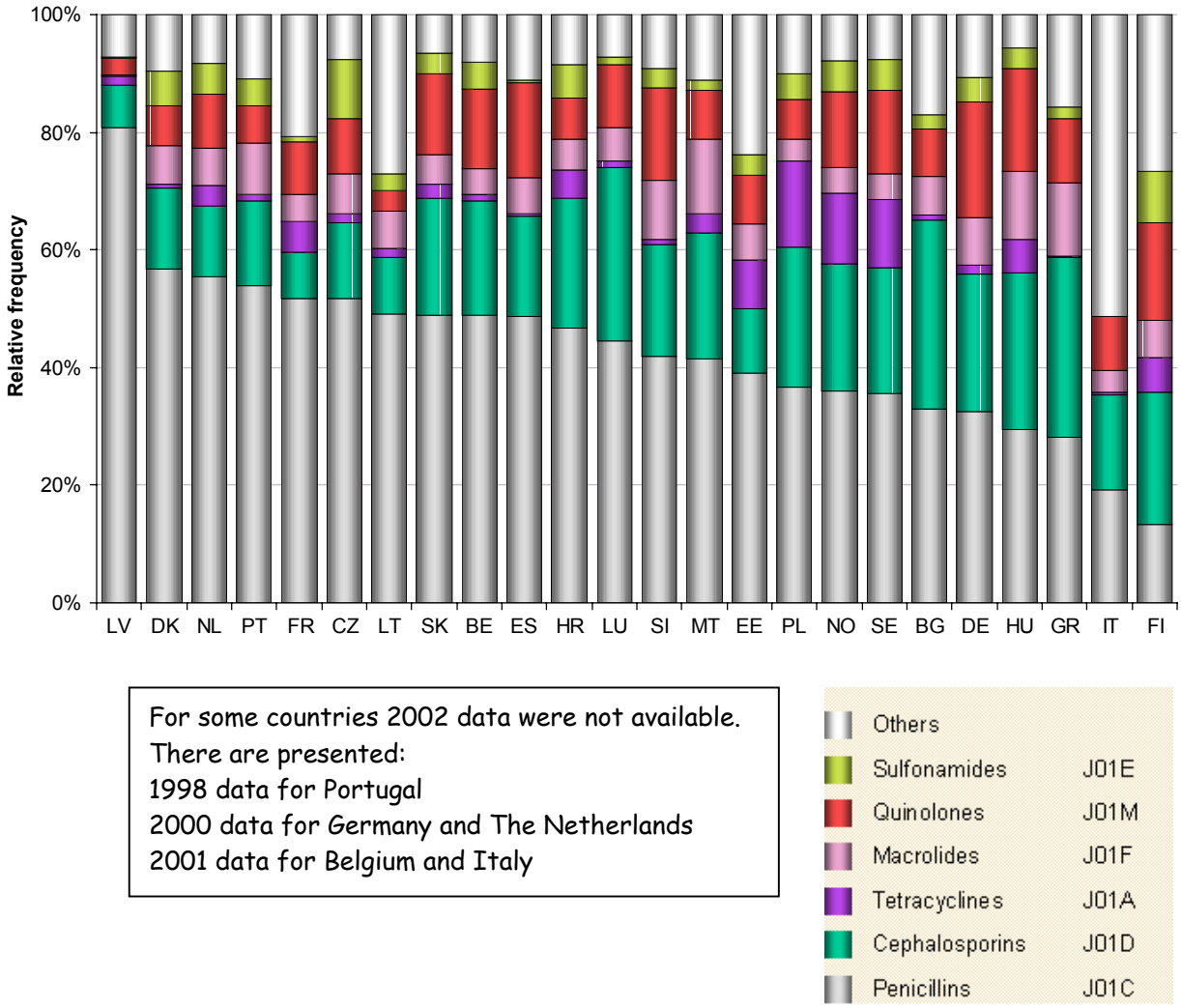


Total hospital use of antibiotics in 2002 varied among 16 countries delivering national data with a factor of 4.5 between the country with the highest (5.8 DID in Latvia) and the country with the lowest (1.3 DID in Norway) hospital use.

These data however must be interpreted with caution as the split between consumption in ambulatory and hospital care was not always explicit and often biased by the divers determination of the ambulatory/hospital mix, as mentioned in the methodological approach section of this report.

In this way proportion of hospital care consumption varied between 6 and 32% within 16 countries shown.

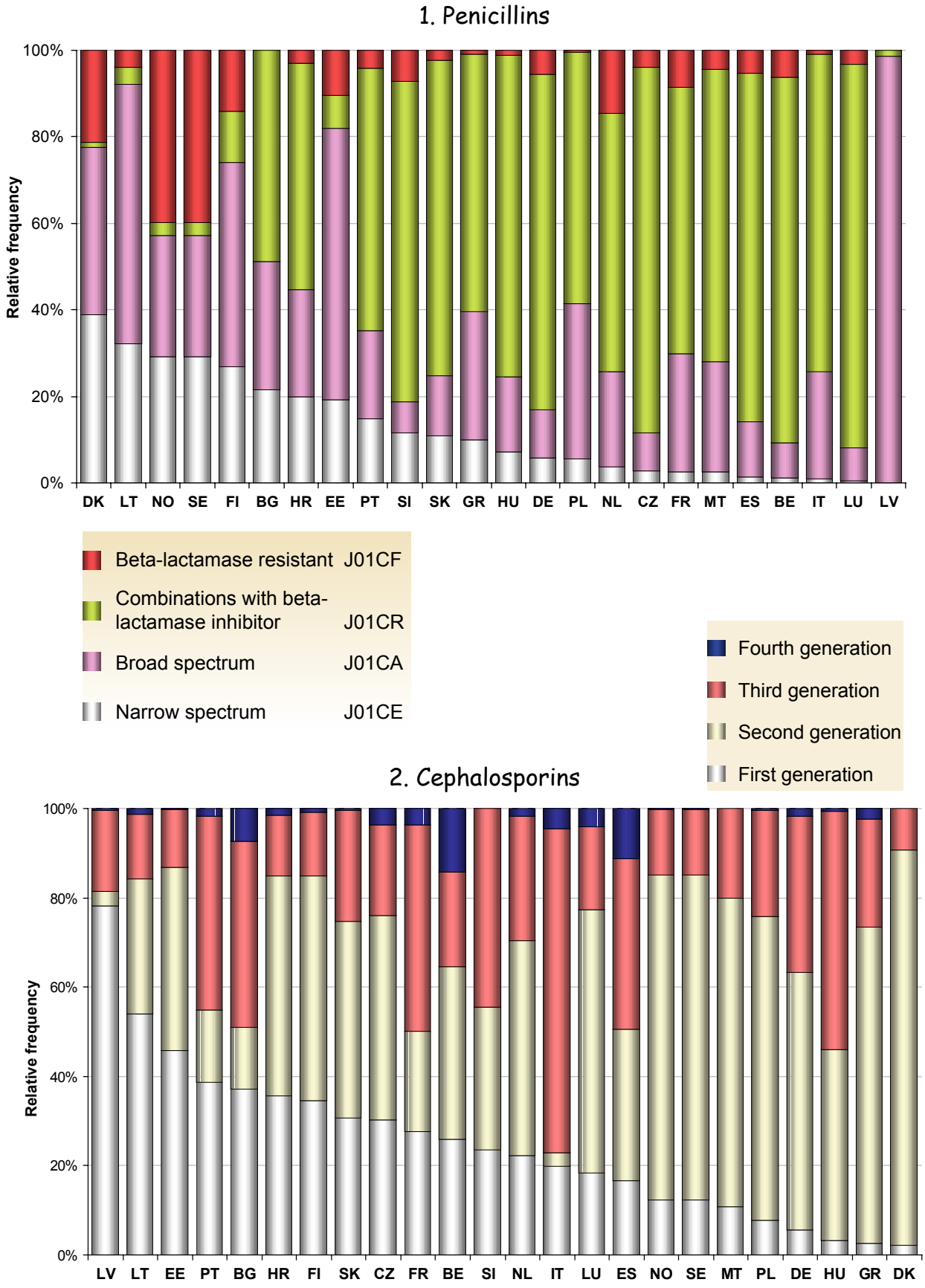
5.2.3 Antibiotic Consumption in Hospital Care in 2002 - Relatively in 24 countries



Additionally to 16 countries able to cover the complete national hospital consumption of antibiotics, another 8 countries were able to deliver hospital care data for a sample of hospitals. Thus relative frequency of different antibiotic classes van be analysed in these countries

Penicillins are the most commonly used drugs in most countries, followed by the cephalosporins. Consumption of these two main groups of antibiotics is further analysed in the following two figures, where they are further divided into subgroups to compare their relative proportion.

5.2.4 Relative Consumption of Penicillins and Cephalosporins in Hospital Care in 2002.



5.3. Relationship between outpatient antibiotic use and resistance.

Beta-lactam resistance data on *S. pneumoniae* were obtained from the EARSS project surveying the antimicrobial susceptibility among invasive (from blood and cerebrospinal fluid) pneumococcal isolates (Bronzwaer S. European antimicrobial resistance surveillance as part of a community strategy. [dissertation]. Groningen: Rijksuniversiteit Groningen; 2003).

Macrolide resistance data on *S. pneumoniae* and *S. pyogenes* were obtained from the telithromycin surveillance project on antimicrobial resistance among isolates from respiratory tract specimens (Goossens H, Elseviers M, Ferech M, Hendrickx E, Vander Stichele R, Bryskier A. Correlation between macrolide use and geographic diversity of erythromycin-resistance among *Streptococcus pneumoniae* and *S. pyogenes* in 17 European countries [Abstract]. ICAAC. Chicago: American Society for Microbiology. 2003, p.111.).

Resistance in *E. coli* isolates was obtained from a pan-European project surveying the antimicrobial susceptibility of urine pathogens from uncomplicated urinary tract infections (Kahlmeter G. An international survey of the antimicrobial susceptibility of pathogens from uncomplicated urinary tract infections: the ECO-SENS project. J Antimicrob Chemother 2003; 51: 69 – 76.).

Table 5.3 (next page) shows the correlations between antibiotic use and resistance. A strong statistical significant correlation was found for all combinations, except for co-trimoxazole use and resistance in *E. coli*, where we observed a trend towards significance.

Table 5.3 - Correlation between antibiotic use and resistance

ORGANISM - YEAR OF ISOLATION *[source of information]*	ANTIBIOTIC RESISTANCE	ANTIBIOTIC USE - ATC GROUP (year of data)	NO. OF COUN-TRIES	SPEARMAN CORRELA-TION (r)	P-VALUE
S. pneumoniae 1999/2000 *[1]*	Erythromycin	Macrolides - J01FA (1998)	16	0.858	< 0.001
S. pneumoniae 2001 *[1]*	Penicillin	Penicillins - J01C (2000) Cephalosporins - J01DA (2000)	18	0.579 0.637	0.012 0.004
S. pyogenes 1999/2000 *[2]*	Erythromycin	Macrolides - J01FA and lincosamides - J01FF (1998)	17	0.588	0.013
E. coli 1999 *[3]*	Ciprofloxacin Co-trimoxazole	Quinolones – J01M (1999) Co-trimoxazole – J01F (1999)	12	0.680 0.566	0.015 0.055

1. Bronzwaer S. European antimicrobial resistance surveillance as part of a community strategy. [dissertation]. Groningen: Rijksuniversiteit Groningen; 2003.

2. Goossens H, Elseviers M, Ferech M, Hendrickx E, Vander Stichele R, Bryskier A. Correlation between macrolide use and geographic diversity of erythromycin-resistance among *Streptococcus pneumoniae* and *S. pyogenes* in 17 European countries [Abstract]. ICAAC. Chicago: American Society for Microbiology; 2003, p.111.

3. Kahlmeter G. An international survey of the antimicrobial susceptibility of pathogens from uncomplicated urinary tract infections: the ECO-SENS project. J Antimicrob Chemother 2003; 51: 69 – 76.

5.4. Conclusions

Outpatient antibiotic use data have been reported using various units of measurement, but in order to compare drug utilisation data from different regions or countries, the data need to be collected and aggregated in a standardised uniform way. ESAC opted for the ATC classification system and the DDD measurement unit, developed by the WHO Collaborating Centre for Drug Statistics Methodology. The DDD is the assumed average maintenance dose per day for its main indication in adults and is assigned by the WHO Collaborating Centre. The DDD is a technical unit, and although the DDDs for antibiotics are as a main rule based on the use in infections of moderate severity, it does not necessarily reflect the current recommended or prescribed daily dose. To control for the size of the population, we expressed antibiotic use as a number of DDD per 1000 inhabitants per day (DID). Use calculated in DID is the only standard measure that provides an estimate of the proportion of the population who may be treated daily with the antibiotic concerned.

A striking finding was the marked differences in antibiotic prescribing in primary care in Europe. In general, antibiotic use was highest in Southern and Eastern Europe, and lowest in Northern Europe. In most countries, we observed a growing use of the newer (i.e. broad-spectrum) antibiotics, such as amoxicillin/clavulanic acid, the new macrolides and quinolones (results not shown) to the detriment of the older (narrower-spectrum) penicillins and cephalosporins. However, the narrow spectrum penicillins and the first generation cephalosporins, are still widely prescribed for the treatment of community-acquired infections in certain Northern European countries. Although antibiotic resistance rates are lower in these Northern European countries, thereby allowing the use of these older drugs, our data suggest that antibiotics are prescribed inappropriately in other countries.

Striking seasonal fluctuations were observed in some countries. High annual levels of antibiotic use were associated with a substantial increase of antibiotic prescribing in these countries during winter seasons. Summers peaks of antibiotic use were also observed, particularly of the beta-lactamase resistant penicillins. This observation was most pronounced in the United Kingdom, where flucloxacillin showed a consistent increase in each summer season, reflecting the prescription of this drug to treat skin infections.

In all but one country (Portugal) we found no seasonal variation of ciprofloxacin use, suggesting that this drug was used mainly for treatment of urinary tract infections. Interestingly, these data (as well as data on the use of norfloxacin, nitrofurantoin and trimethoprim – analysis not shown) also suggest that urinary tract infections are not characterised by seasonal fluctuations. In Portugal, fluctuations in prescriptions for ciprofloxacin are consistent with it being administered as therapy of adult patients with winter seasonal infections,

particularly those of the respiratory tract. We suggest that a low seasonal fluctuation of the earlier quinolones, such as ciprofloxacin, is a good marker of restrained use. Levofloxacin and moxifloxacin have superior activities against pneumococci compared with the earlier agents, and their introduction in Europe was very successful in Belgium and Portugal. The Belgian data are surprising because numerous clinical practise guidelines in Belgium clearly state that these drugs are not first-line therapy for adult respiratory tract infections. However, when sounding the alarm about the peril of rising antibiotic resistance, we may be inadvertently promoting inappropriate use of these new quinolones. This inappropriate use of fluoroquinolone in Belgium will inevitably lead to emergence of not only resistant pneumococci but also of a host of Gram-negative organisms.
Cephalosporin use was high in Greece, Luxemburg and France. In France, cephalosporin use has been increasing for treatment of uncomplicated respiratory tract infection with a presumed aetiology. This high cephalosporin use was due to the markedly high use of oral third generation cephalosporins, i.e. cefpodoxime and cefixime.
Differences in the incidence of community-acquired infections have been proposed as a factor to explain differences in antibiotic use among countries. Although seasonal Influenza outbreaks have been responsible for year-to-year variations in the level of antibiotic use, they represent an unlikely explanation for the large and stable differences observed among European countries. High antibiotic use, which is mainly seen in Southern European countries and is related to increased use during winter seasons, is unlikely to be due to a higher incidence of respiratory tract infections in these countries. However, the high winter peaks of antibiotic use in countries with high annual levels of antibiotics might be related to diagnostic labelling of respiratory tract infections (RTI). Differences in culture and in education have also been proposed as an explanation for differences in antibiotic use observed in Europe.
Differences in drug regulations and in the structure of the national pharmaceutical market may also explain differences in antibiotic use.
Geographic differences in the proportion of resistance can be explained by differential selection pressure for resistance or the dissemination of certain resistant clones in some countries but not in others. The number of DDDs is related to the number of prescriptions and number of persons exposed to antibiotics, and, therefore, the number of DDD per 1000 inhabitants per day is a good indicator for measuring the ecological pressure and should thus be correlated with resistance. The ESAC antibiotic use data were correlated with published data on resistance among *S. pneumoniae*, *S. pyogenes* and *E. coli*, three pathogens causing massive antibiotic prescribing in primary care. Although ecological studies have to be interpreted cautiously, these results support the hypothesis that differences in selection pressure account for geographic variation of resistance. The major selective pressure driving changes in the

frequency of resistance is the level of drug use. It should be noted that antibiotic resistance is not only the effect, but also a cause of consumption of antibiotics (resistant organisms require higher dosages to be eradicated or alternative antibiotics).
In conclusion, the ESAC project represent the first set of publicly available standardised and validated supranational data on antibiotic use in Europe.

6. MEETINGS

Meetings were organised during various stages of the project and whenever appropriate representatives of the Commission, participating countries, scientific societies, European scientific study groups, consumer organisations, pharmaceutical companies or other interested parties were invited as well.

1. Kick off Meeting: European Conference on Antibiotic Use in Europe
15-17 November 2001, Brussels, Belgium

2. First EARSS - ESAC Plenary Meeting
13-15 November 2002, Bath, United Kingdom

3. Second EARSS - ESAC Plenary Meeting
5-7 November 2003, Warsaw, Poland

4. Regional meetings

- The Eastern cluster (EU applicant countries, Turkey)
  12-14 December 2002, Prague, Czech Republic

- The Southern cluster (Spain, Portugal, Greece, France, Italy)
  7-8 March 2003, Verona, Italy

- The Viking Cluster (Nordic and Baltic countries, NL)
  25-26 April 2003, Copenhagen, Denmark

- Ireland, UK and Malta
  15-16 May 2003, Dublin, Ireland

- Bismarck countries
  13-14 June 2003, Brussels, Belgium

6.1. European Conference on Antibiotic Use in Europe

The kick off meeting of the ESAC project was held during the European Conference on Antibiotic Use in Europe (15-17 November 2001, Brussels, Belgium).

On the first day plenary sessions were held on antibiotic consumption in Europe. The following day, participants could join in on workshops, which conclusions and recommendations were presented on the third day. The conference then ended with a presentation on newly EU funded projects, including the ESAC project.

On the next pages, the executive summary of the conference is presented.
The final report of the conference is attached to this report.

Most scientists agree that excessive consumption of antibiotics promotes development of resistance among the microbes that cause infectious diseases. Yet information on consumption of antibiotics across Europe is not freely available, and the factors that determine differences in antibiotic consumption are not fully understood. Experts from 33 countries gathered at the European Conference on Antibiotic Use in Europe (Brussels, Belgium, November 15-17, 2001) to begin a project that will collect data on antibiotic use across Europe, and to discuss the determinants of antibiotic use.

The essential motivation for the Conference is the fear that some common infections may soon be untreatable if the causative organisms acquire resistance to all available antibiotics – a scenario that has been called the "post-antibiotic era". Prescription of antibiotics for diseases that are not susceptible to these medicines drives the development of resistance.

The Conference was the launch meeting for the European Surveillance of Antibiotic Consumption (ESAC) project, funded by the European Commission, which will collect in a standardised manner information on antibiotic use in European Union member states and several other European countries, and make this information available free of charge. Some data on antibiotic consumption are available commercially. These data indicate considerable differences in the amount of antibiotics used in different European countries. For example, compared with the Nordic countries, France, Spain and Portugal consume about twice as many antibiotics per head of population, yet the people of the Nordic countries do not seem to suffer because of their modest consumption of antibiotics. However, these commercial data are expensive and they are not available in the public domain.

The Conference was organised by the Belgian Antibiotic Policy Co-ordination Committee (BAPCOC), endorsed by the European Commission, and supported by the European Agency for the Evaluation of Medicinal Products (EMEA), and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID)

Delegates at the meeting discussed the factors that lead to different patterns of antibiotic consumption in different countries, and came up with a series of recommendations for future initiatives and research. These include development of evidence-based guidelines for appropriate use of antibiotics, and assessment of the impact of these guidelines and better patient education on antibiotic use. Delegates also supported the wisdom of continuing the ban on advertising antibiotics to the public. The recommendations of the six workshops are listed in this report.

The Conference coincided with the adoption by the European Union of a community strategy against antimicrobial resistance, due to be implemented by November 2002. These Council Recommendations were prepared and adopted during the Belgian EU Presidency, and we hope other countries, chairing the EU, will continue to take initiatives against the emergence of antibiotic resistant micro organisms.

6.2. First EARSS – ESAC Plenary Meeting

The first joint EARSS – ESAC meeting took place in Bath, United Kingdom, on 13 – 15 November 2002.
The program, minutes and participants are presented here below. More information can be found in the attached meeting reports.

6.2.1 Detailed Program

DAY 1

EARSS session	
14,00	Welcome on behalf of EARSS
14,10	Welcome on behalf of PHLS
14,20	Latest results EARSS
14,40	Public health action on the problem of AMR in UK
15,00	Introduction "ß—lactamases in *E. coli*"
15,20	Proposal improved ESBL reporting EARSS
15,30	Discussion
15,45	Tea Break
16,15	Routine detection of VISA
16,35	Proposal VISA reporting EARSS
16,45	Discussion
17,00	Breakpoints for surveillance applied to EARSS
17,15	EARSS in Baltic countries
17,30	Update EARSS web-site
17,45	General discussion
18,30	*Close*

DAY 2

EARSS session	
09,00	Denominator information for EARSS
09,15	Collection of EARSS data on representative ness
09,30	Discussion
09,45	Results QA exercise 2002
10,05	Discussion
10,15	Finances, conclusive remarks, future initiatives
10,40	Coffee Break

DAY 2

EARSS-ESAC session	
11,00	EU strategy on the problem of AMR in Europe *(Stef Bronzwaer)*
11,20	Overview EARSS (participants, methods, important results)
11,35	Overview ESAC (participants, methods, important results) *(Herman Goossens)*
11,50	Presentation of EARSS-ESAC partnership *(ESAC: Herman Goossens)*
12,00	Pilot project EARSS-ESAC: presentation of preliminary results *(ESAC: Monique Elseviers)*
12,20	ARmed: Antibiotic Resistance in Mediterranean countries
12,30	Kick-off SAR (Self-medication of AB & resistance levels in EU)
12,55	Presentation of EARSS-ESAC-SAR partnership *(ESAC: Herman Goossens)*
13,00	*Lunch*
ESAC session	
14,00	Welcome + introduction *(Herman Goossens)*
14,20	Retrospective study: Presentation of the results *(Monique Elseviers)*
14,45	*Classification problems encountered* (Matus Ferech)
14,55	Guidance from WHO centre Oslo on ATC/DDD classification problems on antibiotics *(Hege Salvesen Blix)*
15,15	Poster walk: presentation of actual situation about administrative data collection per country
16,15	Coffee Break
16,30	Round table (moderator*: Robert Vander Stichele)* Quality of the retrospective data (45') Requirements of the prospective data collection system (15') Perspectives for the prospective data collection (30')
18,00	*Closure*

DAY 3

ESAC session	
09,00	Development of national register of available antibiotic products: basic requirements *(R. Vander Stichele)*
09,30	Collection of information on ongoing projects *(M. Ferech)*
09,45	Network building and planning of (supra)-national meetings *(R. Vander Stichele)*
10,30	Coffee Break
11,00	Presentation of ongoing projects in the field of antibiotic consumption: ▪ Collection of antibiotic consumption data: example Denmark *(Annemette Anker Nielsen)* ▪ Outcomes of a programme for monitoring 'alert antibiotic' use in hospital *(P.G. Davey)* ▪ Attitudes towards antibiotic use within the Maltese general public *(M.A. Borg)* ▪ Variability in the European reimbursement schemes for antibiotics: Consequences for the ESAC Project *(M. Ferech)*
11,50	Administrative and financial matters *(M. Boets)*
12,00	Other topics: website, Glasgow, collaboration with ARPAC
12,10	Planning: interim report, publication policy, future of ESAC
12,20	Take home session *(moderator R. Vander Stichele)*
12,50	Summary tasks and thanks
13,00	*Close*

6.2.2 Minutes

After the EARSS session the common EARSS – ESAC session was opened by P. Schrijnemakers on behalf of EARSS and H. Goossens on behalf of ESAC.

EARSS–ESAC session: Summary of discussion and conclusions

S. Bronzwaer, on behalf of the European Commission, explained the key areas of DG Sanco: surveillance, prevention & infection control, research & product development and international co-operation. DG Sanco stimulates cooperation between different surveillance networks (EARSS, ESAC, Euro TB, ENTER-Net). DG Sanco also stimulates implementation of Council Recommendation by co-ordinating a working group, aiming:

- to have in place intersectorial coordinating mechanisms at a national level within 1 year to enhance information exchange;
- to develop guidelines for the prudent use of antimicrobials and develop prevention and intervention programmes at a national level;
- to continue and improve EARSS, ESAC, SAR;
- to make a TV-film to explain the problem of AMR to a broad public;
- to coordinate action from other Commission services.

Furthermore the EC gives priority to initiatives enhancing external quality assurance exercises and standardisation of methods between laboratories in Europe.

M. Borg presented the ARmed study that will start in 2003 with collection of data on antimicrobial resistance, usage and infection-prevention and control, in collaboration and according to the methodology of EARSS, ESAC and Harmony. Countries that will participate: Turkey, Jordan, Cyprus, Maroc, Egypt, and Tunisia.

The preliminary results of a pilot-study based on collection of both resistance data and usage data from Belgium and the Netherlands for *S. pneumoniae* were presented on behalf of EARSS and ESAC. The pilot study illustrated that data on antibiotic usage and resistance can be linked at different aggregation levels. Limitations mainly resulted from small numbers of invasive isolates. It will certainly be of added value to combine these data in the near future.
To make this feasible EARSS national representatives/national data managers will be asked to provide coded geographic information of participating laboratories to further explore the possible relationship between resistance and usage data in the near future. For ESAC, it was decided to limit the prospective data collection to the geographical areas according the European NUTS-1 level.

Linkage to resistance data at a lower geographical level is not valuable due to the limited number of isolates.

The Self medication with Antibiotics and Resistance study (SAR) was launched by Flora Haaijer-Ruskamp. The study aims to quantify the consumption of OTC antibiotics and leftovers, to study on the acquisition of antibiotics and self-medication and to investigate the impact of non-prescribed consumption on AB-resistance. National representatives were invited to participate in this study that is performed in close collaboration with EARSS and ESAC. There was a positive response of most of the NR's. An in-depth discussion of the protocol took place during an extra evening session.

Many national representatives, the EC- representative and the management teams of EARSS and ESAC concluded that this 1st common plenary meeting was a big success. It was decided to organise a common meeting next year, preferably in a middle or eastern European country. Suggestions for the venue are welcome. It was suggested to invite ICM (Intersectorial Co-ordination Committee) at the next common meeting.

ESAC session: summary of discussion and conclusions

The afternoon session started with the presentation of the results of the retrospective data collection. There was an in depth presentation of the methodological problems encountered: coverage, denominator, and technical problems of data processing and ATC/DDD classification.
'Bed-days' was considered as the main problem. A more in-depth investigation is necessary. The NR's agreed to present the hospital data for international comparison based on DID until bed-days will be more uniformly defined.

Hege S. Blix represented the WHO-Oslo. She presented the ATC/DDD-methodology focused on antibiotics. H. Goossens proposed to install a working group on antibiotics within the WHO-Oslo-centre.

From 25 countries national data, derived from the retrospective data collection, were presented on a poster. During a guided poster-walk each N.R. had the opportunity to present the strengths and weaknesses of his data-collection system and to give a first presentation of the results. The confrontation of each country with its own results meant a first evaluation of the data collected. It was decided to send out to each country their national poster asking to make possible corrections before making the results available on a national level.

The round table discussion focused on the delivered data sets. These data sets are questioning if comparable, potential pit-falls were treated: incomplete or biased data, variability in denominators and in hospital/ambulatory care mix, discrepancies in ATC/DDD-assignments, time-shifts. The proposal for the prospective data collection was discussed and generally accepted:

- ATC-5 completed with route of administration (problem of privacy-protection for companies if only one product in a category);
- Monthly data-collection will also be a problem in several countries, particularly for the hospital sector. Possible solution: for hospitals: quarterly data collection; for ambulatory care: monthly data collection.

The ESAC morning session started with a more in depth discussion on some technical issues within the ESAC-project:

1. The **national register** will be cleansed by the ESAC management team and returned to the NR's for approval. Instructions will be sent again when requested.

2. A web page for collection of information on **ongoing projects** will be developed on the ESAC-website.

3. For building the **national ESAC network**, the involvement of the national ICM (Intersectorial Co-ordination Committee) is important.
   Suggestion to invite ICM at the next back-to-back-meeting.

4. Organization of **supra-national meetings**:
   - The Eastern cluster (applicant countries + RO + BU + RU + Turkey): planned in Prague, December 12-14, 2002
   - The Viking cluster (Nordic +Baltic countries + NL);
   - The Southern cluster (ES, PT, GR, FR, IT, MT)
   - The Eire and UK cluster (five countries).
   - The Bismarck cluster (DE, AT, CH, LU, BE)

5. For the **clinical classification** of antibiotics a special workgroup will be installed.
   Peter Davey (U.K.), Helmut Mittermayer, (Austria), Waleria Hryniewicz (Poland), Christian Rueff (Switzerland) and Dominique Monnet (Denmark) are interested to participate.

6. **The ESAC new project proposal** will focus on the further development of an established surveillance system of antibiotic consumption in Europe. The central database will contain validated use data of all European countries

accessible by Health care policy makers and researchers. In preparation of the new proposal, a questionnaire will be sent to all NR's asking for further suggestions. It is clear that for the new proposal the accent must be put on "Surveillance', this being the main object of the ESAC-project.

An overview of contracts and financial problems was given. There are still 6 of EU countries without contract signed and 6 of the applicant countries without MoU signed.

All EU countries need a form for declaration of costs for the second year of the project. It was decided to organize personal contacts with each country in other to arrange financial matters and contract problems

Ongoing projects in the field of antibiotic consumption were presented:

- Annemette Anker Nielsen presented the Danish system of data collection of antibiotic use
- Peter Davey presented outcomes of a programme for monitoring 'alert antibiotic' use in hospital and focused on a method to evaluate interventions
- Michael Borg showed the results of a study investigating antibiotic consumption in the general population in Malta and highlighted the problem of OTC consumption
- Anastasia Antoniadou presented a new intervention study planned to control the hospital consumption in Greece
- Matus Ferech demonstrated the high variability in reimbursement schemes in Europe focusing on the consequences for the collection of use antibiotic data

6.2.3 List of participants

EUROPEAN COMMISSION	
Luxemburg	Stef Bronzwaer
ESAC MANAGEMENT TEAM	
Belgium	Herman Goossens, Robert Vander Stichele, Erik Hendrickx, Monique Elseviers, Matus Ferech, Monique Boets
ESAC PARTICIPANTS	
Austria	Helmut Mittermayer
Bulgaria	Boyka Markova
Croatia	Arjana Tambic Andrasevic
Czech Republic	Ludvik Stika
Denmark	Dominique Monnet, Annemette Anker Nielsen
Finland	Pirkko Paakkari
France	Didier Guillemot, Philippe Maugendre
Greece	Helen Giamarellou, Anastasia Antoniadou
Hungary	Gabor Ternak
Iceland	Karl G. Kristinsson
Ireland	Robert Cunney
Italy	Guiseppe Cornaglia
Latvia	Sandra Berzina
Lithuania	Rolanda Valinteliene
Luxemburg	Robert Hemmer
Malta	Michael Borg
Norway	Hege Salvesen Blix
Poland	Waleria Hryniewicz, Pavel Grzesiowski
Romania	Irina Codita
Slovak Republic	Tomas Tesar
Slovenia	Milan Cizman
Portugal	Jose Campos
Sweden	Otto Cars
Switzerland	Christian Ruef
The Netherlands	Margreet Filius
Turkey	Serhat Unal
United Kingdom	Peter Davey
EARSS MT	
The Netherlands	P. Schrijnemakers, E. Tiemersma, N. Bruinsma, L. Monen, C. Schinkel-Jager, J. Degener
SAR PARTICIPANTS	
The Netherlands	F. Haaijer-Ruskamp, L. Grigoryan

6.3. Second EARSS - ESAC Plenary Meeting

The second joint EARSS – ESAC meeting took place in Warsaw, Poland, on 5 – 7 November 2003. The program, minutes and participants are presented here below.

6.3.1 Detailed Program

DAY 1	
ESAC session	
08,30	Welcome
09,00	Wrapping up the retrospective data collection Results of the retrospective data collection 2002 *(H. Goossens)* Overview of the 1997-2002 data *(H. Goossens)* Lessons from the past: validity of delivered data *(R. Vander Stichele)* Turn out from the ESAC pilot project *(M. Elseviers)* Publication policy *(H. Goossens)* Round table: evaluation of the pilot project *(R. Vander Stichele)*
10,00	*Coffee Break*
10,30	Gearing up the data collection in the new project Presentation of the new proposal *(M. Elseviers)* Basic requirements of the administrative data collection *(R. Vander Stichele)* Stratification of hospitals for sample based data collection *(M. Elseviers)* National registers of available antibiotics *(M. Ferech)* Assignment of new DDDs: report of meeting WHO (*M. Rønning)*
12,30	*Lunch*
ESGAP-ESAC session	
13,30	Problems with using the ATC classification and the DDDs * The experience of ARPAC * The experience of ESAC *(R. Vander Stichele)* * Discussion of the above
14,15	Analysing the relationship between antibiotic use and resistance: methods and pitfalls *(D. Monnet)*
14,45	Influence of reimbursement systems on antibiotic consumption in Europe *(M. Ferech)*
15,15	*Coffee Break*
15,45	Antibiotic use and resistance in intensive care units *(H. Hanberger)*
16,15	Containment of antimicrobial resistance in the United States: present and future initiatives *(J.Weber)*
16,45	What do we know about national antibiotic policies in Central and Eastern Europe *(M. Čižman)*
17,15	Variability of ESAC data: possible relationship with treatment recommendations and national antibiotic policies *(H. Goossens)*
18,00	*Close*

DAY 2

ESAC session	
08,30	The future of ESAC 2 EC policy and granting *(H. Goossens)* Using indicators to evaluate national antibiotic use *(R. Vander Stichele)* Call for participation in the ESAC 2 subprojects *(R. Vander Stichele)* ESAC timeline 2004 *(M. Elseviers)*
10,15	Coffee Break
EARSS-ESAC session	
10,30	Welcome
10,35	View of DG SANCO on the surveillance of antimicrobial resistance and consumption in Europe (H. Walerius)
11,05	Resistance and its determinants
11,15	Consumption and its determinants *(H. Goossens)*
11,25	Collaborative initiatives: linking consumption and resistance for *E. coli* and *S. pneumoniae (ESAC: M. Elseviers)*
11,55	First preliminary results of Self-medication with Antibiotics and Resistance (SAR)
12,10	Reconciling EARSS and ESAC data, highlighting policy aspects. (Case studies for some specific countries- *J. Kolman, M. Cizman, J. Campos, O. Lyytikäinen, P. Paakkari)*
12,40	*Lunch - posterwalk*
EARSS session	
14,00	Welcome + introduction
14,10	MRSA; variation in time and place
14,40	Trends in resistance of *S. pneumoniae*
15,10	Will *E. coli* become a difficult to treat pathogen?
15,30	Update: Metallo-beta-lactamase ESBL in Greece
15,35	Update: CTX ESBL in the UK
15,45	Coffee Break
16,15	Laboratory and hospital reference data: results from the questionnaire 2002
16,45	EARSS UK NEQAS: Methodology and preliminary results of EQA 2003
17,15	The EARSS proposal and financial news
17,35	EARSS website: update on innovations
18,00	*Close*

DAY 3

EARSS session	
	Antimicrobial susceptibility testing
09,00	Improve routine susceptibility testing of *S. aureus*: use cefoxitin screen disk?
09,15	Need for an update EARSS protocol for *S. aureus* screening?
09,30	New European clinical breakpoints and epidemiological cut-off values for surveillance - Discussion: Need for protocol adjustments for identifying trends in fluoroquinolone resistance in *S. pneumoniae*?
10,15	Coffee break
	New initiatives
10,45	Internet-based Information System (IBIS-EARSS)
11,15	Methods for strain identification: an overview of different typing approaches for *Staphylococcus aureus* as an example
11,45	Spa tying: a single sequence-based approach
12,15	Discussion: Molecular epidemiological typing within the EARSS network: potential for a new initiative?
12,45	Conclusive remarks
13,00	*Close*

6.3.2 Minutes

ESAC session

The session began with the presentation of the retrospective data collection and an overview of the 1997 to 2002 data.

With what had been learned from the past, the validity of the delivered data was then more thoroughly explained and questions answered when proposed.

After explaining the turn out of the ESAC pilot project and the presentation of the new proposal, a round table was set up to discuss the project and the problems arisen concerning publications and missing DDDs.

Regarding publications and the publication policy, everyone got a good feeling of the possibilities of data analysis with the data now in possession.
The methodological article was well received, as was the possibility to publish as a study group and the possibility for the national representatives to have a final check and approval.

The democratic discussion resulted in a clear choice for yearly data collection (in September) of AC quarterly data and HC yearly data at country level in ATC-5

plus Route of Administration (NUTS-1 will be discussed with the big countries separately).

Relationships with the national representatives
The excellent relations with the NR should be continued, in what is considered also by them (as stated explicitly and repeatedly) as a rewarding mutual cooperation.
The problem of the missing EU countries, Romania and Cyprus, is still considered to be important to be solved in the future, as is the participation of Switzerland.

Participation of the hospital pharmacists
The presence of two representatives of the European hospital pharmacists was very instrumental for the future of the collection of ESAC hospital care data.

The second day, the future of the new ESAC 2 proposal was discussed from different sites, scientific as well as economical and cost-beneficiary. National representatives were invited to participate more closely in the new possible subprojects of ESAC 2.

ESGAP-ESAC session

The problems with using the ATC classification and the DDDs was discussed more in detailed in the following common ESGAP-ESAC session.

The participants appreciated the structural advances made in the collaboration with the WHO, in the resolving of the problems with the missing DDD. Also the proposals with regard to the validation procedures were welcomed and now recognised as an important contribution to the project. But there was some opposition from methodological experts to the use of acronyms such as DID en DPP.

The second part of this session focused upon the relationship between antibiotic use and resistance and examples were given and explained whenever possible. The public was also invited to give their opinion on the matter.

J. Weber from the CDC, Atlanta, Georgia, USA, presented a different point of view, as he addressed present and future initiatives taken in the USA concerning antibiotic resistance.

M. Cizman made a comparable speech as he addressed the situation in Central and Eastern Europe.

The session was closed by addressing possible treatment recommendations and national antibiotic policies, which will have an ongoing impact within the different Member States of the European Community, countries signatories to the Agreement on the European Economic Area and associated countries of Central and Eastern Europe also after the end of the pilot ESAC project.

ESAC-EARSS session

After welcoming the EARSS participants, determinants on resistance and antibiotic consumption were discussed and the proposed initiative of linking both was illustrated by the linking of consumption and resistance for *E. coli* and *S. pneumoniae*.
Furthermore presentations on Spain, Slovenia, and Finland were presented, which served as a nice precursor for country publications, as in these presentations the times series of consumption and resistance were presented on the background of information of the country's antibiotic policy, an important issue to address in ESAC 2.

6.3.3 List of participants

ESAC MANAGEMENT TEAM	
Belgium	Herman Goossens, Robert Vander Stichele, Erik Hendrickx, Monique Elseviers, Matus Ferech, Monique Boets
ESAC PARTICIPANTS	
Czech Republic	Ludvik Stika , Petr Dvorák
Estonia	Ly Rootslane
Finland	Pirkko Paakkari, Tina Voipio
France	Philippe Maugendre
Germany	Katja De With
Greece	Helen Giamarellou, Anastasia Antoniadou
Hungary	Gabor Ternak
Ireland	Robert Cunney
Latvia	Sandra Berzina
Lithuania	Rolanda Valinteliene, Anna Stefanovic
Norway	Hege Salvesen Blix
Poland	Pawel Grzesiowski
Portugal	Luis Caldeira
Slovak Republic	Viliam Foltan, Tomas Tesar
Slovenia	Milan Cizman
Sweden	Gunilla Skoog
The Netherlands	Robert Janknegt
Turkey	Irfan Yengingüc
UK (Scotland)	Douglas Steinke
EARSS/ESAC PARTICIPANTS	
Austria	Helmut Mittermayer
Belgium	Herman Goossens, Erik Hendrickx
Bulgaria	Boyka Markova
Croatia	Arjana Andrasevic
Denmark	Dominique Monnet
Iceland	Karl Kristinsson
Italy	Giuseppe Cornaglia
Luxembourg	Robert Hemmer
Malta	Elizabeth Scicluna
Poland	Waleria Hryniewicz
Romania	Irina Codita
Slovenia	Marija Gubina
Spain	José Campos

EARSS MT	
The Netherlands	P. Schrijnemakers, E. Tiemersma, N. Bruinsma, L. Monen, C. Schinkel-Jager, J. Degener
EARSS PARTICIPANTS	
Czech Republic	Pavla Urbaskova
Estonia	Paul Naaber
Finland	Antti Nissinen, Outi Lyytikäinen
France	Hélène Aubry-Damon, Vincent Jarlier
Germany	Wolfgang Witte
Greece	Alkiviadis Vatopoulos
Hungary	Miklos Füzi
Ireland	Stephen Murchan
Israel	Raul Colodner
Italy	Annalisa Pantosti
Norway	Dag Seeger Halvorsen
Portugal	Manuela Caniça
Slovak Republic	Leon Langsadl
Slovenia	Jana Kolman
Spain	Fernando Baquero
Sweden	Gunnar Kahlmeter, Barbro Olsson-Liljequist
UK	Georgia Duckworth, Christine Walton, Theresa Lamagni
ESGAP PARTICIPANTS	
Austria	Agnes Wechsler-Fördös
Bulgaria	Emma Keuleyan
Croatia	Vera Vlahovic
Denmark	Henrik Westh
Switzerland	Philip Jenkins
The Netherlands	Inge Gyssens
UK	Barry Cookson, Fiona MacKenzie
USA	Todd Weber

6.4. Regional meetings

The meetings were important milestones in the building of a reliable data collection network for monitoring antibiotic consumption in the participating European countries.

The participants were asked

- To present the position of their institution within the national health care system of their country, with special attention to antibiotic policy and antibiotic consumption monitoring.
- To show how their institution can be instrumental for the prospective collection of antibiotic consumption data.
- To share their know-how and experience with their colleagues from other participating countries.

The expected outcomes were

- The exchange of ideas and approaches for prospective data collection from 2002 onwards.
- The guarantee of continuous and fluid data collection in the applicant countries.
- The preparation for the establishment and maintenance of a National Register of available antibiotics, and the organisation of its periodical validation
- An overview of the ongoing projects in the field of antibiotic policy in the participating countries.

The program of the meetings was each time based on the same template, and only adjusted according to the countries participating (see next page).

From all participating countries key persons were invited, such as drug utilisation data providers (national drug institutes, insurance companies), providers of administrative drug data and health care statistics, policy and decision makers and representative of hospital pharmacists, involved in hospital data collection.

Program template of the meetings

DAY 1

1st Plenary session: Introduction	
9,30	Welcome speech
9,45	ESAC Introduction: Objectives and Achievements *(Monique Elseviers)*
10,05	EARSS Introduction: Objectives and Achievements *(EARSS representative)*
10,20	Relationship between consumption and resistance *(Monique Elseviers)*
10,40	Coffee Break
Description of the health care system, antibiotic policy and drug consumption monitoring possibilities	
11,00	General overview of the countries' characteristics *(Matus Ferech)*
11,10 – 11,50	Country by country presentations
12,00	Data sources for antibiotic consumption: reimbursement versus sales data *(Matus Ferech)*
12,30	*Lunch*
2nd Plenary session: ESAC retrospective data collection	
13,30	ESAC retrospective data collection: presentation of the results *(Monique Elseviers)*
13,50	Methodological problems encountered *(Matus Ferech)*
Country retrospective data presentation (National representatives)	
14,05	*Poster Template Presentation* (Matus Ferech)
14,10 – 14,50	Country by country posters
15,00	Discussion: the quality of the retrospective data collection in the participating European countries *(Chairman: Robert Vander Stichele)*
15.30	Coffee Break
16,00	Introduction to prospective data collection: national register, network, basic requirements *(Robert Vander Stichele)*
16,45	Parallel sessions: Country meetings to discuss how to improve ESAC data collection in the different countries (*chaired by National Representatives*)
17,30	*Closure*

DAY 2

3rd Plenary session: Prospective data collection	
9.00	*National register, clinical classification and network building* (Robert Vander Stichele)
Round Table: Country meetings reports (Chairman: Robert Vander Stichele)	
9,30 -10,10	Country by country meeting reports
10,30	Coffee Break
11,00	Pilot project EARSS-ESAC: presentation of preliminary results *(Monique Elseviers)*
11,15	Variability in the European reimbursement schemes for antibiotics: consequences for ESAC *(Matus Ferech)*
11,30	Invited Presentations: free presentations by the participants
12,30	Take home session
13,00	*Lunch*

6.4.1 The Eastern Countries Meeting

The Eastern Cluster Meeting took place in Prague, Czech Republic, on 12-14 December 2002.

The following people of the following countries participated in the meeting.

BULGARIA	
	Markova Boyka University Hospital "Alexandrovska", Clinical Microbiology 1 Georgy Sofiiski St, 1431 Sofia
	Valcheva Jordanka National Health Insurance Fund, Head Drug Policy Department 4, Bigla Str., 1407 Sofia
	Benisheva Tania Ministry of Health, Head Drug Policy Department Nedelia Square N-5, 1000 Sofia
	Popova Maria Bulgarian Drug Agency 26, Yanko Sakazov Blvd., 1504 Sofia
CROATIA	
	Andrasevic Tambic Arjana University Hospital for Infectious, Pharmacovigilance Mirogojska 8, Zagreb
	Lerman Mirjana Ksaver 2004, Zagreb
	Vrsalovic Renata Ministry of Health, Department of Drugs Mirgosska Cesta 8, Zagreb
CZECH REPUBLIC	
	Prokes Michal Clinical Hospital for Infectious Disease, Department of Microbiology Drahobeljova 1404/4, 19003 Prague 9
	Urbaskova Pavla Military Health Insurance Fund, Health Policy Department Srobarova 48, 50005 Hradec Kralove
	Stika Ludvik Public Health institute, EARSS NR Heyrovskeho 1203, 10041 Prague 10
	Vlcek Jiri State Institute for Drug Control, NR Srobarova 48, 50005 Hradec Kralove
	Dvorak Petr Charles University Faculty of Pharmacy Lembitu 10, 10041 Prague 10
ESTONIA	
	Meresmaa Krista State Institute for Drug Control (SUKL), Department of Medicines Gyali ut 2-6, 10114 Tallinn

HUNGARY	
	Fuzi Miklos Estonian Health Insurance Fund, Bacteriology Stikra utca 8, 1097 Budapest
	Benkö Ria National Centre for Epidemiology, Clinical Pharmacy Department Chelmska Street 30/34, 6725 Szeged
POLAND	
	Grzesiowski Pawel University of Szeged, Prevention of Infection Chelmska Street 30/34, 00-725 Warsaw
	Szafraniec Szylwia National Institute of Public Health Georgy
	Cel Malgorzata National Institute of Public Health Georgy
SLOVAKIA	
	Foltan Viliam National Institute of Public Health, ORF Odbojarov 10, 83232 Bratislava
	Tesar Tomas Faculty of Pharmacy, ORF Odbojarov 10, 83232 Bratislava
SLOVENIA	
	Cizman Milan National Drug Institute, Department of Infectious Diseases 1525 Ljubljana
	Pecar Silva Faculty of Pharmacy, Dep. Social Pharmacy Trubarjeva 2, 1525 Ljubljana
	Bajec Tom University Medical Centre Llubljana Subiceva 3, 1000 ljubljana
	Furst Jurji Institute of Public Health 1507 Ljubljana
TURKEY	
	Yengingüc Irfan Sicon d.o.o. Firm, Head of Dep. for Medicinal Products Milli Müdafaa Cad. No. 24, Bakanliklar / Ankara
	Köselerli Rasim Ilkiz Sokak No. 1, Bakanliklar / Ankara

6.4.2 The Southern Countries Meeting

The Southern Cluster Meeting took place in Verona, Italy, on 7-8 March 2003.

The following people of the following countries participated in the meeting.

BELGIUM	
	Robert Vander Stichele ESAC / University of Antwerp, Departement Microbiologie Universiteitsplein 1, 2610 Wilrijk
	Monique Elseviers ESAC / University of Antwerp, Departement Microbiologie Universiteitsplein 1, 2610 Wilrijk
	Matus Ferech ESAC / University of Antwerp, Departement Microbiologie Universiteitsplein 1, 2610 Wilrijk
FRANCE	
	Didier Guillemot Institut Pasteur, Unité des Agents Antibactériens 25 - 28 rue du Dr. Roux, 75015 Paris
	Philippe Maugendre Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSAPS) Blvd. Anatole France 143-147, 93285 Saint-Denis Cedex
GREECE	
	Helen Giamarellou Sismanoglion General Hospital, 4th Department of Internal Medicine 151 26 Maroussi Attikis, 11526 Athens
	Anastasia Antoniadou Sismanoglion General Hospital, 4th Department of Internal Medicine 151 26 Maroussi Attikis, 11526 Athens
	E.Fouza National Organization for Medicines (EOF) Cholargos
	Areti Vardika Institute for Pharmaceutical Research and Technology (IFET) Pallini – Athens
	Alikie Maria Tsakalou Hospital Pharmacist Thessaloniki
ITALY	
	Roberta Joppi Servizio Farmaceutico – ASL 20 Verona
	Giuseppe Cornaglia University of Verona, Institute of Microbiology Strada Le Grazie 8, 37134 Verona
	Bertazzoni Minelli Elisa Policlinico G.B. Rossi Verona

PORTUGAL	
	Luis Caldeira Instituto Nacional da Farmacia e do Medicamento (INFARMED), OMPS, Observatório do Medicamento e Produtos de Saúde Parque de Saude de Lisboa; Av. Brasil, 53 – Pav. 24, 1749 -004 Lisboa, Portugal
	Vasco Maria Faculdade de Medicina de Lisboa Lisboa
	Isabel Mega Hospital de Santa Maria Lisboa
	Antonio Faria Vaz INFARMED Lisboa
	Zilda Mendes CEFAR – National association of pharmacies Lisboa
SPAIN	
	Fernando Baquero Hospital Ramón y Cajal Madrid
	Mercedes Sora Ortega L'Hospitalet de Llobregat Barcelona
	Francisco J. de Abajo Agencia Española del Medicamento Madrid
	Eugenia Mª Cortés Montejano Ministerio de Sanidad y Consumo Madrid
	José Campos Instituto Carlos III Ministry of Health, Centro Nacional Microbiología Cra. Pozuelo, ES-28220 Mazadahonda-Madrid

6.4.3 The Nordic and Baltic Countries Meeting

The Viking Cluster Meeting took place in Copenhagen, Denmark, on 25-26 April 2003.

The following people of the following countries participated in the meeting.

DENMARK	
	Andersen Morten Syddansk Universitet, Institut for Sundhedstjenesteforskning, Klinisk Winsløwparken 19, 5000 Odense C
	Dahl Jensen Vibeke Danish Medicines Agency Frederikssundsvej 378, 2700 Brønshøj
	de Joncheere Kees World Health Organization, Health Technology and Pharmaceuticals Scherfigsvej 8, 2100 Copenhagen
	Hansen Abba Holme The Danish University of Pharmaceutical Sciences, Dept. Social Pharmacy Universitetsparken 2, 2100 Copenhagen
	Monnet Dominique L. Statens Serum Institut, Dept. of Antimicrobial Resistance and Hospital Hygiene Artillerivej 5, 2300 Copenhagen S
	Müller-Pebody Berit Statens Serum Institut Artillerivej 5, 2300 Copenhagen S
ESTONIA	
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FINLAND	
	Paakkari Pirkko National Agency for Medicines Mannerheimintie 166 PB 55, 00301 Helsinki
	Rautakorpi Ulla-Maaija STAKES/FinOHTA, Bureau of Drug statistics Lintulahdenkuja 4, POBox 220, 00301 Helsinki
	Voipio Tinna National Agency for Medicines, Dept. of Pharmacovigilance and Drug Information Mannerheimintie 166 PB 55, 00301 Helsinki
ICELAND	
	Briem Haraldur Directorate of Public Health Austurstrond 4, 170 Seltjarnarnes
	Kristinsson Karl G. Landspitali University Hospital, Dept. of Pharmacovigilance and Drug Information v/Baronstig, 101 Reykjavik
	Sigfusson Eggert Ministry of Health and Social Security Laugaveg 116, 105 Reykjavik

LATVIA	
	Berzina Sandra P. Stradins Clinical University Hospital, Clinical Microbiology 13 Pilsonu Str., 1002 Riga
	Empelis Arnis P. Stradins Clinical University Hospital, Department of Pharmacy 13 Pilsonu Str., 1002 Riga
	Grakolska Aina State Agency of Medicines, Information Dept. 15 Jersikas Str., 1003 Riga
	Sumilo Dana Health Ministry, Dep.of Public Health 25 Baznicas Str., 1010 Riga
LITHUANIA	
	Meizis Viktoras Ministry of Health of the Republic of Lithuania, Foreign Affairs and European Integration Division Vilniaus str. 33, 2001 Vilnius
	Sabaliauskas Romualdas Ministry of Health of the Republic of Lithuania, Head of Public Health Department Vilniaus str. 33, 2001 Vilnius
	Stefanovic Anna Institute of Hygiene, Public Health Research Department Didzioji str. 22, 2001 Vilnius
	Valinteliene Rolanda Institute of Hygiene, Head of Public Health Research Department Didzioji str. 22, 2001 Vilnius
NORWAY	
	Rønning Marit World Health Organization, Collaborating Centre for Drug Statistics Methodology Sven Oftedalsvei 10, 0903 Oslo
	Salvesen Blix Hege Norwegian Institute of Public Health Postboks 4404 Nydalen, 0403 Norway
	Smabrekke Lars RELIS Nord-Norge, Universitetssykehuset i Nord-Norge HF Postboks 79, 9038 Tromse
	Steinbakk Martin Akershus University Hospital, Department of Microbiology 1474 Nobyhagen
SWEDEN	
	Cars Otto STRAMA, Swedish Institute for Infectious Disease Control Nobels Vag 18, 171 82 Solna
	Lundh Kristina STRAMA, Swedish Institute for Infectious Disease Control Nobels Vag 18, 171 82 Solna
	Skoog Gunilla STRAMA, Swedish Institute for Infectious Disease Control Nobels Vag 18, 171 82 Solna
	Stalsby Lundborg Cecilia Dep. of Public Health Sciences/ IHCAR Norrbacka, 171 76 Stockholm

CROATIA	
	Vlahovic-Pacevski Vera Karolinska Institutet , Department of Clinical Pharmacology Kresimirova 42, 51000 Rijeka
THE NETHERLANDS	
	Baart Fedor PO Box 30460, 2500 GL The Hague
	de Neeling Han RIVM, Laboratory for Infectious Diseases and Serological Screening PO Box 1, 3720 BA Bilthoven
	Filius Margreet PO Box 2040, 3000 CA Rotterdam
	Liem Yves PO Box 2040, 3000 CA Rotterdam
	Prins Jan Meibergdreef 9, 1105 AZ Amsterdam

6.4.4. The UK-Ireland-Malta Meeting

The UK-Ireland-Malta Meeting took place in Dublin, Ireland, on 15-16 May 2003.

The following people of the following countries participated in the meeting.

BELGIUM	
	Matus Ferech ESAC / University of Antwerp, Departement Microbiologie Universiteitsplein 1, 2610 Wilrijk
	Monique Elseviers ESAC / University of Antwerp, Departement Microbiologie Universiteitsplein 1, 2610 Wilrijk
	Robert Vander Stichele ESAC / University of Antwerp, Departement Microbiologie Universiteitsplein 1, 2610 Wilrijk
	Luc Proost Belgian Drug Information Center, Drug register specialist Brussels
IRELAND	
	Edmond Smyth Beaumont Hospital, Microbiology Department Beaumont, Dublin 9
	Robert Cunney National Disease Surveillance Centre 25-27 Middle Gardiner Street, Dublin 1
	Noreen Quinn Dep. of Health for Children Ireland
	Ajay Oza National Disease Surveillance Centre Ireland
MALTA	
	Christianne Micallef National Medicines Policy & Audit Unit (NMPAU), Health Department Malta
	Elizabeth Scicluna St Luke's Hospital, Infection Control Unit MSD08 G'Mangia
	Peter Zarb St Luke's Hospital, Infection Control Unit MSD08 G'Mangia
UK-NORTHERN IRELAND	
	Hugh Mc Gavock Antibiotic Resistance Group, UK DURG UK
	Kathryn Turner Family Practitioner Services, Central Services Agency, Pharmaceutical department UK
	Jaqueline Sheridan Family Practitioner Services, Central Services Agency, Information and Research UK

UK-WALES	
	Roger Walker Welsh School of Pharmacy UK
	Dave Hopkins Health Solutions Wales, Prescribing Services Unit UK
	Neil Jenkins Health Solutions Wales, Prescribing Services Unit UK
UK-SCOTLAND	
	Peter Davey Ninewells Hospital, Department of Clinical Pharmacology, Medicines Monitoring Unit Dundee DD1 9SY, Scotland
	Doug Steinke ISD Scotland, Primary Care Information Group UK
	Chris Waugh ISD Scotland, Primary Care Information Group UK
UK-ENGLAND	
	Phil Wiffen SACAR, Department of Health UK
	Anne Emery Department of Health, Statistics Division UK
	Kay Goodyear Veterinary Medicines Directorate, Policy Division UK
	John Threlfall Health Protection Agency, Laboratory Genetic Pathogens UK
	Helen Kendall PPA, Pharmaceutical Directorate UK
	Paul Frosdick NHS Information Authority, Aqueous II UK

6.4.5 The "Bismarck" Countries

The Bismarck Countries Meeting took place in Brussels, Belgium, on 13-14 June 2003.

The following people of the following countries participated in the meeting.

AUSTRIA	
	Mair Alfred Oberösterreichische Gebietskrankenkasse Gruberstr. 77, 4020 Linz
	Metz Sigrid Krankenhaus der Elisabethinen Linz, Institut für Hygiene, Mikrobiologie und Tropenmedizin Fadingerstrasse 1, 4020 Linz
	Mittermayer Helmut Krankenhaus der Elisabethinen Linz, Institut für Hygiene, Mikrobiologie und Tropenmedizin Fadingerstrasse 1, 4020 Linz
	Wieninger Peter Hauptverband der Sozialversicherungsträger Kundmanngasse 21, 1031 Vienna
	Windischbaur Sabine Krankenhaus der Elisabethinen Linz Fadingerstrasse 1, 4020 Linz
GERMANY	
	de With Katja University Hospital, Abteilung Medizin 2, Infektiologie Hugstetter Str. 55, 79106 Freiburg
	Kaemmerer Regine Bundesministerium für Gesundheit und Soziale, Referat 310 Am Propsthof 78A, 53108 Bonn
	Kern Winfried University Hospital, Abteilung Medizin 2, Infektiologie Hugstetter Str. 55, 79106 Freiburg
LUXEMBOURG	
	Bruch Marcel Direction de la Santé, Division de la Pharmacie et des Medicaments Allée Marconi, 2120 Luxembourg
	Hansen/Koenig Danielle Direction de la Santé (Ministère de la Santé) Villa Louvigny / Allée Marconi, 2120 Luxembourg
	Hemmer Robert Centre Hospitalier de Luxembourg, Service National des Maladies Infectieuses 4 rue Barblé, 1210 Luxembourg
THE NETHERLANDS	
	Janknegt Robert Maasland Ziekenhuis, Klin. Farmacie en Toxicologie P.O. Box 5500, 6130 MB Sittard

BELGIUM	
	Bruynseels Patrick RIZIV Tervurenlaan 211, 1150 Brussel
	De Falleur Marc RIZIV Tervurenlaan 211, 1150 Brussel
	De Smedt Marcella Landsbond der Christelijke Mutualiteiten Haachtsesteenweg 579, 1031 Brussel
	De Swaef André RIZIV Tervurenlaan 211, 1150 Brussel
	Devriese Els RIZIV Tervurenlaan 211, 1150 Brussel
	Mensaert Antoon RIZIV, Geneeskundige Verzorging Tervurenlaan 211, 1150 Brussel
	Mertens Raf Landsbond der Christelijke Mutualiteiten Haachtsesteenweg 579, 1031 Brussel
	Vandenbroele Henk RIZIV, Geneeskundige Verzorging Tervurenlaan 211, 1150 Brussel
	Goossens Herman ESAC / University of Antwerp, Departement Microbiologie Universiteitsplein 1, 2610 Wilrijk
	Elseviers Monique ESAC / University of Antwerp, Departement Microbiologie Universiteitsplein 1, 2610 Wilrijk
	Ferech Matus ESAC / University of Antwerp, Departement Microbiologie Universiteitsplein 1, 2610 Wilrijk
	Vander Stichele Bob ESAC / University of Antwerp, Departement Microbiologie Universiteitsplein 1, 2610 Wilrijk
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7. DISSEMINATION OF RESULTS

7.1 International Meetings

7.1.1 ECCMID 2003

- ECCMID OPENING PRESS CONFERENCE
- ECCMID PRESENTATIONS
    - Data collection performance in the European surveillance of antibiotic consumption: Results for the 1997-2001 retrospective data collection
    - Methodological problems encountered within the ESAC retrospective data collection
    - Consumption of antibiotics in ambulatory care in Europe: first results of the ESAC retrospective data collection
    - Consumption of antibiotics in hospital care in Europe: first results of the ESAC retrospective data collection
    - Country posters

7.1.2 EACPT 2003

- An exploration of the therapeutic arsenals of antibiotics in European countries using the drug utilisation 90% method
- Regional clusters in antibiotic consumption in Europe

7.1.3 ICAAC 2003

- Correlation between macrolide use and geographic diversity of Erythromycin-resistance among *Streptococcus pneumoniae* (SPN) and *S. pyogenes* (SPY) in 17 European countries

7.1.4 ISPOR 2002 – 2003

- Variability in European reimbursement schemes for antibiotics: consequences for European Surveillance of Antibiotic Consumption
- Consumption of antibiotics in Europe: results of the ESAC retrospective data collection

7.1.5 EUPHA 2004

- Consumption of antibiotics in Europe: results of the ESAC retrospective data collection

7.2 Publications

7.3 The ESAC Website

7.1 International meetings

7.1.1. ECCMID 2003

7.1.1.1 The ECCMID Opening Press conference

ECCMID OPENING PRESS CONFERENCE
"Emerging Infectious Diseases in the 21st Century

16.00 Welcome and introduction

16.05 Travel – Europe's new health threat?

16.25 Questions

16.35 The Hazards of Hospitals

16.55 Questions

17.05 Antibiotic consumption in Europe: first report of the European Surveillance of Antibiotic Consumption (ESAC) retrospective data collection *(Spokesperson - Herman Goossens)*

Determinants of antibiotic use in Europe
Measuring selective pressure with regard to resistance

17.25 Questions

17.30 Press conference ends

7.1.1.2. ECCMID 2003 Presentations

DATA COLLECTION PERFORMANCE IN THE EUROPEAN SURVEILLANCE OF ANTIBIOTIC CONSUMPTION: RESULTS FOR THE 1997-2001 RETROSPECTIVE DATA COLLECTION

ECCMID 2003 ORAL PRESENTATION

R. Vander Stichele, M. Ferech, M. Elseviers, and H. Goossens
ESAC Management Team, University of Antwerp, Belgium

Objectives
ESAC (European Surveillance of Antibiotic Consumption, granted by DG SANCO of the EC) is an international network of national surveillance systems, aiming to collect comparable antibiotic consumption data in Europe. During the first phase, date accessibility and validity, as well as strengths and weaknesses of national systems were assessed. Quarterly data were to be collected retrospectively (1997-2001) from ambulatory (AC) and hospital care (HC) in 31 countries, using ATC/DDD classification (WHO, version 2002),

Methods
Data were collected according to a pre-established protocol, defining a common format. Additional information was collected by questionnaire: midyear country population, covered population, and nature of the ATC/DDD assignment process, data provider characteristics, and country bed days.

Results
Data from 26 countries were delivered. Two current EU countries were yet missing (Germany and Ireland) and two first wave EU countries (Cyprus, Estonia). In addition, data from Bulgaria, Croatia, Iceland, Norway and Turkey were available.
Two countries could only deliver aggregated total data (Iceland, Turkey), 2 countries only AC data (Austria, England), 1 country only HC data (Malta), two countries only total and HC data (Bulgaria, Czech Republic), and 19 countries were able to deliver both AC/HC data separately. Hence, AC data were available from 25 countries and HC data from 22 countries.
AC data were reimbursement data in 11 countries; in the remaining 14 countries, sales data were provided, collected from companies in 2 (France, Greece), from wholesalers in 9 (Bulgaria, Croatia, Finland, Iceland, Latvia, Norway, Poland, Turkey,) and from community pharmacists in 3 countries (Denmark, the Netherlands, Sweden); in 4 countries (Austria, Lithuania, The Netherlands, Poland), sample (not census) data were collected.
In all but 1 country (Belgium), HC data were sales data (as hospitals are budgeted in most countries).
Nine countries (Belgium, Denmark, England, Finland, Greece, The Netherlands, Poland, Slovenia, and Sweden) were able to deliver quarterly AC data for all five years.

Conclusions
For the first time, a credible alternative to industry sources has been established for the collection of internationally comparable data on antibiotic consumption in Europe, based on cooperation between regulatory authorities, scientific organisations, health insurers, and professional organisations.

METHODOLOGICAL PROBLEMS ENCOUNTERED WITHIN THE ESAC RETROSPECTIVE DATA COLLECTION

ECCMID 2003 ORAL PRESENTATION

M. Ferech, M. Elseviers, R. Vander Stichele and H. Goossens
ESAC Management Team, University of Antwerp, Belgium

Objectives
ESAC (European Surveillance of Antibiotic Consumption, granted by DG SANCO of the EC) is an international network of national surveillance systems, aiming to collect comparable antibiotic consumption data in Europe. During the first phase, date accessibility and validity, as well as strengths and weaknesses of national systems were assessed. Quarterly data were to be collected retrospectively (1997-2001) from ambulatory (AC) and hospital care (HC) in 31 countries, using ATC/DDD classification (WHO, version 2002).

Methods
Data were collected by a pre-established protocol, defining a common format. Additional information was collected by questionnaire: mid-year country population, covered population, nature of ATC/DDD assignment process, data provider characteristics; the number of country bed days (BD) and the BD calculation technique. AC data were to be expressed in DDD/1000 inhabitants/day (DID), while HC data in DDD/100 BD.

Results
The following methodological problems were encountered:
Data originate from disparate sources (sales/reimbursement, census/sample data)
Bias is possible from extrapolation from sample data or incomplete census data.
The ATC/DDD assignment process may not be streamlined; most countries stated to have used ATC/DDD 2002 versions, but we observed non-standardised assignment of DDDs for combinations and substances without official DDD and failure to shift G04A (urinary antiseptics) into J01.
The number of BD's is a problematic denominator; it proved difficult to reliably and timely estimate BD's and to determine the proportion of long-term rehabilitation or psychiatric BD's.
The mix between AC/HC is varying, as data from nursing homes, day care centres and policlinic prescribers are differently assigned to AC or HC.
In reimbursement data, bias in comprehensiveness is possible in Austria, Lithuania, Spain, and Portugal, either because of OTC sales or peculiarities in the reimbursement system.
In sales data, parallel export or import needs to be determined, as it may distort the validity of the population exposure estimate (e.g. Greece).

Conclusions
Due to uncertain reliability of BD data, their application as a comparable denominator at the international level is jeopardised; hence, we decided to express national HC use data in DID, as in AC. In the upcoming prospective ESAC data collection, it will be possible to adequately deal with most of the methodological problems, encountered in the retrospective data collection.

CONSUMPTION OF ANTIBIOTICS IN AMBULATORY CARE IN EUROPE: FIRST RESULTS OF THE ESAC RETROSPECTIVE DATA COLLECTION.

ECCMID 2003 ORAL PRESENTATION

M. Elseviers, M. Ferech, R. Vander Stichele and H. Goossens.
ESAC Management Team, University of Antwerp, Belgium.

Objectives
ESAC (European Surveillance of Antibiotic Consumption, granted by DG SANCO of the EC) is an international network of national surveillance systems, aiming to collect comparable antibiotic consumption data in Europe. During the first phase, data accessibility and validity, as well as strengths and weaknesses of national systems were assessed. Quarterly data were to be collected retrospectively (1997-2001) from ambulatory (AC) and hospital care (HC) in 31 countries, using ATC/DDD classification (WHO, version 2001), and expressing results in DDD/1000 inhabitants per day (DID).

Methods
25 countries provided AC use data; 19 were suitable for international comparison. The remaining 5 were not comprehensive (AT, LT), or not separable from total data, including HC (BG, CZ, IS, TR).

Results
In 2001, AC use in Europe varied between 10.0 DID (NL) and 32.9 DID (FR). Other high consumers were (in decreasing order) GR, IT, LU, PL, PT, BE and SK, all with a total use > 24 DID. During the observation period of 5 years, consumption clearly increased in GR and PL and decreased in BE and ES. High seasonal fluctuations in AC use (mean increase >30% in quarter 1 and 4 compared to quarter 2 and 3) were observed in BE, GR, PL and SI. High seasonal fluctuations were particularly noted in countries with high consumption (r=0.77). In 2001, median (range) proportional use of penicillins (PEN), cephalosporins (CEP), tetracyclines (TET), macrolides (M) and quinolones (Q) was 45 (31-63), 11 (<1-23), 10 (2-23), 15 (6-23) and 7% (1-14) of total use, respectively; the median (range) proportion of small spectrum PEN, ampicillin/amoxicillin and combination with clavulanic acid was 10 (<1-66), 45 (12-84), and 32% (<1-59) of total PEN use, respectively.
Large regional differences could be observed in consumption patterns. Northern European countries (NO, SE, FI, DK, NL, LV) are low consumers using relatively narrow spectrum PEN and TET more extensively and less CEP and Q. Southern European countries (PT, IT, GR, FR) are high consumers using no longer narrow spectrum PEN, but exceptionally high proportions of CEP, M and Q.

Conclusions
Intriguing high variation in AC use in Europe was observed and needs to be related to determinants of use and variation in resistance patterns.

CONSUMPTION OF ANTIBIOTICS IN HOSPITAL CARE IN EUROPE: FIRST RESULTS OF THE ESAC RETROSPECTIVE DATA COLLECTION.

ECCMID 2003 ORAL PRESENTATION

M. Elseviers, M. Ferech, R. Vander Stichele and H. Goossens.
ESAC Management Team, University of Antwerp, Belgium.

Objectives
ESAC (European Surveillance of Antibiotic Consumption, granted by DG SANCO of the EC) is an international network of national surveillance systems, aiming to collect comparable antibiotic consumption data in Europe. During the first phase, data accessibility and validity, as well as strengths and weaknesses of national systems were assessed. Quarterly data were to be collected retrospectively (1997-2001) from ambulatory (AC) and hospital care (HC) in 31 countries, using ATC/DDD classification (WHO, version 2001), and expressing results in DDD/1000 inhabitants per day (DID).
Methods
HC use data were provided sent by 22 countries; 2 were unsuitable for international comparison, due to late data delivery in an idiosyncratic format (CZ, PT). In 6 countries (BG, ES, HR, IT, LT, PL), sample (not census) data were collected.
Results
In 2001, HC use in Europe varied between less than 1.5 DID in NL, NO, SE, SK and DK to more than 3.5 DID in FI and FR. HC use varied between 5 (SK) and 17% (FI) of total consumption in the different European countries. The median (range) proportion of use in 2001 of penicillins (PEN), cephalosporins (CEP), carbapenems (CAR), glycopeptides (GLYC) and quinolones (Q) represented 46% (14-86), 19% (1-35), 1% (<1-3), 1% (0-3) and 9% (1-16) of total HC use, respectively; the median (range) CEP generations represented (from first to fourth): 20% (2-39), 51% (3-87), 25% (8-73) and 1% (0-5) of total CEP use. Consumption was particularly low for PEN (<20%) in BG, FI, and IT and was low for CEP (<7%) in FR and LV. Consumption was high for: CARB (>2%) in ES and SE; for GLYC (>2%) in ES, GR, and IT; for Q (>13%) in ES, FI, SE, SI, and SK.
Conclusions
In HC, a wide variation in total use of PEN, CEP and Q, as well as within the CEP generations were observed. Countries do not seem to cluster in regional supra-national consumption patterns.

The ESAC country posters on the consumption of antibiotics are attached to this report (Results of the retrospective data collection 1997 – 2001, posters presented at ECCMID, Glasgow, 2003).

7.1.2. EACPT 2003

AN EXPLORATION OF THE THERAPEUTIC ARSENALS OF ANTIBIOTICS IN EUROPEAN COUNTRIES USING THE DRUG UTILISATION 90% METHOD

EACPT 2003 POSTER PRESENTATION

M. Ferech, R. Vander Stichele, M. Elseviers, and H. Goossens
ESAC Management Team, University of Antwerp, Belgium

Objectives

ESAC (European Surveillance of Antibiotic Consumption, granted by DG SANCO of the EC) is an international network of national surveillance systems, aiming to collect comparable antibiotic consumption data in Europe. Within the project, the aim of this study was to investigate the number and nature of commonly used antibiotics in different countries, using the DU90 method.

Methods

An attempt was made to retrospectively collect data from ambulatory care (AC) in 31 countries, using the Anatomic Therapeutic Clinical Classification (ATC-WHO, version 2002), and expressing results in Defined Daily Doses (DDD) for the period 1997-2001.

For each of the 206 antibiotics (including combinations), currently listed in the ATC J01 group (Antiinfectives for systemic use), the volume of use in terms of DDD was determined in each country, and ranked in a Lorenz curve distribution, with a cut off at 90% of the total consumption.

Results

The ESAC team succeeded to collect acceptable AC data for 1997-2001 from 16 European countries. Of the 206 available ATC codes, no consumption whatsoever was recorded in any country for 67 ATC codes; 24 ATC codes were used in only one country; 115 ATC codes were used in at least two countries. The median number per country of ATC codes with some traceable consumption was 60 (P25-P75 48-66), with Norway at the extreme low range (32) and Spain at the extreme upper range (75).

When the analysis was limited to the DU90 segment, the median number of ATC codes was 14 (P25-P75 13-15), with Slovenia at the extreme low range (9) and France at the extreme upper range (21).

Within the DU90, 48 antibiotics occurred in at least one country (15 substances only in one single country); one ATC code (amoxicillin) was a component of DU90 segment in all countries; and another one (doxycycline) in all but one country (Denmark).

Conclusions

In 2001 only for 67.5% of the antibiotics with assigned ATC codes some trace utilisation was recorded in the ambulatory sector within 16 European countries. The segment with substantial utilisation (with the cut off determined by the DU90 method) was limited to 23.3%. Remarkable differences between the therapeutic arsenals of antibiotics were identified within a representative sample of European countries. This variability may reflect differences in quality of care and explain the diverging patterns of emergence of antibiotic resistance in Europe. The historical, cultural and economic determinants of this variability merit further research.

REGIONAL CLUSTERS IN ANTIBIOTIC CONSUMPTION IN EUROPE

EACPT 2003 POSTER PRESENTATION

Monique M. Elseviers, Robert H. Vander Stichele, Matus Ferech and Herman Goossens
ESAC management team, University of Antwerp, Belgium

Introduction

Within the framework of the ESAC project (European Surveillance of Antibiotic Consumption, EU project granted by DG/SANCO), retrospective data of antibiotic use in ambulatory care (AC) and hospital care (HC) for the period 1997-2001 was collected on a quarterly base. Although wide variation in consumption patterns between different European countries could be observed, the question arises if this variation showed regional clustering as previously also observed in European resistance patterns.

Methods

Consumption of antibiotics was expressed according to ATC/DDD classification (WHO, version 2002) and volume was presented in DDD/1000 inhabitants per day (DID). Antibiotic use data were provided by 26 countries; AC use data of 19 countries and HC use data of 22 countries were suitable for international comparison. European countries were geographically clustered in North (LT, LV, NL, NO, SE, DK, FI), South (ES, IT, PT, GR, MT, FR), Central (BE, LU), East (BG, HU, SK, SI, HR, PL) and West (UK). Antibiotic consumption between clusters was compared using ANOVA.

Results

In 2001, total AC use (mean, range) differed significantly between regional clusters and was low in the North (14.5 DID (10.0-19.8)) and the West (14.6 DID), moderate in the East (20.6 DID (17.4-24.8)) and high in Central (25.3 DID (24.3-26.4)) and South (26.6 DID (18.8-32.9)). High seasonal fluctuations in AC use (mean increase > 30% in quarter 1 and 4 compared to quarter 2 and 3) were observed in South, Central and East while in North and West the increase in consumption during winter was limited to 20%. Large regional differences could be observed in the proportional use of different antibiotic classes. North was using low proportions of cephalosporins (CEP) and quinolones (Q) and higher proportions of tetracyclines (TET). In contrast, in South and Central, the proportional use of CEP, macrolides (M) and Q was exceptionally high. Only in North and East, small spectrum penicillins were still extensively used. In 2001, total HC use varied between 1.6 DID in East and 2.7 DID in South, showing no significant differences between regional clusters. In HC, a wide variation in total use of PEN, CEP and Q, as well as within the CEP generations, was observed. Proportional use of CEP varied between 6 and 35% of total HC consumption and was high in BG, LU, GR, HR and NO. Proportional use of Q varied between 1 and 10% and was high in FI, SK, SE, ES and SI. Although variations between countries are also substantial, countries do not seem to cluster in regional consumption patterns for HC use.

Conclusion

In AC, the high variation in antibiotic use observed between different European countries was clearly related to geographical clustering. In HC, regional clustering of observed variation could not be documented.

7.1.3. ICAAC 2003

CORRELATION BETWEEN MACROLIDE USE AND GEOGRAPHIC DIVERSITY OF ERYTHROMYCIN-RESISTANCE AMONG STREPTOCOCCUS PNEUMONIAE (SPN) AND S. PYOGENES (SPY) IN 17 EUROPEAN COUNTRIES

ICAAC 2003 POSTER PRESENTATION

H. Goossens[1] , M. Elseviers[1], M. Ferech[1], E. Hendrickx[1], R. Vander Stichele[1], A. Bryskier[2] and ESAC national representatives
ESAC Management Team, University of Antwerp, Belgium[1]; Aventis, France[2]

Background
There are huge country-to-country differences in antibiotic use and resistance in Europe and there is a complex relationship between resistance and selective pressure.
Methods
A total of 4202 SPN and 4179 SPY collected in 1999 from respiratory tract specimens in 17 European countries were included. MICs for erythromycin A (ERY) were tested according to the NCCLS guidelines. Macrolide (M) resistance genes {*erm* (A), *erm* (B), *mef* (A), *mef* (E)} were detected by PCR. M use in ambulatory care in 1998 was obtained from ESAC (European Surveillance of Antibiotic Consumption), using ATC/DDD classification (WHO, version 2002), and expressing results in DDD/1000 inhabitants per day (DID). Spearman correlation coefficients were calculated. P values < 0.05 were considered statistically significant and < 0.1 regarded as a trend towards significance.
Results
M use in Europe varied between 1.05 (NL) and 5.21 (GR) DID; short-acting (SA), intermediate-acting (IA) and long-acting (LA) M use varied between 0.12 (NL) and 1.98 (UK), 0.47 (UK) and 4.11 (GR), 0.03 (UK) and 1.39 (SI) DID, respectively. In SPN, statistically significant correlations were found for the following combinations: ERY-resistance (MIC>1 µg/mL) and use of M (P<0.001) and IA-M (P=0.003); *erm* (B) prevalence and use of M (P=0.002) and IA-M (P=0.006). We found a trend towards significance for ERY-resistance and use of LA-M (P=0.08). In SPY, we found a significant association between: ERY-R and use of M (P=0.02) and IA-M (0.007); *mef* (A) prevalence and use of M (P=0.007) and IA-M (P=0.006).
Conclusions
M resistance was found to be correlated with the intensity of the M selective pressure, particularly of IA-M use in *erm* (B)-positive SPN and *mef* (A)-positive SPY. Dissemination of resistant clones could not be assessed because genetic typing was not performed.

7.1.4. ISPOR

VARIABILITY IN EUROPEAN REIMBURSEMENT SCHEMES FOR ANTIBIOTICS: CONSEQUENCES FOR EUROPEAN SURVEILLANCE OF ANTIBIOTIC CONSUMPTION (ESAC PROJECT)

ISPOR 2002 POSTER PRESENTATION

Ferech M, Elseviers MM, Vander Stichele RH, Goossens H., University of Antwerp, Belgium

Objective
The ESAC project was funded by the European Commission to collect reliable and comparable data on antibiotic consumption in all European countries. The aim of this study is the identification of reimbursement status of antimicrobials in participating countries, to assess its impact on the comparability of utilization data, collected in national databases.
Methods
Structured questionnaire was sent to local experts in all EU and applicant countries and obtained data were validated by comprehensive literature search. We limited this pilot analysis to reimbursement rules for uncomplicated acute infection in adult persons (economically active), as co-payment schemes often vary widely, dependent on health and social status of patient.
Results
Thirty countries participated. Two axes of differentiation were discovered in the reimbursement systems. Firstly, the axis of homogeneity: is the reimbursement rate fixed and identical across and among antibiotic classes or not? Secondly the axis of initial private payment: is the reimbursement system without limitations or does the reimbursement start only above a fixed threshold co-payment (prescription cap) or a threshold co-payment for multiple prescriptions over a given period? Homogeneity without threshold co-payment was observed most frequently (n=13). Homogeneity, with threshold co-payment was observed in 8 countries. In the remaining 9 countries reimbursement status differs across antibiotic classes, without reimbursement limitation in 6 countries, with threshold co-payment in 3 countries
Conclusions
In many European countries, claims databases based on dispensed reimbursed medication suffice to record antibiotic usage in a valid way, as all antibiotics are to some extent reimbursed. In the other countries, where not all antibiotics are reimbursed and/or where reimbursement starts only above a threshold co-payment, data from claims databases will not reflect the actual level of utilization and need to be completed with alternative methods of data collection.

CONSUMPTION OF ANTIBIOTICS IN EUROPE: RESULTS OF THE ESAC RETROSPECTIVE DATA COLLECTION.

ISPOR 2003 POSTER PRESENTATION

Ferech M, Elseviers M, Vander Stichele R, Goossens H.
ESAC Management Team, University of Antwerp, Antwerp, Belgium

Objectives
ESAC (European Surveillance of Antibiotic Consumption, granted by DG SANCO of the EC) is an international network of national surveillance systems, aiming to collect comparable antibiotic consumption data in Europe. During the first phase, data accessibility and validity, as well as strengths and weaknesses of national systems were assessed. METHODS Quarterly data were to be collected retrospectively (1997-2001) from ambulatory (AC) and hospital care (HC) in 31 countries, using ATC/DDD classification (WHO, version 2001), and expressing results in DDD/1000 inhabitants per day (DID).
Results
AC use data were provided by 25 countries; 21 were suitable for international comparison. The remaining 3 were not comprehensive or not in a format enabling international comparison (TU). Quarterly AC data were delivered by 10 countries. HC use data were provided by 23 countries; 21 were suitable for international comparison, 14 of them were based on a limited sample. In 2001, AC use in Europe varied between 10.0 DID (NL) and 32.9 DID (FR). Other high consumers were (in decreasing order) GR, IT, LU, PL, PT, BE and SK, all with a total use exceeding 24 DID. During the observation period of 5 years, consumption clearly increased in GR and PL and decreased in BE and ES. High seasonal fluctuations in AC were observed in BE, GR, PL and SI. Large regional differences could be observed in consumption patterns. Northern European countries (NO, SE, FI, DK, NL) are low consumers using commonly narrow spectrum penicillins while Southern European countries are high consumers using broad spectrum penicillins and exceptionally high proportions of cephalosporins, macrolides and quinolones.
Conclusions
An intriguingly high variation in antibiotic use in Europe was observed and needs to be related to social, cultural and economic determinants of use as well as to variation in resistance patterns. Especially in AC, countries seem to cluster in regional consumption patterns.

7.1.5. EUPHA 2004

CONSUMPTION OF ANTIBIOTICS IN EUROPE: RESULTS OF THE ESAC RETROSPECTIVE DATA COLLECTION.

EUPHA 2004 POSTER PRESENTATION

M. Ferech, M. Elseviers, R. Vander Stichele and H. Goossens.
ESAC Management Team, University of Antwerp, Belgium.

Objectives
ESAC (European Surveillance of Antibiotic Consumption, granted by DG SANCO of the EC) is an international network of national surveillance systems, aiming to collect comparable antibiotic consumption data in Europe. During the first phase, data accessibility and validity, as well as strengths and weaknesses of national systems were assessed.
Methods
Quarterly data were to be collected retrospectively (1997-2001) from ambulatory (AC) and hospital care (HC) in 31 countries, using ATC/DDD classification (WHO, version 2001), and expressing results in DDD/1000 inhabitants per day (DID).
Results
AC use data were provided by 25 countries; 21 were suitable for international comparison. The remaining 3 were not comprehensive or not in a format enabling international comparison (TU). Quarterly AC data were delivered by 10 countries. HC use data were provided by 23 countries; 21 were suitable for international comparison, 14 of them were based on a limited sample.
In 2001, AC use in Europe varied between 10.0 DID (NL) and 32.9 DID (FR). Other high consumers were (in decreasing order) GR, IT, LU, PL, PT, BE and SK, all with a total use > 24 DID. During the observation period of 5 years, consumption clearly increased in GR and PL and decreased in BE and ES. High seasonal fluctuations in AC use (mean increase >30% in quarter 1 and 4 compared to quarter 2 and 3) were observed in BE, GR, PL and SI. Large regional differences could be observed in consumption patterns. Northern European countries (NO, SE, FI, DK, NL, LV) are low consumers using commonly narrow spectrum penicillins while Southern European countries (PT, IT, GR, FR) are high consumers using broad spectrum penicillins and exceptionally high proportions of cephalosporins, macrolides and quinolones.
Conclusions
An intriguingly high variation in anibiotic use in Europe was observed and needs to be related to social, cultural and economic determinants of use as well as to variation in resistance patterns. Especially in AC, countries seem to cluster in regional consumption patterns.

7.2 Publications

List of proposed publications

PROPOSED TOPIC	PRINCIPLE AUTHOR
Outpatient Antibiotic Use in Europe: Determinants of Use and Impact on Resistance. *	Herman Goossens
European Surveillance of Antimicrobial Consumption (ESAC): Data Collection Performance and Methodological Approach **	Bob Vander Stichele
Correlation between macrolide use and geographic diversity of Erythromycin-resistance among *Streptococcus pneumoniae* (SPN) and *S. pyogenes* (SPY) in 17 European countries	Eric Hendrickx
Critical assessment of the volume of outpatient use of the broad spectrum penicillins and their combinations in Europe	Matus Ferech
Availability of antibiotics in European countries: Registers of Antibiotics	Matus Ferech
Variability in European Reimbursement Schemes for Antibiotics: Consequences for European surveillance of antibiotic consumption (ESAC project)	Matus Ferech
Trends of antibiotic use and link with guidelines	Samuel Coenen
Trends of use, European regional clusters, seasonal variations	Monique Elseviers
Fluoroquinolones use in ambulatory care	ESAC NR
Macrolide use in ambulatory care	ESAC NR
Outpatient use of beta-lactam antibiotics	ESAC NR
Antibiotic consumption in the United kingdom	Matus Ferech
Utilisation of antibiotics in Europe (1997-2001): Hospital Care	Monique Elseviers
Investigating the relationship between consumption of antibiotics and resistance to *Streptococcus pneumoniae*: linkage between the ESAC and EARSS databases.	Monique Elseviers
Indicators of antibiotic use	Bob Vander Stichele
Utilisation of antibiotics in Belgium (1997-2001): An attempt to collect comprehensive, valid and internationally comparable data.	Samuel Coenen

*Submitted to The Lancet

** Accepted in The British Journal of Clinical Pharmacology

7.3 The ESAC Website

During the ESAC project a website has been developed, accessible for the general public using the following link: http://www.ua.ac.be/esac/ .

Comprehensive information about the ESAC project has been gathered on this website.

Information about the background and the global structure of the project, the management team, the participating countries and NR's, and collaborating organisations, is displayed, as well as information about the different international meetings and conferences with ESAC participation that took place, data on ongoing projects and links to related projects

Downloadable pdf files are available of these topics, such as the oral and poster presentations held at the different international meetings, the program, minutes and participants to the different ESAC meetings, and some technical documents such as the ABC-calculator.

Further information about the ESAC project as well as more detailed consumption data can be obtained on request, after submission of the research protocol.

8. FINAL CONCLUSIONS ABOUT THE WHOLE ACTIVITY

The ESAC project represent the first set of publicly available standardised and validated supranational data on antibiotic use in Europe.
Our results show that (i) countries in Southern and Eastern Europe generally consume more antibiotics than in Northern Europe, (ii) there is a tendency to use new antibiotics, which fail to offer substantial improvements over other available drugs, and (iii) the variation in resistance between different European countries can be explained by variation in selection pressure for resistance.
The critical level of antibiotic use required to trigger the emergence of resistance to significant levels should be studied. Population-based studies are needed to determine the motivations, expectations and incentives that lead persons to use or not use antibiotics. Genetic studies should explore: differences in symptomatic response to infection in Europe, the influence of host genetics on colonisation and dissemination of bacterial clones, and the pharmacokinetic differences of antibiotics among human populations which may influence the selection of resistant bacteria. The ethics of promoting antibiotics in clinical settings where they are unnecessary should be given serious consideration.
The ESAC data allow audit of patterns of antibiotic prescribing, educational and other interventions, evaluation of guidelines and policies, and monitoring of the outcomes of the interventions. Studies are urgently needed to identify which patients benefit from antibiotic treatment, particularly in primary care and for lower RTI. Given the emergence of bacterial resistance and the observed decline in the rate of development of novel antibiotics, we must study and implement (novel) effective professional and public strategies to encourage appropriate prescribing of antibiotics. If not, we will loose the miracle drugs of the 20th century.

9. SUMMARY OF THE PROJECT

9.1 Background

Antibiotic consumption is increasingly recognised as the main driver for antibiotic resistance, a major European and global public health problem.
Differential selection pressure of antibiotics agents may be responsible for some of the observed geographic differences of the proportion of resistance to various classes of antibiotics in Europe.
However, data on antibiotic use are scarce and not freely available, and the factors that determine differences in antibiotic use are not fully understood

9.2 Aims

The main objectives of the ESAC project were to consolidate the continuous collection of comprehensive antibiotic consumption data, for ambulatory care and hospitals, in all participating European countries and to use this European database to develop health indicators of antibiotic use and to use a set of core indicators to give feedback to the participating countries.
The consumption data might also be assessed in relation to resistance patterns, incidence of infectious diseases and guidelines for treatment of infections.

9.3 Methods

The collection of administrative data on antibiotic consumption was performed on a bi-annual base to construct an ESAC database. Data were then validated by the use of a national register showing the linkage to the ATC/DDD classification (WHO, Collaborating centre for Drug Statistics Methodology, Oslo) for all available antibiotics in the countries.

9.4 Findings-Results

A database on antibiotic consumption in the participating ESAC countries was constructed. To further disseminate the knowledge in the field of antibiotic consumption, an interactive ESAC website was developed, including aggregated consumption data as well as an electronic bibliography of European published and ongoing studies in the field of antibiotic consumption. This website is accessible for the general public. For health authorities and scientists, more detailed consumption data will be available on request.
National authorities annually received feedback on their national antibiotic consumption profile using a well-established set of core indicators.

ESAC also published yearbooks on antibiotic consumption handling the main topics of the ESAC surveillance system of the preceding year.
Scientific papers will continue to be published, focusing on the development of indicators, the linkage of consumption to antibiotic resistance, consumption patterns in specific groups and the pharmaco-economic evaluation of antibiotic consumption.
ESAC organised annual meetings for the national representatives and regional meetings for the national ESAC networks to stimulate and enhance the activities at the national level.

9.5 Conclusions

The ESAC project provides for the first time publicly available antibiotic use data. Antibiotic use was clearly correlated with levels of resistance across Europe. These data might provide a tool for assessing public health strategies aiming to reduce antibiotic selective pressure.

10. FINANCIAL REPORT

SI2.325736 (52001CVG4-016)
Scientific evaluation on the use of antimicrobial agents in human therapy
acronym : ESAC

FINANCIAL REPORT IN EURO (1.11.2001-31.01.2004)

EXPENSES		INCOME	
DIRECT ELIGIBLE COSTS (D)		**Commission (funding requested) (S)**	
		max. 70% of eligible costs	533,440.00
Personnel costs	403,256.80		
		Contribution pertaining to national officials	
Travel and subsistence expenses	202,116.83	N.A.	0.00
Miscellaneous services	196,687.30	**Applicant's financial contribution (C)**	
		applicant	
Administration	22,550.38	own contribution of participating countries	171,971.08
Reserve for unexpected costs	0.00	**Income generated by the project (R)**	
		NA	0.00
INDIRECT ELIGIBLE COSTS (I)			
General costs (7%)	37,796.40	**Other external resources (R)**	
		Ministry of Public Health	93,993.03
		ESGAP	46,803.60
CONTRIBUTION IN KIND (K)		Ministry	13,200.00
		EURODURG	3,000.00
NA			
		Other current funding applications (R)	
		NA	0.00
		CONTRIBUTION IN KIND (K)	0.00
		NA	
INTERIM TOTAL (D+I+K)	**862,407.71**	**GRAND TOTAL (C+R+S+K)**	**862,407.71**

Prof. Dr. Herman GOOSSENS
ESAC Project Leader

Prof. Dr. Francis VAN LOON
Rector of University of Antwerp

DETAILS OF EXPENDITURE IN EURO

DIRECT ELIGIBLE COSTS: costs directly linked to the project

PERSONNEL COST

Fees

Description	Amount
Salaries	397,044.80
	397,044.80

Other personnel costs

Description	Amount
Others	6,212.00
	6,212.00

TOTAL PERSONNEL COSTS **403,256.80**

TRAVEL/ACCOMODATION/SUBSISTENCE

Travel expenses

Description	Cost €
Travel expenses	109,657.38
	109,657.38

Subsistence

Description	Cost €
Subsistence	92,459.45
	92,459.45

202,116.83

MISCELLANEOUS SERVICES

Information costs (e.g. printing, computer support, conference programme, distribution)

Description	Amount
Information	2,761.87
Sub-total	2,761.87

Cost of reports/translation

Description	Amount
reports	16345.26
Sub-total	16,345.26

Subcontracting costs

Description	Amount
participating countries payments based on signed subcontract	139,500.32
Sub-total	139,500.32

Interpreting costs

Description	
Sub-total	0.00

Audit/evaluation costs

Description	Amount
Audit	2,677.13
Sub-total	2,677.13

Other services (please specify)

Description	
Others	35402.72
Sub-total	35,402.72

TOTAL MISCELLANEOUS SERVICES **196,687.30**

PROJECT ADMINISTRATION

Equipment (purchase, rent or leasing)

Description	Amount
IT equipment	5,933.66
Sub-total	5,933.66

Cost of consumables and supplies

Description	
Consumables	15,548.35
Sub-total	15,548.35

Cost of financial services (cost of banking transactions, insurance)

Description	Amount
Banking transactions	1,068.37
Sub-total	1,068.37

Cost of certificates/sureties (bank guarantee)

Description	Amount
Sub-total	0.00

TOTAL PROJECT ADMINISTRATION 22,550.38

RESERVE FOR UNEXPECTED COSTS

Maximum 5% of direct eligible costs (personnel costs + travel/subsistence + miscellaneous services + project administration)

Description	Amount

TOTAL RESERVE FOR UNEXPECTED COSTS **0.00**

INDIRECT ELIGIBLE COSTS

GENERAL COSTS

Maximum 7% of direct eligible costs (personnel costs + travel/subsistence + miscellaneous services + project administration)

Description	Amount
overhead University of Antwerp	37,796.40

TOTAL GENERAL COSTS **37,796.40**

TOTAL EXPENDITURE **862,407.71**