ESAC – European Surveillance of Antimicrobial Consumption

FINAL SCIENTIFIC REPORT

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LIST OF ABBREVIATIONS

AC	Ambulatory Care
AIDS	Almost Ideal Demand System
ARMED	Antimicrobial Resistance Surveillance and Control in the Mediterranean Region
ARPAC	Antibiotic Resistance: Policy and Control
ATC	Anatomical Therapeutic Chemical
BAPCOC	Belgian Antibiotic Policy Coordination Committee
DDDs	Defined Daily Doses
DID	Defined Daily Doses per 1000 inhabitants per day
DPP	DDD per package
EARSS	European Antimicrobial Resistance Surveillance System
EBug Pack	Development and dissemination of a school antibiotic and hygiene education pack and website across Europe
EC	European Commission
ESAC	European Surveillance of Antimicrobial Consumption
ESCMID	European Society of Clinical Microbiology and Infectious Diseases
ESF	European Science Foundation
ESPRIT	ESCMID Study Group on Primary Care Topics
EuroDURG	European Drug Utilisation Research Group
GP	General Practioner
GRACE	Genomics to combat Resistance against Antibiotics in Community-acquired LRTI in Europe
GRIN	General Practice Respiratory Infections Network
HC	Hospital Care
IC	Infection Control
ICD	International Statistical Classification of Diseases and Related Health Problems
ICPC	International Classification of Primary Care
IPH	Institute of Public Health Brussels
IPSE	Improving Patient Safety in Europe
LTC	Long Term Care Facility
MOSAR	Mastering Hospital Antimicrobial Resistance and its spread into the community
MT	Management Team
NH	Nursing Homes
NR	National Representative
PPS	Point Prevalence Survey
RoA	Route of Administration
SAR	Self-Medication with Antibiotics and Resistance Levels in Europe
TC	Total Care
WHO	World Health Organisation

1 INTRODUCTION

ESAC, granted by DG/SANCO of the European Commission (Agreement number: 2003/211), is an international network of national surveillance systems, collecting comparable and reliable antibiotic use data. After a successful pilot phase of the ESAC project (2001-2004), another three-year term was approved by DG SANCO for the period 2004-2007. The main objectives of ESAC-2 were:

- To consolidate the continuous collection of comprehensive antibiotic consumption data in all European countries, for ambulatory care and hospitals,
- To disseminate its knowledge in the field of antibiotic consumption by the development of an interactive ESAC website,
- To develop health indicators of antibiotic use based on consumption data, to validate these indicators and to use a set of core indicators to give feedback of the antibiotic consumption in the participating countries.

To deepen the knowledge of antibiotic consumption, collecting additional data on a pilot basis was organised:

- for ambulatory care, to link data on antibiotic use to patients' sex and age, prescriber and indication,
- for nursing homes, to collect data for individual nursing homes and to assess the assignment of these data to either ambulatory care data or hospital care data,
- for hospital care, to collect data for individual hospitals to link antibiotic use data to the hospitals' characteristics;
- additionally to perform a pharmaco-economic evaluation, including an assessment of determinants of use and regional variation.

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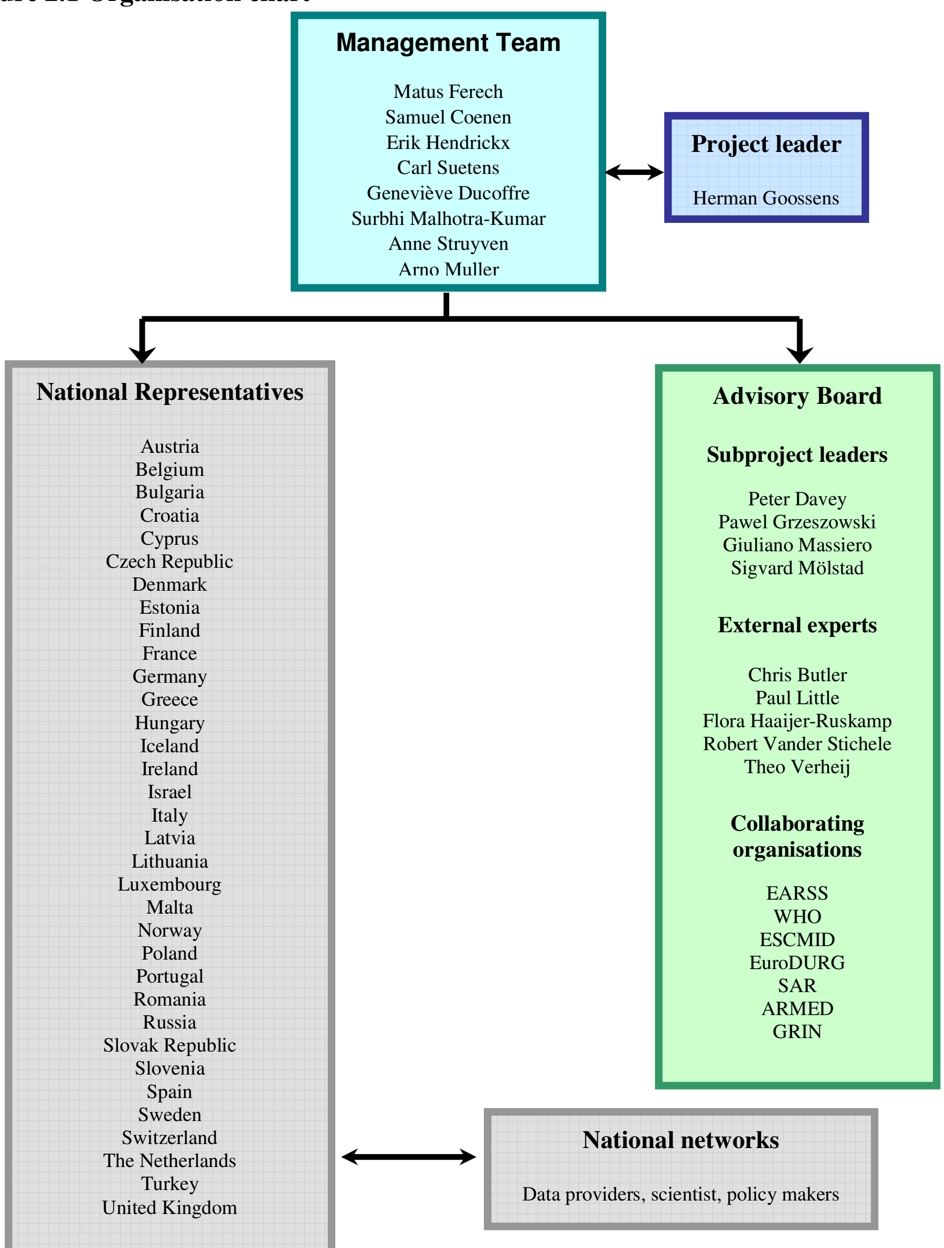
2 PARTNERS – ORGANISATION OF THE PROJECT

2.1 Organisation chart

Figure 2.1 presents the structure of the ESAC project. In this project a 'network of networks' approach was taken. A multidisciplinary management team (a chief microbiologist plus 3 full-time equivalents in pharmaco-epidemiology, medical sociology, pharmaco-economics and administrative assistance) established a network of dedicated national representatives (predominantly microbiologists), collaborating on a voluntary basis. In each country, the national representative was to contact potential data providers, and to liase with the national body co-ordinating antibiotic policy (where present) and with the relevant public health authorities. The objective of the central management team was to build viable national data collection networks in each country, in close co-operation with all the interested parties at national level. In 2005, 34 countries participated in the ESAC project, including all 25 EU countries, 4 applicant countries (Bulgaria, Croatia, Romania and Turkey), 3 of the 4 members of the European Free Trade Association (Iceland, Norway and Switzerland, not Liechtenstein).

Figure 2.1 Organisation chart



Project management

Herman Goossens as the ESAC project leader has concentrated on antimicrobial resistance and consumption during the last 10 years. The University of Antwerp and its several relevant departments (Microbiology, General Practice, Public Health) are committed to supporting its members to contribute to the Network. The Laboratory of Medical Microbiology has taken the lead in research on antimicrobial resistance and consumption in Europe. Moreover, Herman Goossens has co-ordinated several national and international clinical studies. He is or was also a partner of several ongoing EU funded relevant studies, such as ARPAC (Antibiotic Resistance: Policy and Control), EBug Pack (Development and dissemination of a school antibiotic and hygiene education pack and website across Europe), MOSAR (Mastering Hospital Antimicrobial Resistance and its spread into the community), ARMED (Antimicrobial Resistance Surveillance and Control in the Mediterranean Region). Herman Goossens is also the coordinator of GRACE (Genomics to combat Resistance against Antibiotics in Community-acquired LRTI in Europe). Finally, Herman Goossens has organised several international meetings on antibiotic resistance and has co-ordinated nationally and internationally funded research projects. Therefore, he has the skills to lead this ambitious project.

An integrated management of knowledge and intellectual properties are located at the University of Antwerp. Communication between the partners were organised through the interactive website. The central management structure coordinated the administrative and financial reports, managed the flow of results of the ESAC project, organised the meetings, coordinated the dissemination of results, prepared articles for newspapers, assisted radio and TV interviews, and provided the interface with the industry, academia, patient organisations and the public.

The project management applied international project management standards. The activities comprised:

- To manage the project start, the implementation of the work, and the project close down,
- to draft and amend the project reports on a regulary basis,
- to perform the project planning,
- to perform the project controlling,
- to manage any project discontinuity,
- to draft the project reports for the EC,
- to survey the financial management,
- to deal with the contractual matters,
- to issue the project templates and project results,
- to ensure the overall quality of the outputs were achieved.

To discuss the project scientific, administrative and financial matters, weekly meetings with the project leader and the management team were organised. Besides the annual and regional meetings, other communication with the participating countries was held through emails and phone calls. Herman Goossens was responsible for the project, but the day-to-day running was undertaken by the staff members and the clerical administrator.

In this project a 'network of networks' approach was taken. A multidisciplinary management team (such as a chief microbiologist and 3 full-time equivalents in pharmaco-epidemiology, medical sociology, pharmaco-economics and administrative assistance) established a network of dedicated national representatives (predominantly microbiologists), collaborating on a voluntary basis. In each country, the national representative contacted potential data providers, liaised with the national body co-ordinating antibiotic policy (where present) and with the relevant public health authorities.

The objective of the central management team was to build viable national data collection networks in each country, in close co-operation with all the interested parties at national level.

2.2 Members of the ESAC Management Team

ESAC Management team

The following persons contributed to the ESAC Management Team (MT):

Table 2.1 ESAC Management Team (2004 – 2007)

FUNCTION	NAME	E-MAIL
Project leader	Herman Goossens	herman.goossens@uza.be
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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 co-ordination 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**
    - Co-ordinate the NR's as well as the ESAC Management team
    - External representative of the project
    - Communicate with all the partners and European Commission.

- **Coordinator**
    - Lead the ESAC network building process
    - Disseminate of the ESAC results
    - Edit reports, yearbooks and other publications
    - Co-ordinate the ESAC subprojects

- **Data manager**
    - Support the representatives of the participating countries
    - Operate and maintain the central database
    - Write algorithms for automated checking, linking and analysis

- **Clinical Scientists, Clinical Epidemiologist**
    - Support to the representatives of the participating countries
    - Create the questionnaires
    - Assist the interpretation of data at central level
    - Analyse data
    - Write papers and scientific reports

- **Network Facilitator**
    - Gather information on the feasibility of establishing a national ESAC project and at the same time making an inventory of expected problems

- **Administrator**
    - Organisation of the different meetings (preparatory, kick off, evaluation meeting and final conference)
    - Correspondence: send invitations, documents etc.

- **Communicator**
    - Prepare materials for the website, update the website
    - Develop the communication policy

- **Web designer**
    - Develop and maintain the ESAC website
    - Construct the interactive database

2.3 ESAC National Representatives

List of ESAC National Representatives (NR)

The list with all ESAC NRs is presented in table format (Table 2.2). The participating countries are listed in alphabetical order with the particulars of each NR mentioned below.

Tasks of the ESAC NRs

The following tasks were appointed to the ESAC NRs:

- The collection of antibiotic consumption data for the period 2003-2006 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 ESAC-meetings
- To set up and maintain a national ESAC-network

Table 2.2 Participating countries and National Representatives

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2.4 Advisory Board

The advisory board was composed of the ESAC subprojects leaders and invited external experts from other European projects and collaborating organisations: EARSS, WHO, ESCMID, EuroDURG, SAR, ARMED, GRIN.

Main tasks were:
- To support intended activities
- To give scientific input on methodology, guidelines/standards and scientific output of the ESAC surveillance system
- To advice on future activities and new projects

The advisory board met in the context of the subprojects. The first meeting was in February 2005, the second just before the ESF Workshop in September 2005 and the last meeting was held in September 2006.

2.5 Subproject coordinators

The ESAC project aimed to deepen the knowledge of antibiotic consumption by collecting additional data on a pilot basis. For this purpose four subprojects were agreed upon by all national representatives: Hospital care, Ambulatory care, Nursing homes and pharmaco-economic. Therefore, four Associated Beneficiaries were allocated an additional budget to cover personnel according to the needs of the project. Each subproject is assisted by a member of the ESAC MT.

2.6 Objectives of the ESAC project

Main objectives

The main objective of the ESAC project was to consolidate the continuous collection of comprehensive antibiotic consumption data, for ambulatory care and hospitals, in all 34 participating European countries. The European database was used to develop health indicators of antibiotic use and a set of core indicators was used to give feedback to the participating countries. The consumption data were assessed in relation to resistance patterns, incidence of infectious diseases and guidelines for treatment of infections.

In addition, limited but in-depth consumption patterns in specific groups of patients were investigated, and a pharmaco-economic evaluation was carried out.

Finally we aimed to disseminate our knowledge in the field of antibiotic consumption by the development of an interactive ESAC website.

Additional objectives

The ESAC project was successful in its retrospective data collection. However, future efforts should be needed to consolidate and enhance the quality of the surveillance of antibiotic consumption, for a better understanding of the emergence of antimicrobial resistance and for fostering appropriate prescribing.

We aimed to deepen the knowledge of antibiotic consumption by collecting additional data on a pilot basis. For this purpose four subprojects were agreed upon by all national representatives aiming:

- For ambulatory care to link data on antibiotic use to patients' sex and age, prescriber and indication.

- For nursing homes to collect data for individual nursing homes and to assess the assignment of these data to either ambulatory care data or hospital care data.

- For hospital care to collect data for individual hospitals to link antibiotic use data to the hospitals' characteristics.
- In addition, we aimed to perform a pharmaco-economic evaluation, including an assessment of determinants of use and regional variation.

3 METHODOLOGICAL APPROACH

3.1 ESAC data collection

The aim of the ESAC project was to collect comparable and reliable data on antibiotic use in Europe from publicly available sources, and to assess the time trends in human exposure to antibiotics.

After a thorough international debate on desirability and feasibility, the following common goals were set at the launch of the project:

- to collect data on the consumption of systemic antibiotics for human use,
- to collect data for ambulatory (AC) and hospital (HC) care separately,
- to collect quarterly data for AC and yearly for HC, as from 1997,
- to collect data at the level of the active substance (5th level of the ATC classification), using the taxonomy of the Anatomical Therapeutic Chemical (ATC) classification system, as recommended by the World Health Organisation (WHO)
- to express data in number Defined Daily Doses (DDD) per day and 1000 inhabitants (midyear population per year derived from the WHO Health for all database) according to the most recent ATC/DDD index (WHO Collaborating Centre for Drug Statistics Methodology Oslo, www.whocc.no)

Data on antibiotic consumption were collected from either distribution or reimbursement systems. Distribution or sales data were based on reports from the pharmaceutical companies, wholesalers, pharmacies or market research companies. Reimbursement data were collected by the third party payer on the basis of financial claims from legitimate beneficiaries, from prescribers or from dispensing pharmacies (community or hospital).
Prior to the inclusion to the ESAC database, the validity of the consumption data provided was evaluated by means of a checklist including possible sources of bias (Table 3.1). This checklist was developed during the project, as experience with methodological problems grew. During the project, feedback on problems with the data set was given to the national representatives, who discussed this with their data providers. Whenever possible, corrective action was taken. After this round of corrections, the validity of the data sets was evaluated using the checklist with possible biases and scored into 5 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; data provided in non-compatible form and no data provided (Tables 3.2 and 3.3).

Table 3.1 Checklist for the evaluation of the data validity

1. Problems with population coverage
Sample bias in samples of less than 90 % of the population, not or incorrectly extrapolated.
Census bias in census data, covering less than 90% not or incorrectly extrapolated
Under detection or over detection bias by parallel import and export (in data collection systems based on distribution data).
2. Problems with drug coverage
Measurement bias by problems with ATC/DDD assignment.
3. Problems with ambulatory care/hospital care mix
Assignment of data from nursing homes, day care centres and dental care to one of both settings (AC or HC).
Assignment of specialist prescribing (prescribing by specialists based in ambulatory care; prescribing by hospital-based specialists to outpatients; dispensing by hospital pharmacists to outpatients).

Table 3.2 Availability and quality of data on hospital utilisation of antibiotics (ATC J01) within the ESAC project in 15 European countries providing valid data sets in 2002

Country	1997	1998	1999	2000	2001	2002	2003	2004	2005
EUROPEAN UNION COUNTRIES									
Belgium	●	●	●	●	●	●	●	●	●
Bulgaria	○	○	○	○	○	○	○	○	•
Czech Republic	•	•	•	•	○	○	○	•	•
Denmark	●	●	●	●	●	●	●	●	●
Estonia	•	•	•	•	•	●	●	●	●
Finland	**○**	**○**	**○**	**○**	**○**	**○**	**○**	**○**	**○**
France	●	●	●	●	●	●	●	●	●
Germany	•	⊙	⊙	⊙	•	•	⊙	•	•
Greece	**○**	**○**	**○**	**○**	**○**	**○**	**○**	***TC** only*	***TC** only*
Hungary	•	•	•	•	●	●	●	●	●
Ireland	•	•	•	•	•	•	•	●	●
Italy	⊙	⊙	⊙	⊙	⊙	•	•	•	**○**
Latvia	•	•	•	•	•	○	○	○	○
Luxembourg	●	●	●	●	●	●	●	●	●
Malta	●	●	●	●	●	●	●	●	●
Poland	**○**	**○**	**○**	**○**	**○**	**○**	•	•	•
Portugal	•	⊙	•	•	•	•	•	•	•
Slovakia	***TC** only*	***TC** only*	**○**	●	●	●	●	●	●
Slovenia	○	●	●	●	●	●	●	●	●
Spain	⊙	⊙	⊙	⊙	⊙	⊙	•	•	•
Sweden	●	●	●	●	●	●	●	●	●
The Netherlands	●	●	●	●	●	●	•	•	•
APPLICANT COUNTRIES									
Croatia	•	•	•	●	●	●	●	●	●
Turkey	•	•	•	•	•	•	•	**○**	**○**
OTHER EUROPEAN COUNTRIES									
Israel	•	•	•	•	•	●	●	●	●
Norway	•	○	•	•	○	●	●	●	●
Russia	•	•	•	•	•	•	•	•	○

TC = total care data, incl. hospital use
• = no data provided
⊙ = data provided in non-compatible form
○ = data with major bias, invalidating exposure estimation;
○ = data available, but with minor bias, not invalidating exposure estimation;
● = valid data available

Table 3.3 Availability and quality of data on volume of outpatient antibiotic use (ATC J01) in Europe within the ESAC project.

Country	1997	1998	1999	2000	2001	2002	2003	2004	2005
EUROPEAN UNION COUNTRIES									
Austria	•	⭘	⭘	⭘	⭘	⭘	⭘	⭘	⭘
Belgium	●	●	●	●	●	●	●	●	●
Bulgaria	•	•	•	•	***TC** only*	***TC** only*	***TC** only*	***TC** only*	•
Cyprus	*Participant not yet able to provide data*								
Czech Rep.	•	●	●	●	●	●	●	●	●
Denmark	●	●	●	●	●	●	●	●	●
Estonia	•	•	•	•	•	●	●	●	●
Finland	●	●	●	●	●	●	●	●	●
France	●	●	●	●	●	●	●	●	●
Germany	●	●	●	●	●	●	●	●	●
Greece	⭘	⭘	⭘	⭘	⭘	⭘	⭘	***TC** only*	***TC** only*
Hungary	•	●	●	●	●	●	●	●	●
Ireland	●	●	●	●	●	●	●	●	●
Italy	•	•	●	●	●	●	●	●	●
Latvia	•	•	•	•	○	○	○	○	⭘
Lithuania	•	•	•	○	○	•	○	○	○
Luxemburg	●	●	●	●	●	●	●	●	●
Malta	•	•	•	•	•	•	•	•	•
Poland	⭘	⭘	⭘	⭘	⭘	⭘	•	⭘	⭘
Portugal	●	●	●	●	●	●	●	●	●
Romania	*Participant not yet able to provide data*								
Slovakia	***TC** only*	***TC** only*	●	●	●	●	●	●	●
Slovenia	●	●	●	●	●	●	●	●	●
Spain	⭘	⭘	⭘	⭘	⭘	⭘	⭘	⭘	⭘
Sweden	●	●	●	●	●	●	●	●	●
The Netherlands	●	●	●	●	●	●	●	●	●
UK	●	●	●	●	●	●	●	●	●
APPLICANT COUNTRIES									
Croatia	•	•	•	●	●	●	●	●	●
Turkey	⊙	⊙	⊙	⊙	⊙	⊙	⊙	⊙	⊙
OTHER EUROPEAN COUNTRIES									
Iceland	***TC** only*	***TC** only*	***TC** only*	***TC** only*	***TC** only*	***TC** only*	***TC** only*	***TC** only*	***TC** only*
Israel	•	•	•	•	•	⭘	⭘	⭘	⭘
Norway	•	⭘	•	•	⭘	●	●	●	●
Russia	•	•	•	•	•	•	•	○	○
Switzerland	•	•	•	•	•	•	•	○	•

TC = total care data, incl. hospital use
• = no data provided
⊙ = data provided in non-compatible form
○ = data with major bias, invalidating exposure estimation;
⭘ = data available, but with minor bias, not invalidating exposure estimation;
● = valid data available

3.2 Data collection protocol

3.2.1 Version 2003

In all participating countries, retrospective data on volume of antibiotic consumption was collected for 2003, separately for ambulatory care (AC) and hospital care (HC), according the ATC/DDD classification, 2004 version. If the data were delivered to the National Representative, according the ATC/DDD classification but in another format, the ESAC MT had to be contacted to investigate the possibility to deliver the data in the existing format.

Scope of the data collection

- Volume:
  - DDDs (number of defined daily doses 'consumed' in a given period , area and sector) + valid national register of available antibiotics with DDD values applied for calculations and DPP (DDD per package) indicated and
  - number of packages if possible
- Classification:
  - ATC – 5^{th} level
  - Separated between Oral/Parenteral form for ATC codes with multiple DDDs if possible or
  - Medicinal product package level if possible
- Time frame: 2003
- Periodicity: quarterly for AC, total year for HC (quarterly if possible)
- Area: country
- Sector: AC - HC

Guidelines for sector delineation

Situations could have been different in several countries concerning inclusion/exclusion of particular segments of antibiotic consumption. If possible, the following rules had to be respected:
Coverage of ambulatory care included:

- Hospital specialists prescribing for patients of the outpatient clinic with delivery of antibiotics by community pharmacists
- Ambulatory care specialists prescribing for ambulatory care patients with delivery of antibiotics by community pharmacists
- Antibiotic consumption for dental care
- Consumption of nursing homes and day care centers

Coverage of hospital care included consumption of psychiatric clinics.
All exceptions to these rules needed to be carefully noted on the questionnaire.

Structure of the retrospective database (RETROdata)
ATC classification

For the retrospective data, a fixed framework for data collection was used, based on the ATC 5 classification (and Route of Administration if possible), version 2004. Data collection 2003 was limited to antimicrobials belonging to the ATC class J01.

- If raw data needed to be aggregated specifically for the ESAC project, the ATC version 2004 had to be used for conversion
- If an active ingredient was not mentioned in the list, this category had to be added to the end of the list
- If "WHO" ATC's or DDD's were missing for some of the active ingredients, the DDD applied had to be clearly indicated in the **register** or number of **Packages/Units** had to be delivered.

Structure of the questionnaire (RETROquestionnaire)

In order to obtain more insight in the format of the 2003 data collected, a small questionnaire was added which consisted of an AC and an HC sheet. These sheets were used to identify the data providers and the ATC version used and to gather more information concerning the coverage of the data provided. If a particular segment of consumption was only partly included (e.g. only a sample of hospitals), additional information had to be given, particularly an estimation of the data coverage.

3.2.2 Version 2004

Data collection protocol for the 2004 data collection was agreed during the 3rd EARSS-ESAC Plenary Meeting, held in Madrid (Spain) on November 10th –12th, 2004 with some adjustments:

- It was concluded to collect use data on the package level from 2004 onwards (countries not able to provide detailed data should aggregate them according to the route of administration)
- It was concluded to include antimycotics for systemic use in the ESAC standard data collection protocol.
- It was concluded to collect the use of antivirals and antimycobacterials on a pilot basis.
- It was concluded that the NRs would validate their J01 data by assessing the impact of the following substances:
    - *combinations for eradication of Helicobacter pylori (A02BD),*
    - *oral metronidazole, ornidazol (P01),*
    - *oral vancomycin and colistin (A07AA).*

Collecting data on the package level represented a new challenge for the ESAC MT. As the number of products available varies significantly, design of a common data collection form was not feasible. In order to reduce any eventual additional workload, NRs were allowed to submit their national 2004 data in any readily available format, preferably compatible with the Excel worksheet, separately for ambulatory and hospital care.

Parameters of the data collection (product level)

- Volume:
    - number of packages per medicinal product (used in a given period , area and sector) + valid national register of available antibiotics with DDD values assigned.
- Classification:
    - Medicinal product package level
- Time frame: 2004
- Periodicity: quarterly for AC, total year for HC (quarterly if possible)
- Area: country
- Sector: AC / HC
- ATC/DDD version 2005

In the participating countries, where data on package level were not available due to legal constraints, data on volume of antibiotic consumption for 2004 were collected on the ATC-5 level, separated according to their route of administration (RoA), at least for ATC codes with multiple DDDs, using a pre-defined form "*Data2004form.xls*".

Parameters of the data collection (substance level)

- Volume:
    - DDDs (number of defined daily doses 'consumed' in a given period , area and sector) + valid national register of available antibiotics containing DDD values applied for calculations and DPP (DDD per package) indicated,
    - number of packages if possible
- Classification:
    - ATC – 5th level
    - Separated between Oral/Parenteral form for ATC codes with multiple DDDs
- Time frame: 2004
- Periodicity: quarterly for AC, total year for HC (quarterly if possible)
- Area: country
- Sector: AC / HC
- ATC/DDD version 2005

Scope of data collection

Data collection 2004 included for the first time antimicrobials classified outside of the ATC class J01.

According to the conclusions from Madrid data on J02 class (Antimycotics for systemic use) were included in the routine data collection in addition to J01.

Use of Antimycobacterials (J04), Antivirals (J05), combinations for eradication of Helicobacter pylori (A02BD), oral metronidazole, ornidazol (P01), oral vancomycin and colistin (A07AA) was collected on a voluntary basis.

Timing of the data collection

The new provisions introduced in the new data extraction protocol required some additional time burden. As no ESAC Plenary Meeting was scheduled in autumn 2005, the deadline for 2004 data collection was more flexible than in previous years and was finalized by the end of March 2006.

3.2.3 Version 2005

Data on antibiotic use in 2005, for both ambulatory care (AC) and hospital care (HC), according the ATC/DDD classification (2006 version) were delivered at the product level, expressed in number of packages in a database format (Excel worksheet). Moreover a valid national register of available antibiotics (including number of DDDs per product package - PDD) had to be enclosed.
For the participating countries not able to deliver data on a product level due to objective constraints, data on the volume of antibiotic consumption in 2005 was collected on the ATC5 + Route of Administration (RoA) level. As the number of antibiotics with multiple DDDs for an “Oral” and “Parenteral” is increasing over the time, Oral/Parenteral form was separated for all ATC codes to allow retrospective data adjustments.

Parameters of the routine data collection

- Volume:
    - number of packages per medicinal product (used in a given period , area and sector) + valid national register of available antibiotics with DDD values assigned per each medicinal product package.
- Classification:
    - medicinal product package level (defined by ID key)
- Time frame: 2005
- Periodicity: quarterly for AC, total year for HC (quarterly if available)
- Area: country
- Sector: AC / HC
- Scope:
    - J01 +J02 + additional substances (Antimycobacterials (J04), Antivirals (J05), combinations for eradication of *Helicobacter pylori* (A02BD), oral metronidazole, ornidazol (P01), oral vancomycin and colistin (A07AA) on a voluntary basis).
- National register:
    - Worksheet format was recommended; with all entries in separate columns allowing further calculations
- *Required fields*:
    - national ID number, commercial name of product (label), route of administration (e.g. oral), number of administration units per package (e.g. 16), quantity of active substance per administration unit (e.g. 500), measuring unit (e.g. mg), ATC code, number of DDDs per package (or per administration unit if applicable).

Table 3.4 Providers of data on antibiotic consumption per country

Country	Data sources and providers
Austria	Social Insurance Companies provided reimbursement data (100% coverage). Hospital care data was collected from a sample of collaborating hospitals (since 1998).
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. For 2005 also reimbursement data were provided.
Croatia	Sales data was provided in collaboration with the National Institute of Public Health and the National Institute for Statistics, with almost 100% coverage for ambulatory and hospital care.
Cyprus	The Ministry of Health is providing comprehensive data from public sector, but not from private sector. Therefore difficult to separate ambulatory care and hospital care data.
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, two hospitals have 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 the 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 after 2000. Hospital care data was estimated from the SARI project covering 35 intensive care units located in 17 different regions, and from the MABUSE programme, which is run by the Universities of Freibourg, 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 was provided by the National Health Insurance for ambulatory care since 1998. For hospital care, complete sales data was delivered by the same data provider since 2001. Also reimbursement data is available.
Iceland	Total sales data from pharmaceutical companies was provided by the Ministry of Health. Differentiation between ambulatory and hospital care use is made possible since 2005 on a pilot basis.
Ireland	Hospital care data is available from a sample of private and public hospitals. Community pharmacy sales data were obtained from IMS Health to calculate AC data and were compared with data from the General Medical Services (GMS) reimbursement scheme data.
Israel	Reimbursement data were provided by Clalit Health Services (C.H.S.) and cover 65% of about 6.5 mill. inhabitants in Israel, and 7 out of 23 medical centers for acute

	care patients.
Italy	Sales data was provided by the Ministry of Health since 1999. Prescribed, non-reimbursed and OTC antibiotics were all included. For hospital care, data was collected from a sample of hospitals since 1997. Also reimbursement data is available.
Latvia	The State Medicinal Agency provided sales data from wholesalers, separately for ambulatory and hospital care since 2001. The quality of the data improved since 2002.
Lithuania	Ambulatory care data was provided by the State Patient Fund, but was not comprehensive. Hospital care data was provided from an enlarging sample of hospitals.
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 community pharmacies was weighted and extrapolated. For hospital care, SWAB requested data from all Dutch hospital pharmacists; covering about 60 % of the hospitals.
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.
Russia	Sales data was provided by the research company 'Remedium Group of Companies' based on a pharmacy audit covering 51 regions. Similarly, a hospital audit was realized covering 27 regions/hospitals in Russia.
Slovakia	Wholesaler data was provided by the Slovak Institute for Drug Control. Since 1999 data has been split between ambulatory and hospital care delivered.
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 was comprehensive since 2001.
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) until 2001. For 2002, 2004 and 2005 IMS data are also available.
Sweden	Sales/prescription data was provided by the National Corporation of Swedish Pharmacies (Apoteket AB).
Switzerland	Total sales data for ambulatory care were provided by IHA-IMS from 2002.
Turkey	Only incomplete sales data expressed in units was available from a market research company for ambulatory care from 1997-2002, but is incompatible with ATC-DDD methodology. Hospital care data is available from a sample of hospitals for 2004 and

	2005.
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. Hospital care data is available from a sample of hospitals.

4 RESULTS OF 2005 DATA COLLECTION

Thus far data have been collected as of 1997 until 2005. The overall data are shown in Table 4.1.

Table 4.1: Overall outpatient antibiotic use from 1997 to 2005

Country	1997	1998	1999	2000	2001	2002	2003	2004	2005
Austria		12,51	13,19	12,34	11,86	11,75	12,49	12,61	14,47
Belgium	25,44	26,36	26,21	25,26	23,73	23,82	24,22	22,90	24,29
Bulgaria			15.11	20.18	22.60	17.24	15.34	16.39	
Croatia				18.42	17.65	21.61	23.50	23.02	23.38
Czech Republic		18.27	18.62	18.56	18.49	17.09	16.65	15.58	17.32
Denmark	12.22	12.74	12.13	12.19	12.82	13.32	13.58	14.15	14.62
Estonia					14.37	11.67	11.34		11.70
Finland	19.38	18.44	18.41	18.97	19.70	17.83	18.73	17.27	18.11
France	33.02	33.56	34.33	33.24	32.71	32.05	28.97	27.09	28.94
Germany	14.57	14.63	14.94	14.89	13.82	13.76	13.90	11.09	14.61
Greece	25.06	24.86	28.50	29.13	29.43	30.53	31.40	33.38	34.73
Hungary		18.62	23.92	18.91	19.11	17.05	19.63	18.59	19.54
Iceland	22.12	22.98	21.58	20.47	20.28	20.98	20.36	21.44	23.31
Ireland	16.94	16.65	18.21	17.80	18.99	19.04	20.44	20.69	20.54
Israel						19.55	20.06	19.69	20.55
Italy			24.50	24.03	25.16	24.38	25.69		
Latvia						12.55		11.80	12.14
Luxembourg	25.78	25.48	26.72	25.68	26.08	26.42	27.34	24.17	25.19
Netherlands	10.21	10.07	10.09	9.86	9.93	9.83	9.78	9.75	10.51
Norway		15.45			15.67	15.84	15.72	15.88	16.75
Poland	16.56	20.70	22.18	22.64	24.77	21.14			19.61
Portugal	23.67	23.63	25.79	25.73	25.10	26.13	25.66	23.84	28.01
Russia							11.79	9.15	9.16
Slovakia			29.09	25.59	27.99	25.57	26.63	22.43	25.03
Slovenia	17.51	19.30	19.79	18.01	17.36	16.40	17.10	16.82	16.54
Spain	21.39	20.90	20.45	19.43	18.70	19.35	20.58	18.70	19.29
Sweden	14.64	15.53	15.82	15.50	15.81	15.42	14.88	14.67	14.87
United Kingdom	16.87	15.76	14.46	13.98	14.48	14.49	14.90	15.21	15.45

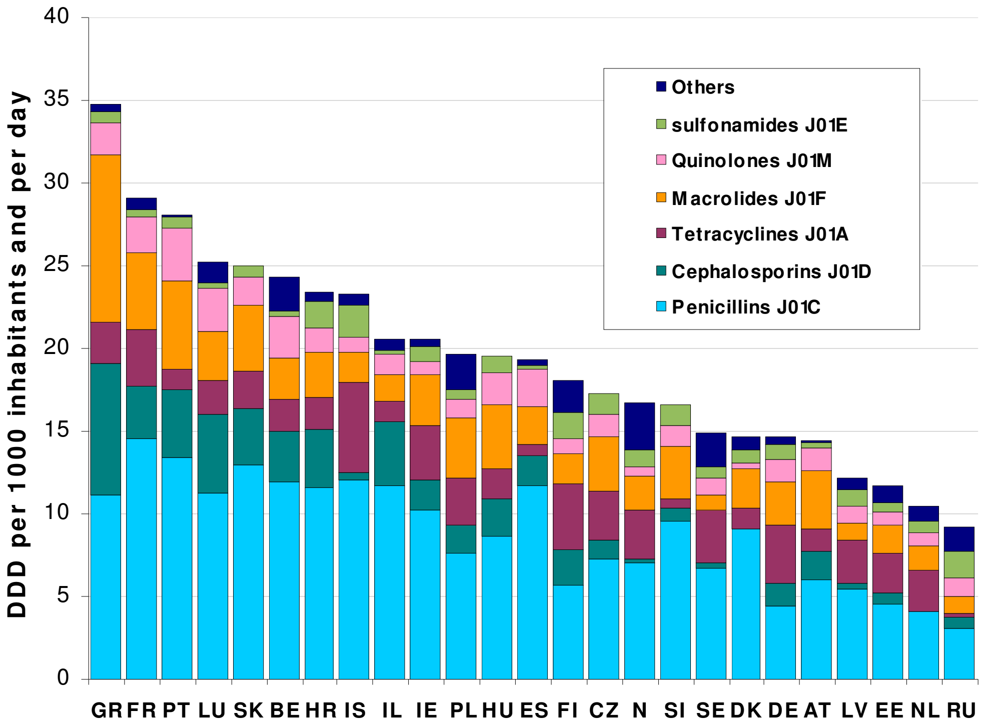
Data from 1997 until 2004 has been published in peer-reviewed journals, as well as in-depth analysis of the use in ambulatory care and hospital care. The detailed unpublished results of the 2005 data collection are mentioned below (4.1-4.3).

4.1 Ambulatory care

Of the 34 (27 member states, 2 applicant countries and 5 others) participating countries 24 were able to deliver outpatient data on antibiotic use, while Iceland provided only total data, covering both AC and HC use. According to the ATC/DDD, 2006 version, total outpatient use values in 2005 varied with a factor of 3.6 between the countries with the highest (33.4 DID in Greece) and lowest (9.2 DID in Russia) use. The difference between the highest outpatient antibiotic user Greece and the second France, which has introduced the nationwide campaign to improve antibiotic use in 2002, further increased in 2005, although the continuous boost of antibiotic sales in Greece could be partially explained by the emergence of parallel exports to EU countries with higher medicine prices.

Figure 4.1 shows outpatient antibiotic use subdivided into major antibiotic groups according to the ATC classification [penicillins (J0IC), cephalosporins (J01D), macrolides (J01F), quinolones (J01M), tetracyclines (J01A), sulphonamides (J01E), and other antibiotics [concatenation of amphenicols (J01B), aminoglycosides (J01G), combinations of antibacterials (J01R) and other antibacterials (J01X)] in 25 European countries.

Figure 4.1: Outpatient antibiotic use in 2005 subdivided into major antibiotic groups

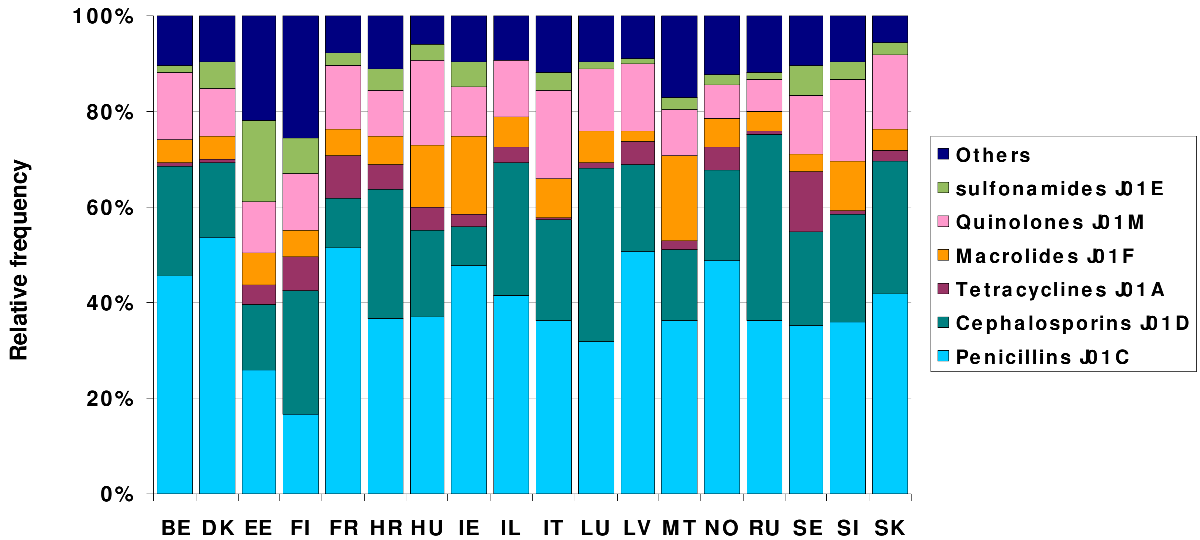


Penicillins represented the most frequently prescribed antibiotics in all countries, ranging from 30% (Germany) to 63% (Denmark) of the total outpatient antibiotic use. For cephalosporins, the proportional use ranged from 0.2% (Denmark) to 22% (Greece), for macrolides from 6% (Sweden) to 29% (Greece), and for quinolones from 2% (Denmark) to 13% (Russia) of the total outpatient antibiotic use.

4.2 Hospital care

Of the 34 participating countries 18 were able to deliver data on antibiotic use in hospitals in 2005 (sample data for Ireland and Israel). As many countries derive their data from the samples which cannot be extrapolated to the national level, shows figure 4.3 relative proportions of major antibiotic groups according to the ATC classification [penicillins (J0IC), cephalosporins (J01D), macrolides (J01F), quinolones (J01M), tetracyclines (J01A), sulphonamides (J01E), and other antibiotics [concatenation of amphenicols (J01B), aminoglycosides (J01G), combinations of antibacterials (J01R) and other antibacterials (J01X)] within hospital antibiotic use.

Figure 4.2: Patterns of hospital antibiotic use in 2005



The proportion of penicillins use ranged from 54% to 32% in 16 countries, but was much lower in Estonia (26%) and in Finland (17%). The proportion of cephalosporins use was high in Russia (39%) and in Luxembourg (36%) but low in France (11%) and in Ireland (8%). Tetracyclines use was relatively high in Sweden (12%). Macrolides use ranged between 18% in Malta and 2% in Estonia; and quinolones use between 18% in Hungary and Italy, and 7% in Norway and Russia.

Nevertheless the reliability of the estimation of national aggregates of hospital antibiotic consumption must be critically evaluated. Some countries derive a reliable estimate for national hospital exposure to antibiotics from wholesale data or from detailed consumption registration in all hospitals. In other countries, only consumption data from a sample of hospitals, expressed in DDD per 100 bed days, are available. Moreover the validity of the hospital data is much more vulnerable for biases in ambulatory/hospital case mix. Specifically in Finland, where some remote primary health care centres and nursing homes are included into the hospital data, proportional use of "other antibiotics" was 26% (in contrast to 6.4% of the "hospital specific antibiotics"), predominantly due to use of oral methenamine, nitrofurantoin and trimethoprim.

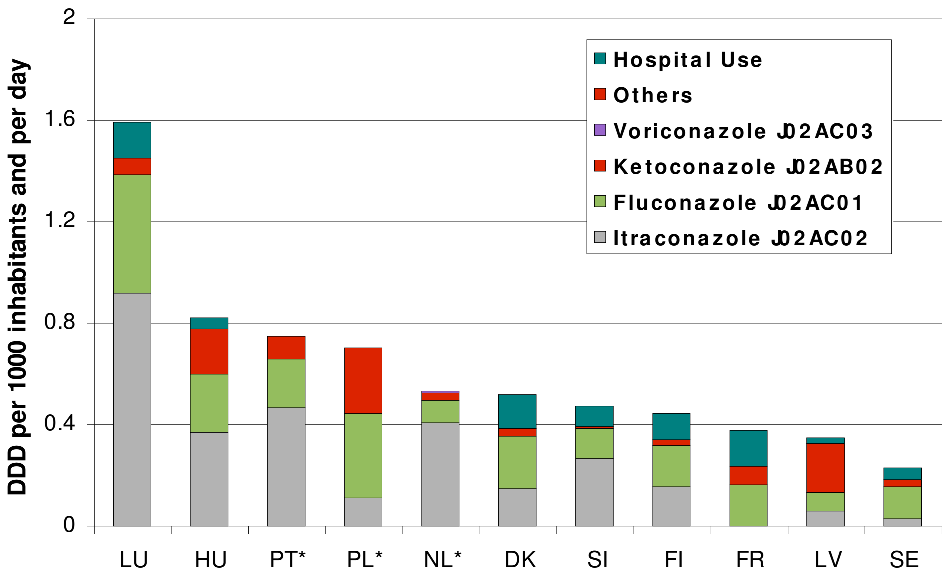
4.3 Antimycotic use in Europe

For the second year, the ESAC project collected data on consumption of antimycotics. In addition to data on antibiotic use, 11 countries were able to deliver data on outpatient and hospital antimycotic use (J02) in 2005.

Figure 4.3 shows the outpatient antimycotic use 2005 for 11 European countries expressed in DID (aggregated hospital use is added for 8 countries). Total outpatient antimycotic use varied with a factor of 9 between the country with the highest (1.59 DID in Luxembourg) and lowest (0.23 DID in Sweden) use.

Itraconazole, fluconazole and ketoconazole represented more than 99% of total outpatient antimycotic use in all countries, except for Sweden (voriconazole use 2.7%). Itraconazole, overall the most frequently prescribed antimycotic, represented more than 75% of the antimycotic use in the Netherlands and more than 60% in Luxembourg, Portugal and 47 in Hungary. Conversely, Fluconazole which represented more than 50% of the total use in Denmark, France and Sweden, was also the most used antimycotic in Poland. Ketoconazole was the most used antimycotic in Latvia (59%) and was used more than 30% in France and Poland.

Figure 4.3: Outpatient and hospital antimycotic use in 2005



*hospital data not available

5 ANTIBIOTIC PRESCRIBING QUALITY INDICATORS

Quality assessment and improvement in health care is a major issue in many countries. Information on quality of health care is being demanded by policy makers, health-care professionals and the general public. With the majority of doctor-patient encounters in general practice resulting in a prescription for drug treatment, the quality of prescribing in general practice is an important issue. Prescribing also has a major influence on well being and accounts for a substantial part of health care expenditure. The above statements hold truth for antibiotic use as well. In addition, antibiotic consumption is increasingly recognised as the main driver for resistance. If we want to improve it, we have to be able to measure the quality of antibiotic use in Europe.
Therefore, we aimed to develop a set of valid drug specific quality indicators for outpatient antibiotic use in Europe, which can be derived from ESAC data, taking into account the recommendations of DURQUIM (Drug Utilisation Research Quality Indicator Meeting).

5.1 Developing a set of quality indicators

To produce a list of proposed quality indicators for outpatient antibiotic use in Europe based on ESAC data, a proposal for an ESF EMRC EXPLORATORY WORKSHOP on Antibiotic Prescribing Quality Indicators was submitted and granted, and a workshop was convened in Antwerp, 7-9 September 2005. This provided the unique opportunity to build on the interdisciplinary expertise within EuroDURG (European Drug Utilisation Research Group; www.eurodurg.com), GRIN (General Practice Respiratory Infections Network), ESPRIT (ESCMID Study Group on Primary Care Topics; www.escmid.org/esprit), BAPCOC (Belgian Antibiotic Policy Coordination Committee; www.bapcoc.be), WHO (World Health Organization; www.who.int), ESAC and other experts in this field.

A scientific advisory board was set up to prepare the workshop. Members of Euro DURG (Flora Haaijer-Ruskamp, Robert Vander Stichele), GRIN/ESPRIT (Paul Little, Theo Verheij) and of the ESAC MT (Samuel Coenen, Matus Ferech, Herman Goossens) decided that the programme of the workshop should allow discussing the development of antibiotic prescribing quality indicators from both the perspective of professionals and policy makers and should result in ESAC based antibiotic prescribing quality indicators, a roadmap for the development of antibiotic prescribing quality indicators in general and a research agenda for the assessment of the validity of antibiotic prescribing quality indicators in particular.

The workshop included smaller work groups and plenary sessions. A series of background presentations in plenary sessions helped to set the scene and to prepare for the following discussions in small groups.
For the break out sessions the participants were split up in advance in two groups with similar distribution of gender and affiliation, and wide variation in nationalities. Each group was facilitated by one member of the scientific advisory board, with two other members serving as rapporteurs.
In plenary sessions, results of the work groups were presented, compared and discussed by all participants. These sessions were tape-recorded.

After two days of relevant background presentations, constructive feedback and fruitful discussions we ended up with a useful set of proposed indicators related to the quality of antibiotic prescribing in ambulatory care and some so-called structural indicators.
A list of proposed antibiotic prescribing quality indicators was developed using a general format and further elaborated by Samuel Coenen and Matus Ferech, based on the audio-recording after the workshop.
The numbered list is shown in table 5.1 and in the full scientific report of the ESF Workshop[1] at www.esf.org and on the ESAC website.

Table 5.1: List of proposed quality indicators for outpatient antibiotic use in Europe

1: Consumption of antibacterials for systemic use (J01) expressed in DID†	[J01_DID]
2: Consumption of tetracyclines (J01A) expressed in DID†	[J01A_DID]
3: Consumption of penicillins (J01C) expressed in DID†	[J01C_DID]
4: Consumption of cephalosporins (J01D) expressed in DID†	[J01D_DID]
5: Consumption of sulfonamides and trimethoprim (J01E) expressed in DID†	[J01E_DID]
6: Consumption of MLS, i.e. macrolides, lincosamides and streptogramins (J01F) expressed in DID†	[J01F_DID]
7: Consumption of quinolones (J01M) expressed in DID†	[J01M_DID]
8: Consumption of tetracycline (J01A) expressed as percentage‡	[J01A_%]
9: Consumption of penicillins (J01C) expressed as percentage‡	[J01C_%]
10: Consumption of cephalosporins (J01D) expressed as percentage‡	[J01D_%]
11: Consumption of sulfonamides and trimethoprim (J01E) expressed as percentage‡	[J01E_%]
12: Consumption of macrolides, lincosamides and streptogramins (J01F) expressed as percentage‡	[J01F_%]
13: Consumption of quinolones (J01M) expressed as percentage‡	[J01M_%]
14: Consumption of β-lactamase sensitive penicillins (J01CE) expressed as percentage‡	[J01CE_%]
15: Consumption of comb. of penicillins, incl. β-lactamase inhibitor (J01CR) expressed as percentage‡	[J01CR_%]
16: Consumption of 3rd & 4th generation of cephalosporins {J01(DD+DE)} expressed as percentage‡	[J01DD+DE_%]
17: Ratio of the consumption of broad spectrum {J01(CR+DC+DD+(F-FA01))}to the consumption of narrow spectrum penicillins, cephalosporins and macrolides {J01(CE+DB+FA01)}	[J01_B/N]
18: Consumption of fluoroquinolones (J01MA) expressed as percentage‡	[J01MA_%]
19: Seasonal variation* of the total antibiotic consumption (J01)	[J01_SV]
20: Seasonal variation* of quinolone consumption (J01M)	[J01M_SV]
21: Seasonal variation* of quinolone consumption (J01M) multiplied by their use in DID†	[J01M_SVDID]
22: Index of longitudinal trends of antibiotic consumption	[J01_TT]
Structural indicators	
23: Diversity of the therapeutic arsenal of antibacterials for systemic use (J01)	[J01_DU99]
24: Number of items recorded in the national register of available antibacterials for systemic use (J01)	[J01_NR]

† Defined Daily Doses (DDD) per 1000 inhabitants per day.
‡ Percentage of the total consumption of antibacterials for systemic use (J01) in DID†.
* Over use in the winter quarters (October – December & January - March) compared to the summer quarters (July-September & April - June) of a one year period starting in July and ending the next calendar year in June, expressed as percentage: [DDD(winter quarters)/DDD(summer quarters)-1] * 100.

5.2 Assessing a set of quality indicators

After the workshop all 27 participants from 15 countries have been asked to score the proposed indicators in a way similar to the scoring during the workshop itself, i.e. to score the relevance of each of the proposed indicators to:

1. reducing antimicrobial resistance,
2. patient health benefit,
3. cost-effectiveness, and
4. public health policy makers,

using a scale ranging from 1 (= completely disagree), over 5 (= uncertain) to 9 (= completely agree).

The scores were processed according to the UCLA-RAND appropriateness method and taking into account the participants' comments. Proposed indicators were judged relevant if the median score was not within the 1-6 interval and if there was consensus, i.e. if the number of scores within the 1-3 interval was less than one third of the panel. To define the final set only relevant indicators were selected. From relevant indicators providing overlapping information only the one with the highest scores for relevance was selected for the final set of quality indicators.

The set of proposed quality indicators was developed using 1997-2003 ESAC data on outpatient antibiotic use in Europe. The values of the final set of relevant indicators were calculated using the most recent, i.e. 2004 ESAC data. For each of the indicators we grouped the indicator values into four quartiles, and used this grouping in maps depicting the indicator values for all countries participating in ESAC.

5.3 Applying a final set of quality indicators

We received the scores from 22 participants from 12 countries (Table 5.2).

Nine indicators were rated as relevant antibiotic prescribing indicators on all four dimensions (indicators 1, 13-19 and 20), and five additional indicators were rated valid if only relevance to reducing antimicrobial resistance and to public health policy makers was taken into account (3, 4, 6, 7 and 21). The information provided by 'Consumption of quinolones (J01M) in percentage' and 'Seasonal variation of quinolone consumption (J01M) multiplied by their use in DID' overlapped with the information provided by 'Consumption of fluoroquinolones (J01MA) in percentage' and 'Seasonal variation of quinolone consumption (J01M)', respectively, but the latter indicators scored higher for relevance.

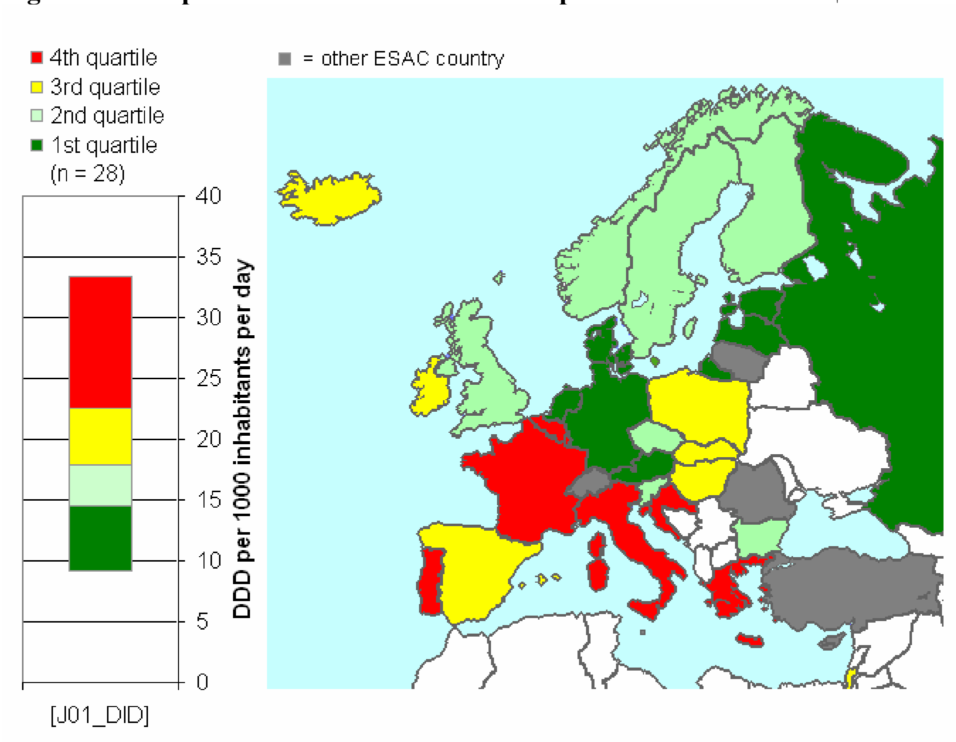
Table 5.2 Relevance of the proposed quality indicators for outpatient antibiotic use in Europe: scores for and consensus on their relevance to reducing antimicrobial resistance, patient health benefit, cost-effectiveness, and public health policy.†

	RESISTANCE			PATIENT HEALTH BENEFIT			COST-EFFECTIVENESS			PUBLIC HEALTH POLICY		
	Median	**N**	**Consensus**	**Median**	**N**	**Consensus**	**Median**	**N**	**Consensus**	**Median**	**N**	**Consensus**
1. J01_DID‡	8	22	+	6.5	22	+	7	21	+	8	22	+
2. J01A_DID	6	22	+	5	22	+	5	21	+	5	22	+
3. J01C_DID‡	7	22	+	6	22	+	6	21	+	7	22	+
4. J01D_DID‡	7	22	+	6	22	+	6	21	+	6.5	22	+
5. J01E_DID	6.5	22	+	5	22	+	6	21	+	5.5	22	+
6. J01F_DID‡	7.5	22	+	6	22	+	6	21	+	7	22	+
7. J01M_DID‡	8	22	+	6	22	+	7	21	+	7.5	22	+
8. J01A_%	5.5	22	+	5	22	+	5	21	+	6	22	+
9. J01C_%	5.5	22	+	5.5	22	+	5	21	+	6.5	22	+
10. J01D_%	6	22	+	5.5	22	+	6	21	+	6.5	22	+
11. J01E_%	5	22	+	5	22	+	5	21	+	6	22	+
12. J01F_%	7	22	+	6	22	+	6	21	+	6	22	+
13. J01M_%‡	7	22	+	6.5	22	+	7	21	+	7	22	+
14. J01CE_%‡	8	22	+	7	22	+	8	21	+	8	22	+
15. J01CR_%‡	7	22	+	7	22	+	7	21	+	7	22	+
16. J01DD+DE_%‡	7	22	+	7	22	+	8	21	+	7.5	22	+
17. J01_B/N‡	7	22	+	7	22	+	7	21	+	7	22	+
18. J01MA_%‡	7	22	+	7	22	+	7	21	+	7.5	22	+
19. J01_SV‡	7	22	+	7	22	+	7	21	+	7.5	22	+
20. J01M_SV‡	7	21	+	7	21	+	7	20	+	7	21	+
21. J01M_SVDID‡	7	21	+	7	21	+	7	20	+	7	21	+
22. J01_TT	6	21	+	6	21	+	7	20	+	7	20	+
23. J01_DU99	5	21	-	5	21	+	6	20	+	7	21	+
24. J01_NR	5	22	-	5	22	+	6	21	+	6.5	22	+

† A scale ranging from 1 (= completely disagree), over 5 (= uncertain) to 9 (= completely agree) was used.
‡ Proposed indicators were judged relevant and potentially valid if the median score for relevance was not within the 1 – 6 interval and if there was consensus, i.e. if the number of scores within the 1-3 interval was less than one third of the panel. The information provided by indicators 13 and 20 overlapped with that provided by indicators 18 and 21, respectively.

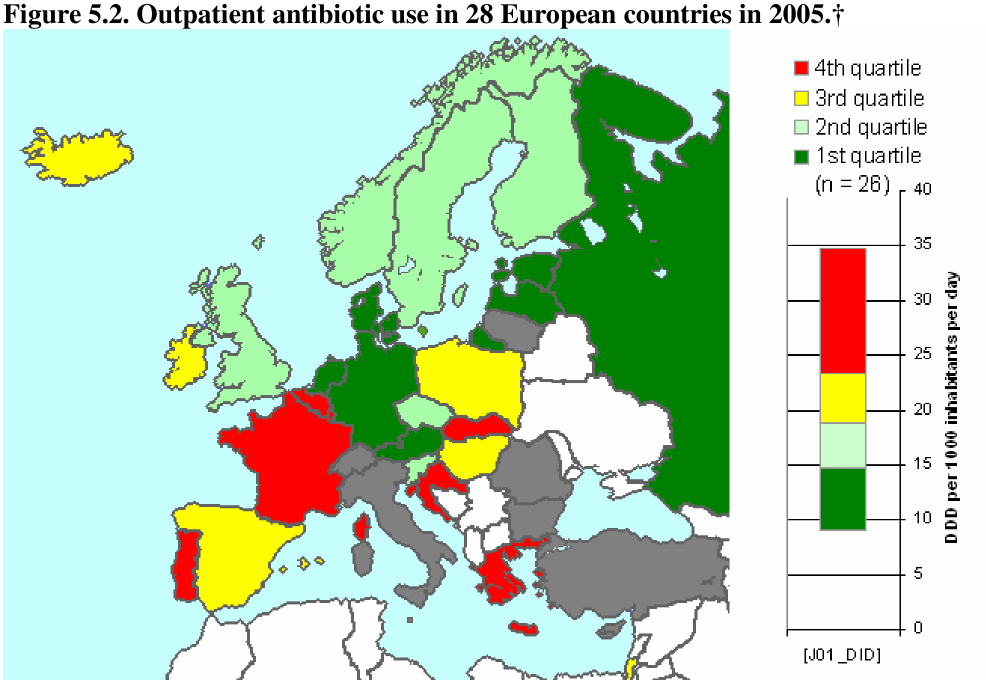
For indicator 1 'Consumption of antibacterials for systemic use (J01) expressed in, Figures 5.1 and 5.2 depict the grouping of the participating countries based on the distribution of the indicator values in four quartiles for 2004 and 2005, respectively.

Figure 5.1. Outpatient antibiotic use in 28 European countries in 2004.†



† Consumption of antibacterials for systemic use (ATC J01) in ambulatory care is expressed in DDD per thousand inhabitants per day; for Greece and Iceland total data are used, for Poland 2002, and for Estonia and Italy 2003 data.

Figure 5.2. Outpatient antibiotic use in 28 European countries in 2005.†



† Consumption of antibacterials for systemic use (ATC J01) in ambulatory care is expressed in DDD per thousand inhabitants per day; for Greece and Iceland total data are used.

Tables 5.3 and 5.4 shows the values for the set of 12 indicators scored valid for participating European countries in 2004 and 2005, respectively. The indicator values allow individual countries to position themselves and to define their own benchmark, based on the epidemiology of infectious diseases and national guidelines.

These results were presented at several international conferences. [2-4] The indicator values will also be made available through the ESAC website. A scientific paper is accepted for publication in Quality and Safety in Health Care.[5]

1. Coenen S, Ferech M, Goossens H. ESF EMRC Exploratory Workshop: Antibiotic Prescribing Quality Indicators. Scientific Report. Antwerp, University of Antwerp, 2005.
2. Coenen S, Ferech M, Goossens H and the ESAC Project Group. Developing valid antibiotic prescribing quality indicators for ambulatory care based on European Surveillance of Antimicrobial Consumption (ESAC) [oral presentation]. 16th ECCMID, 1-4 April 2006, Nice, France. Abstracts book.
3. Ferech M, Coenen S., and Goossens H. European Surveillance of Antimicrobial Consumption (ESAC): Developing Valid Antibiotic Prescribing Quality Indicators for Ambulatory Care [Abstract ID# 13142]. ISPOR 9th Annual European Congress, 28-31 October 2006, Copenhagen, Denmark.
4. Coenen S, Ferech M, Haaijer-Ruskamp FM, Butler CC, Vander Stichele RH, Verheij TJM, Monnet DL, Little P, Goossens H and the ESAC Project Group. European Surveillance of Antimicrobial Consumption (ESAC): Quality indicators for outpatient antibiotic use in Europe. GRIN Meeting, 6-7 October 2006, Stockholm, Sweden.
5. Coenen S, Ferech M, Haaijer-Ruskamp FM, Butler CC, Vander Stichele RH, Verheij TJM, Monnet DL, Little P, Goossens H and the ESAC Project Group. European Surveillance of Antimicrobial Consumption (ESAC): Quality indicators for outpatient antibiotic use in Europe. Qual Saf Health Care. In Press.

Table 5.3 Quality indicators for outpatient antibiotic use in Europe: indicator values for 28 European countries in 2004.

Country	[J01_DID]	[J01C_DID]	[J01D_DID]	[J01F_DID]	[J01M_DID]	[J01CE_%]	[J01CR_%]	[J01DD+DE_%]	[J01MA_%]	[J01_B/N]	[J01_SV]	[J01M_SV]
Austria	12,61	5,12	1,56	3,05	1,50	8,4%	24,3%	11,8%	11,9%	5,17	27,6%	16,8%
Belgium	22,90	10,60	3,16	2,35	2,48	0,6%	28,3%	0,0%	10,8%	27,73	36,1%	18,4%
Bulgaria	16,39	7,71	1,68	1,02	1,60	5,2%	8,5%	0,9%	9,8%	1,43		
Croatia	23,02	11,82	3,42	2,25	1,46	7,3%	21,7%	1,7%	6,3%	2,37	29,7%	16,1%
Czech Republic	15,58	6,81	0,95	2,67	1,27	12,3%	16,7%	0,0%	8,1%	2,86	25,1%	2,9%
Denmark	14,15	8,87	0,02	2,25	0,28	37,0%	0,4%	0,0%	2,0%	0,22	17,3%	7,9%
Cyprus												
Estonia*	11,34	4,52	0,61	1,08	0,64	2,1%	5,5%	0,0%	5,6%	1,59	42,2%	9,2%
Finland	17,27	5,11	2,14	1,89	0,83	9,1%	4,8%	0,0%	4,8%	0,75	19,6%	5,8%
France	27,09	12,83	3,07	4,31	2,08	0,6%	19,2%	5,7%	7,2%	20,47		
Germany	11,09	3,43	1,07	1,81	0,98	9,0%	1,5%	2,8%	8,8%	1,96	37,8%	26,6%
Greece	33,38	10,47	7,23	9,85	1,89	0,8%	15,6%	0,7%	5,7%	24,34	20,3%	-32,0%
Hungary	18,59	8,56	2,25	3,16	1,67	6,0%	24,9%	2,4%	9,0%	7,38	37,8%	5,4%
Iceland	21,44	11,07	0,44	1,67	0,65	13,6%	12,8%	0,3%	3,0%	1,01	17,8%	8,6%
Ireland	20,69	9,98	1,95	2,93	0,77	4,1%	23,0%	0,7%	3,6%	4,59	21,3%	7,8%
Israel	19,69	11,66	3,50	1,51	1,09	8,2%	17,2%	0,1%	5,5%	2,81	16,1%	-5,8%
Italy*	25,69	12,35	3,37	5,01	3,02	0,0%	22,5%	7,7%	10,6%	50,87	37,0%	22,5%
Latvia	11,80	5,38	0,33	0,92	0,90	1,6%	10,1%	0,1%	7,1%	2,98		
Lithuania												
Luxembourg	24,17	10,49	4,59	2,68	2,41	0,7%	26,2%	0,0%	10,0%	14,97		
Malta												
Netherlands	9,75	3,76	0,05	1,38	0,84	4,3%	14,1%	0,1%	8,4%	5,12	15,3%	0,4%
Norway	15,88	6,63	0,28	1,82	0,44	24,8%	0,0%	0,0%	2,8%	0,15		
Poland**	21,14	9,86	2,04	2,37	1,10	2,2%	10,2%	0,1%	4,5%	6,04	38,6%	14,8%
Portugal	23,84	11,21	3,23	3,67	3,05	0,4%	30,7%	2,1%	12,8%	13,48	31,8%	12,8%
Romania												
Russia	9,15	2,22	0,19	0,96	1,30	1,8%	3,2%	0,4%	13,4%	2,18		
Slovakia	22,43	12,50	2,15	3,30	1,33	20,3%	15,2%	0,4%	5,9%	1,67	41,3%	3,0%
Slovenia	16,82	9,91	0,72	3,21	1,12	14,9%	24,1%	0,4%	6,5%	3,03	29,4%	8,8%
Spain	18,70	10,85	1,82	2,45	2,33	0,5%	34,7%	2,6%	12,0%	40,00	30,3%	14,9%
Sweden	14,67	6,61	0,40	0,83	0,99	26,8%	1,3%	0,1%	6,8%	0,15	9,6%	5,4%
Switserland												
Turkey												
United Kingdom	15,21	7,02	0,78	2,27	0,50	4,2%	6,1%	0,0%	3,2%	0,56	15,2%	5,7%

*2003 data; ** 2002 data

Table 5.4 Quality indicators for outpatient antibiotic use in Europe: indicator values for 26 European countries in 2005.

Country	[J01_DID]	[J01C_DID]	[J01D_DID]	[J01F_DID]	[J01M_DID]	[J01CE_%]	[J01CR_%]	[J01DD+DE_%]	[J01MA_%]	[J01_B/N]	[J01_SV]	[J01M_SV]
Austria	14,47	6,00	1,67	3,43	1,42	6,8%	24,7%	5,3%	9,8%	6,20	34,5%	16,3%
Belgium	24,29	11,93	3,05	2,51	2,47	0,5%	28,5%	0,0%	10,2%	34,59	36,1%	15,9%
Bulgaria												
Croatia	23,38	11,55	3,54	2,73	1,52	5,9%	22,3%	1,7%	6,5%	2,93	37,9%	4,6%
Cyprus												
Czech Republic	17,32	7,24	1,19	3,36	1,37	10,9%	16,3%	0,0%	7,9%	3,48	36,4%	-1,2%
Denmark	14,62	9,09	0,03	2,34	0,32	36,0%	0,5%	0,0%	2,2%	0,26	18,3%	5,4%
Estonia	11,70	4,50	0,71	1,71	0,76	3,4%	7,3%	0,0%	6,5%	3,13	31,3%	6,4%
Finland	18,11	5,67	2,21	1,86	0,83	8,8%	5,3%	0,0%	4,6%	0,76	13,9%	5,1%
France	28,94	14,43	3,22	4,55	2,18	0,5%	21,0%	5,9%	7,1%	28,83		
Germany	14,61	4,38	1,46	2,62	1,36	7,6%	1,6%	2,8%	9,3%	2,47	43,4%	29,9%
Greece	34,73	11,13	7,93	10,08	1,89	0,8%	15,1%	0,6%	5,4%	26,75		
Hungary	19,54	8,64	2,32	3,90	1,91	4,1%	26,7%	2,5%	9,8%	11,73	53,3%	22,0%
Iceland	23,31	12,01	0,52	1,83	0,80	13,1%	13,8%	0,3%	3,4%	1,16	16,6%	10,3%
Ireland	20,54	10,21	1,82	3,12	0,84	3,9%	24,1%	0,4%	4,1%	5,02	14,8%	1,5%
Israel	20,55	11,74	3,79	1,64	1,19	7,1%	17,7%	0,1%	5,8%	3,31		
Italy												
Latvia	12,14	5,40	0,42	1,08	1,02	1,5%	11,9%	0,2%	7,9%	3,95	33,0%	18,7%
Lithuania												
Luxembourg	25,19	11,19	4,81	2,93	2,54	0,6%	27,4%	0,0%	10,1%	17,79	43,0%	19,8%
Malta												
Netherlands	10,51	4,09	0,05	1,50	0,86	4,2%	14,2%	0,1%	8,0%	5,39	16,9%	1,0%
Norway	16,75	7,00	0,23	2,04	0,48	25,2%	0,0%	0,0%	2,8%	0,16		
Poland	19,61	7,57	1,72	3,61	1,14	1,5%	3,1%	0,0%	5,8%	9,67		
Portugal	28,01	13,44	4,09	5,33	3,26	0,1%	33,1%	2,2%	11,6%	15,88	58,3%	27,1%
Romania												
Russia	9,16	3,08	0,61	1,00	1,19	2,7%	5,6%	1,6%	12,3%	1,71		
Slovakia	25,03	13,01	3,39	3,93	1,67	17,7%	16,5%	0,4%	6,7%	2,29	48,2%	14,5%
Slovenia	16,54	9,57	0,72	3,27	1,17	11,7%	25,3%	0,2%	6,9%	4,04	37,4%	10,2%
Spain	19,29	11,73	1,83	2,32	2,26	0,4%	39,0%	2,8%	11,3%	51,52	34,3%	20,5%
Sweden	14,87	6,66	0,38	0,87	0,99	26,3%	1,5%	0,1%	6,6%	0,16	10,8%	2,5%
Switserland												
Turkey												
United Kingdom	15,45	7,16	0,78	2,29	0,52	4,3%	6,5%	0,0%	3,4%	0,61	14,3%	6,0%

6 SUBPROJECTS

To deepen the knowledge of antibiotic consumption, four subprojects were agreed with all national representatives during the 3rd ESAC annual meeting aiming:

- For ambulatory care to link data on antibiotic use to patients' sex and age, prescriber and indication.
- For nursing homes to collect data for individual nursing homes and to assess the assignment of these data to either ambulatory care data or hospital care data.
- For hospital care to collect data for individual hospitals to link antibiotic use data to the hospitals' characteristics.
- In addition, we aimed to perform a pharmaco-economic evaluation, including an assessment of determinants of use and regional variation.

6.1 Ambulatory care subproject

The project is lead by Sigvard Mölstad and the ESAC MT liaison person is Samuel Coenen.

Background and Objectives
Besides the main objectives of ESAC II the contract stated an additional objective, i.e. to deepen the knowledge of antibiotic consumption.
For ambulatory care (AC) we therefore aimed to collect use data for specific prescriber groups, for specific age and sex categories, and to deliver antibiotic prescription data related to indications to assess to what extent the additional information explains differences in antibiotic use in ambulatory care

Methods and achievements
During the **ESAC Meeting** in Madrid (10-12 November 2004) all national representatives of the ESAC project (NRs) were asked to complete a questionnaire concerning their participation in the proposed subproject, and all returned this questionnaire (Table 6.1.1). Sigvard Mölstad and Samuel Coenen were assigned to this subproject as subproject leader and contact person within the ESAC MT, respectively.

Table 6.1.1 The ability to provide data for the subproject in ambulatory care (12 November 2004)

TOPICS COUNTRIES	SEX AND AGE	PRESCRIBER	INDICATION
AT	0	1	0
BE	1	1	0
BG	0	?	?
CH	?	?	?
CZ	1	1	0
DE	1	1	1
DK	1	1	1
EE	0	0	0
ES	?	?	?
FI	0	0	0
FR	0	0	0
GR	?	?	?
HR	0	0	0
HU	0	0	0
IE	1	0	0
IL	0	0	0
IS	1	1	0
IT	0	0	0
LU	0	0	0
LV	0	0	0
LT	0	0	0
NL	1	1	1
NO	1	1	0
PL	0	0	0
PT	0	1	0
RO	1	1	1
SE	1	0	1
SI	0	0	0
SK	1	1	1
UK	1	1	1
TOTAL	12	12	7

A **Subprojects Kick-off Meeting** was held in Antwerp 17-18 February 2005. At this meeting only the subproject leaders and the ESAC MT contact persons were present. This meeting was the official start of the development of the AC subproject protocols. First a questionnaire to refine the assessment of data availability was developed and sent to all national representatives (NRs) in June 2005, or to the alternative persons they suggested. We wanted to know how many countries could actually deliver valid and comparable national data linking antibiotic use in ambulatory care with patients' age and sex and the prescriber and/or sample data linking antibiotic use in ambulatory care with indication and regimen (national data are not available). Additionally we asked whether ambulatory care use included prescriptions for nursing home patients, patients recently dismissed from hospital, …; what the denominator population was (we preferred inhabitants over patients over patient visits over prescribers); what the outcome measure for antibiotic use was (we preferred prescriptions, incl. regimen and prescriber over packages over DDD, and want use data at ATC 5 level); what the format for data on patients' age was (we preferred years over age groups) and gender and the prescriber; what the format was for data on the indication (we preferred ICPC2-R codes over ICD10 codes); whether sample data were nationally representative; how this could be assessed; whether the sample data provided sufficient data for less common diagnoses; what the data sources were (insurance data, scientific database, studies or computerised records)?

Their response, as well as a first draft of the protocols, distributed among the subproject group members in August 2005 was discussed during the **Subprojects Protocol Meeting** 7 September 2005 in Antwerp,

i.e. preceding the European Science Foundation Exploratory Workshop on Antibiotic Prescribing Quality Indicators.
In total, 20 countries answered the questionnaire (Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Israel, Luxenbourg, Poland, the Netherlands, Norway, Slovakia, Slovenia, Sweden and UK (England and Scotland)). In 15 countries data linking antibiotic use (=dispensing) and patients's age and gender were available (Austria, *Belgium*, Czech Republic, *Denmark*, *Finland*, Germany, Iceland, Ireland, *Luxembourg*, *the Netherlands*, Norway, Slovakia, *Slovenia*, *Sweden* and UK (England and Scotland). In 14 countries data linking antibiotic use (=dispensing) and the prescriber were available (Austria, *Belgium*, Czech Republic, *Denmark*, *Finland*, Germany, Iceland, Ireland, *Luxembourg* , *the Netherlands*, Norway, Slovakia, *Sweden* and UK (England and Scotland). In 8 countries data linking antibiotic use (=prescribing) and patients's age and gender, and the indication were available (*Belgium*, *Denmark*, Finland, Iceland, the Netherlands, Slovakia, *Sweden* and UK. Only two of these countries (the Netherlands, Slovakia) can provide data on a national base for GPs, most countries can only provide sample data for GPs. In 8 countries data linking antibiotic use (=prescribing) and the prescribed regimen (dosage and length of treatment) were available (Belgium, Denmark, Finland, Iceland, the Netherlands, Slovakia, UK (England and Scotland).
It was decided that we would need two separate protocols to address A. antibiotic dispensing by age, gender and prescriber, and B. GPs' antibiotic prescribing by age, gender and indication, and that we would not pursue to address the therapeutic regimen in this subproject, because of limited availability of data, nor any new data collection.
The outcome measures, route of administration, data collection period, and samples were discussed. Regarding age, gender, prescriber and indication, we preferred collecting data per year of birth over collecting data per age groups, because this is clinically more relevant, e.g. different recommendation for AOM treatment for different ages, we will differentiate between GPs, paediatricians and other prescribers and it was decided that all diagnosis should be recoded into ICPC-2.
After a summary of the Subprojects Protocol Meeting was be circulated for approval (October 2005), Sigvard Mölstad and Samuel Coenen piloted the approved data extraction protocol in Sweden and Belgium, respectively (November 2005 – April 2006). After assessing the outcome of this pilot, the final study protocols were designed and sent to all NRs (May 2006). Sending out the protocols earlier would have interfered with the yearly work to produce yearbooks (Nethmap, Danmap, Swedres, …).

During the last **ESAC Meeting** in Stockholm (21-22 September 2006) national data on A. antibiotic dispensing by prescriber (GP, paediatrician and others), age and gender were available for *Denmark*, *Finland*, *Israel* (2005 data), *Belgium*, *Sweden* and *the Netherlands* (2004) and were presented to the participants. For data on B. GPs' antibiotic prescribing by age, gender and diagnosis only national data was available for *Denmark* (2005, not only prescriptions by GPs), for *Belgium* (2004) and *Sweden* (2005) sample data was available, but the data were not compatible. More countries were asked for data for A or to update their data to 2005. For B, however, it was suggested that a workable solution should be designed to collect data on the link between indication and antibiotic use in countries not (yet) able to deliver such data and be promoted by ESAC.

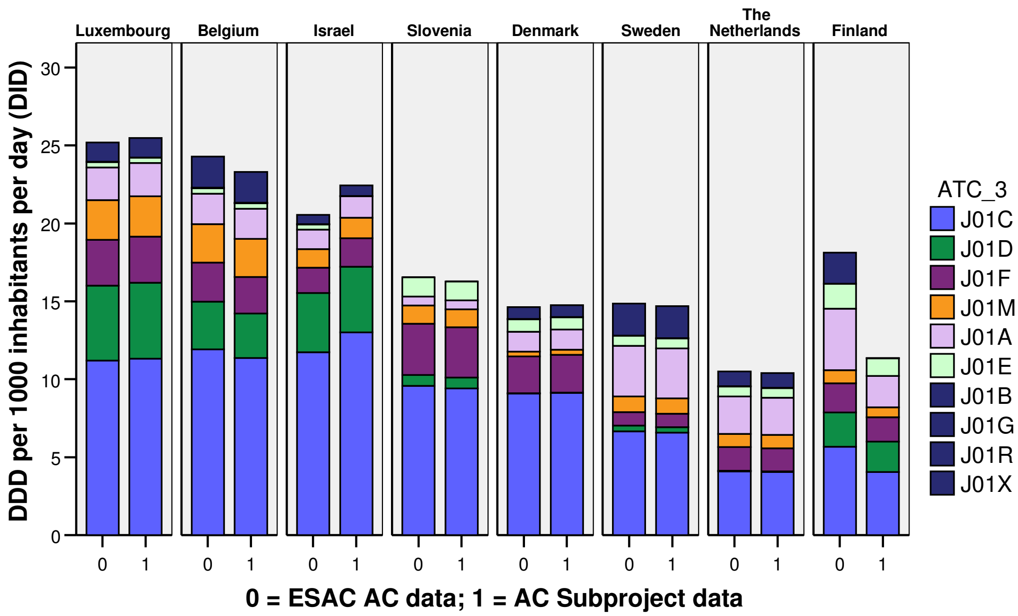
In this final report we present the antibiotic use by the patients' age and gender, and the prescribers' speciality for 8 European countries. An overview of the available data shows that all participating countries were able to deliver 2005 antibiotic use data in DDD per 1000 inhabitants per day (DID), i.e. according the ESAC methodology, by gender (Table 6.1.2). Only one country used age groups in stead of age in years. The prescribers' speciality is missing for Israel (and for the use in DID also for Sweden). Except for Israel, all countries also provided antibiotic use data with prescriptions or packages – a proxy for prescriptions - as outcome measure.
The antibiotic use data available for this subproject are similar to the ESAC data for AC for all countries, except for Finland where the data for this Subproject are reimbursement data and the ESAC data for AC are sales data (Figures 6.1.1a and 6.1.1b). The other figures present the results of this subproject for all 8 participating countries using DID as outcome measure and ranking countries from the highest to the lowest consuming country, with the result for Finland in the end as their data for the Ambulatory Care Subproject differ from the ESAC AC data.

Table 6.1.2 Characteristics of the data available for the ESAC Ambulatory Care Subproject

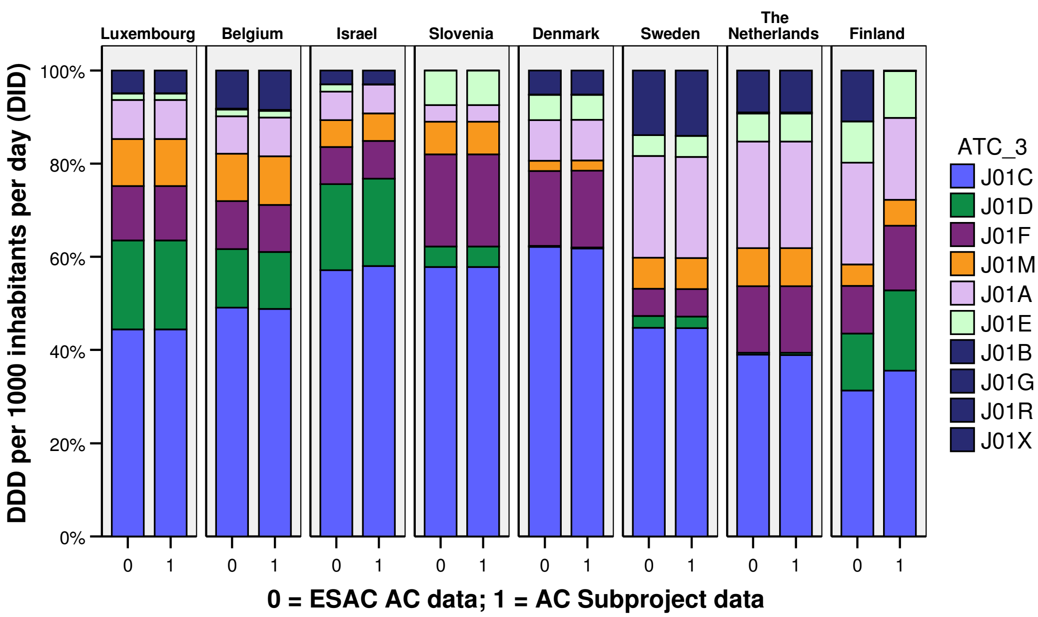
		Patients'		Prescribers'	Outcomes		
	Time frame	Age in years	Gender	Speciality	DDD	Packages	Prescriptions
BE	2005	yes	yes	yes	yes	yes	no
DK	2005	yes	yes	yes	yes	yes	no
FI	2005	yes	yes	yes	yes	yes	no
IL	2005	yes	yes	no	yes	no	no
LU	July 2004 -June 2005	yes	yes	yes	yes	yes	no
NL	2005	yes	yes	yes	yes	no	yes
SI	2005	5 year age groups	yes	yes	yes	yes	no
SE	2005	yes	yes	only for prescriptions	yes	yes	yes

Figure 6.1.1 Total antibiotic use in 8 European countries: comparison between ESAC ambulatory care and Ambulatory Care Subproject data

a.



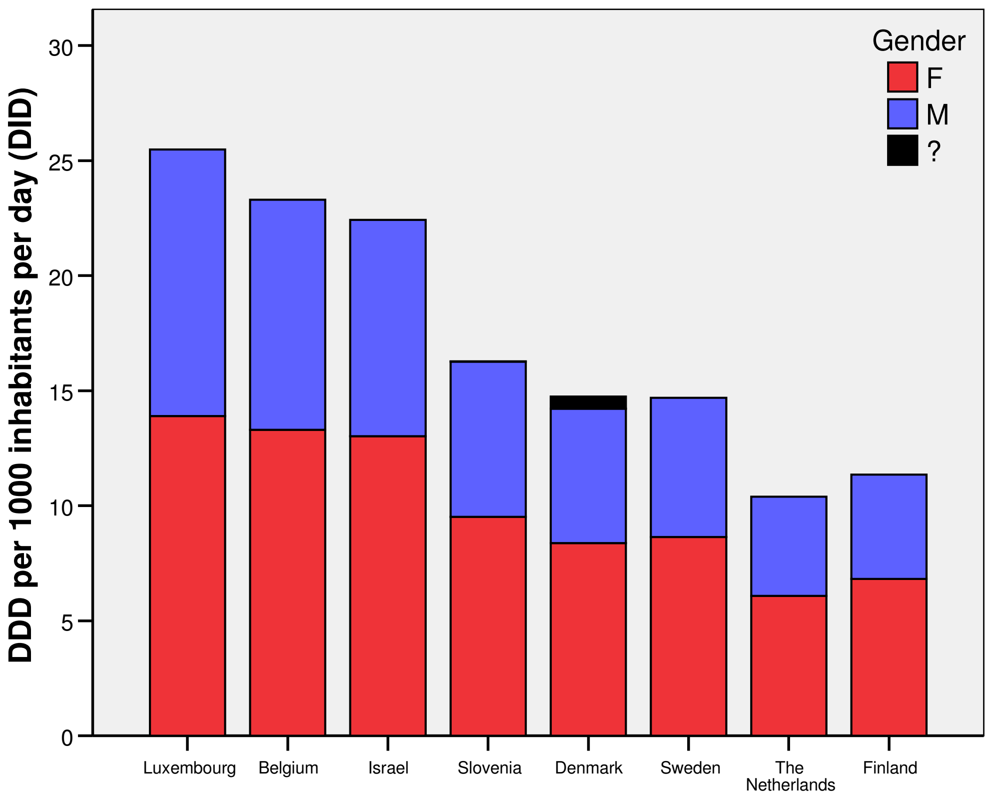
b.



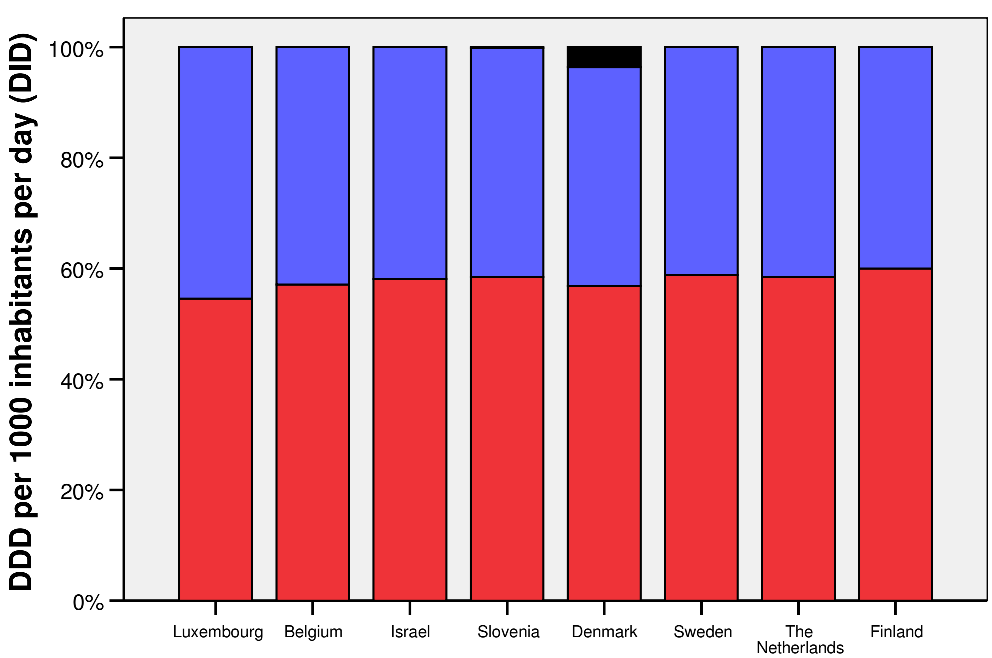
***J01C**: Penicillines; **J01D**: Cephalosporines; **J01F**: Macrolides, lincosamides and streptogramines; **J01M**: Quinolones; **J01A**: Tetracyclines; **J01E**: Sulphonamides and trimethoprim; **J01B, J01G, J01R and J01X**: Other antimicrobials for systemic use.*

Figure 6.1.2 Antibiotic use in primary care by gender in 8 European countries

a.



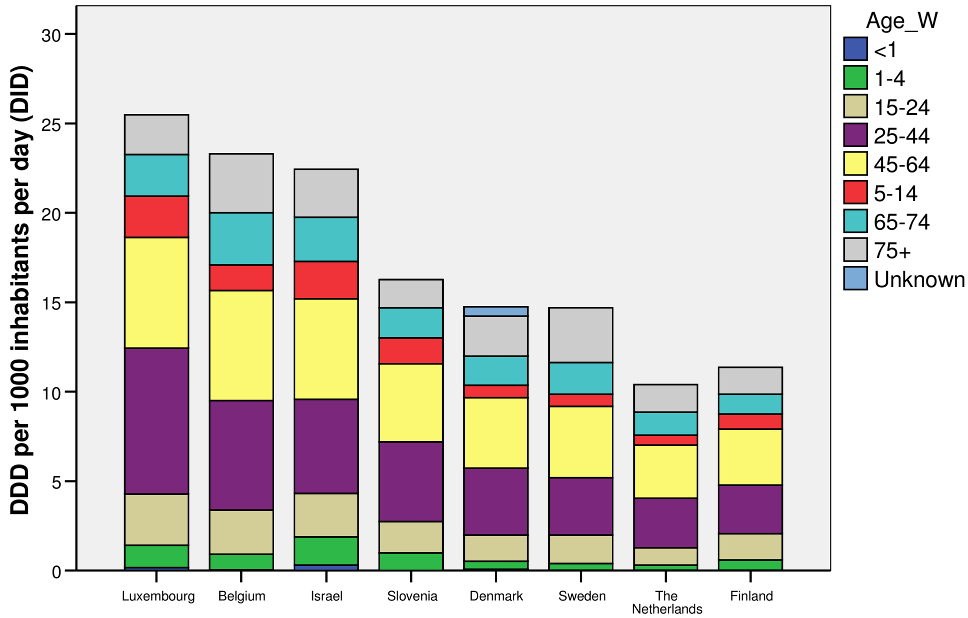
b.



***M**: Male; **F**: Female; **?**: Unknown*

Figure 6.1.3 Antibiotic use in primary care by Wonca age groups in 8 European countries

a.



b.

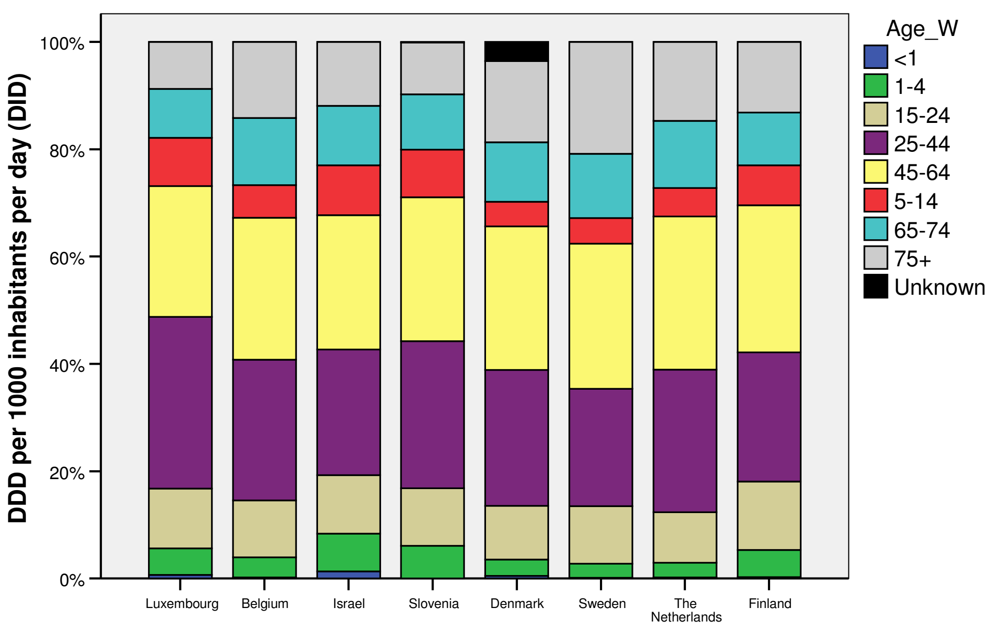
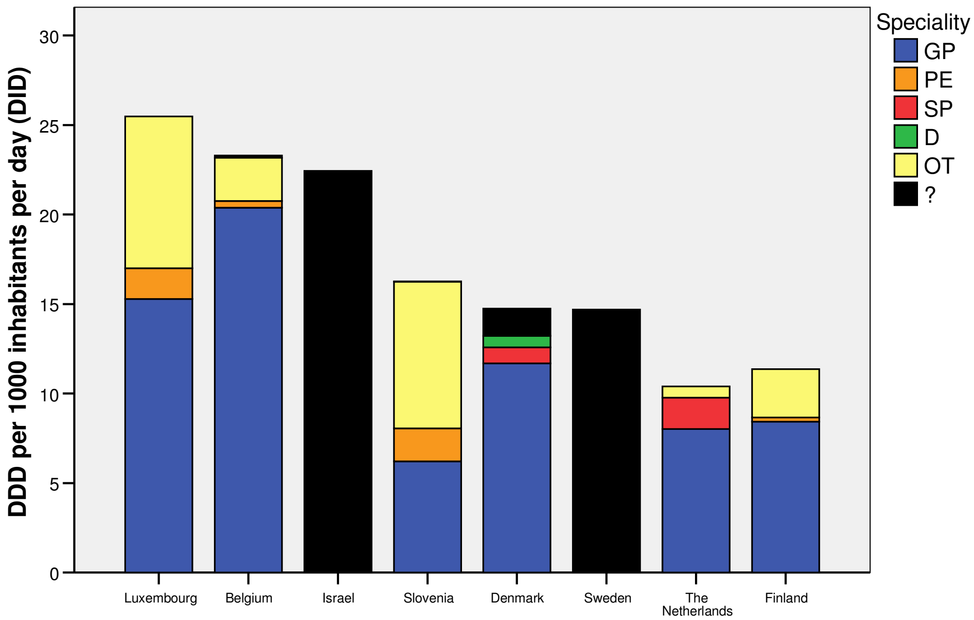
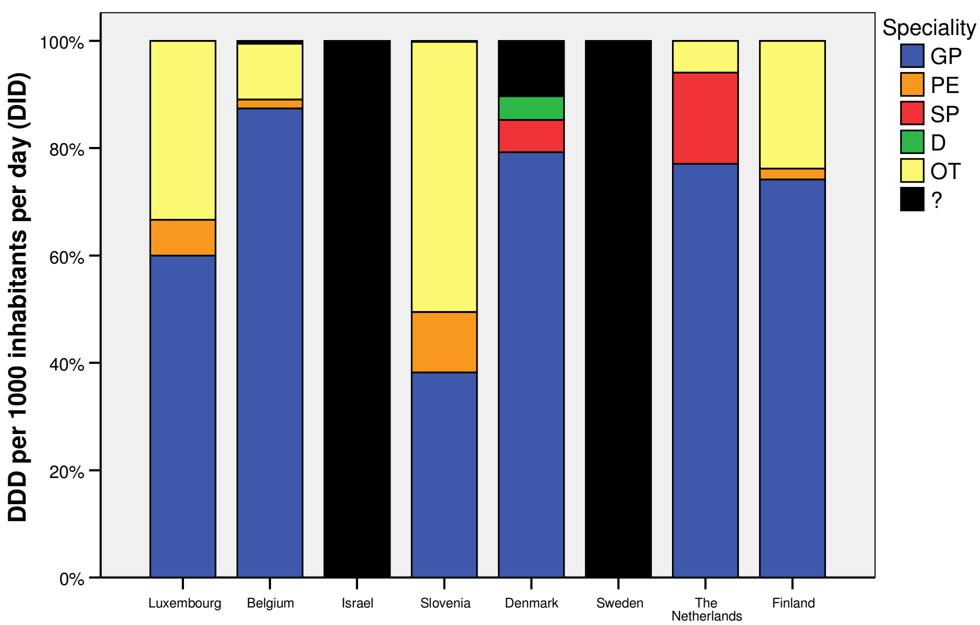


Figure 6.1.4 Antibiotic use in primary care by speciality of the prescriber in 8 European countries

a.



b.



***GP**: General practitioner; **PE**: Paediatrician; **SP**: Specialist; **D**: Dentist; **OT**: Other; **?**: Unknown*

6.2 Hospital care subproject

The Project is lead by Peter Davey (United Kingdom). The data management team (Faranak Ansari and Angela Johnston) is based in the Health Informatics Centre at the University of Dundee. The ESAC MT liaison person is Herman Goossens.

Objectives

Our objective was to collect data about hospital antibiotic use with standardised methods applied across hospitals in different European countries.

We have used the data to answer three questions:

1. What is the trend in hospital antibiotic use over the study period?
2. What effect do different denominators (bed days or admissions) have on longitudinal analysis of hospital antibiotic use?
3. What is the relationship between the DDD calculated from total antibiotic use and the actual daily doses prescribed in each hospital?

Methods

In order to prepare and agree on detailed objectives, methods, and recruiting meetings have beenwere held in February 2005, June 2005, Sep 2005 and January 2006. An additional meeting was held on Sunday 2nd April 2006 from 12:00-14:00 during 16th ECCMID meeting in Nice where the final software for the Point Prevalence Survey was demonstrated.

Members of ESAC II- HC came from 23 countries: Austria, Belgium, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Greece, Germany, Latvia, Lithuania, Malta, Netherlands, Norway, Poland, Slovenia, Sweden, Turkey and the four countries of the UK (England, Northern Ireland, Scotland and Wales). From participating hospitals, two hospitals (Lithuania and Malta) will participate in point prevalence study and one-year (2005) longitudinal study and another hospital (Wales) will participate in longitudinal study only.

One hospital was selected from each country (including one hospital each from the four UK countries, England, Northern Ireland, Scotland and Wales). For countries with pre-existing networks of hospitals the ESAC national representative was asked to identify one hospital that was able to support both the longitudinal and point prevalence components of the HC subproject.

Given that the main question of the study required analysis of time trends in antibacterial use, the details of country and hospital demography were of lesser importance. Nonetheless, a questionnaire about country health-care system and hospital demographics was designed to identify potential explanatory variables in future comparisons between countries or hospitals. However, the HC Subproject team were clear from the outset that no European benchmarking would be performed in this subproject.

Numerator: Antibiotic Use

The study focused on systemic antibacterials in the J01 sub-class according to ATC classification by the WHO Collaborating Centre for Drug Statistics plus oral metronidazole, oral vancomycin and colistin.

Participants were asked to provide the number of dosage forms dispensed from hospital pharmacy to the hospital as a whole.

Minimum database requirements were:

- A list of all drugs, preferably by generic name and translated into English.
- Dosage form with complete information on strength, package and route of administration
- The inpatient destinations for dispensing
- Preferably in generic name and in English language however French, Dutch and German language were accepted.

The amounts of each product were converted to WHO Defined Daily Doses (DDDs) at HIC in Dundee. DDDs were those that were current when the analysis began. Any products without a WHO DDD were assigned a temporary ESAC HC DDD.

Estimated PDD (Prescribed Daily Dose) were provided by participant hospitals based on their local antibiotic policy or local or national formularies. These data were compared with actual PDD data collected in the point-prevalence survey. It was anticipated that estimated PDDs will would be inaccurate and that this information would be important in demonstrating the added value of cross sectional, point prevalence studies.

Denominator: Clinical Activity

The project compared two denominators: bed days and admissions. It was anticipated that annual increments in antibiotic use would be less when the number of patients (admissions or discharges) was the denominator *versus* the number of bed days. [1]

We asked hospitals to define the methods that they used to measure bed days or admissions. We anticipated that the following methods would be in use but agreed to record other methods if they arose.

Bed days

1. Occupied bed days (OBD) calculated from daily census of the number of occupied beds at a specified time (e.g. midnight).
2. Hospital care days calculated from daily census of the number of patients that have occupied each bed in a 24 hour period (can be >1 patient per day).
3. Patient days (based on length of stay, e.g. date of discharge-date of admission -1)

Admissions

1. Does the number of admissions include day cases? If so can day cases be excluded? If not does the hospital have data about % day cases by year?
2. How are birth admissions included? Do they count as one admission or two? Has a consistent method been used throughout the study period?

Time period

Monthly data were collected for 6 years starting from January 2000 until December 2005. 2 hospitals provided 4 year data and another one 5 year data.

Use indicators- DDD/100 bed-days and DDD/100 admissions were the study indicators.

Analysis- Time trends in antibacterial usage will were analysed for each participant hospital within the 6-year period using time series analysis with statistical test for trend based on linear regression.

Longitudinal data analysis

An Access database was designed for each hospital to calculate DDD/100 OBD, DDD/100 for all antibacterials, J01 subgroups, parenteral antibacterials and single drugs on a monthly, quarterly and yearly basis. This automated method also provided DU75% (drugs accounted for 75% percent of total use) for each year.

Estimation of other clinical activity factors

From the information about clinical activity that we had (OBD and AD), we obtained the following measures:

- Number of in-patients discharged(DIS) , denoted by *R* here, using the stock adjustment equation below where *DPM* is the number of days per month, *A* number of in-patients admitted, *B* number of OBDs.

$$\frac{B_t}{DPM_t} = \frac{B_{t-1}}{DPM_{t-1}} + A_t - R_t \,;$$

- Length of stay (LOS) by an average in-patient, denoted by *L* here, using the approximation

$$L_t = \frac{B_t}{\frac{A_t + R_t}{2}}$$

Statistical analysis

For time series analysis we built the following dynamic regression model

$$Y_t = \sum_{s=0}^{S}\left(a_s Y_{t-1-s} + \beta_s A_{t-s} + \gamma_s B_{t-s} + \delta_s R_{t-s} + \phi_s L_{t-s}\right) + \sum_{j=0}^{J}\mu_j t^j + \sum_{i=2}^{12}\theta_i DM_{i,t} + \sum_{k=1}^{K}\lambda_k DI_{k,t} + \varepsilon_t \quad (1)$$

Where Y is amount of antibacterials sin DDDs. $\alpha_s, \beta_s, \gamma_s, \delta_s$ and ϕ_s are the coefficients which capture the impact of these variables with s lags (assuming a finite lag order of $S \geq 0$); t refers to time associated with the observation date; the μ_j coefficients capture the intercept and trend (assuming some finite polynomial in time of degree $J \geq 0$); DM_i s are seasonal dummies which assumes 1 for month i and 0 otherwise and whose coefficients, θ_i s, capture the shift in month i relative to the first month (January is set as the bench month and we use dummies for February to December – i=2,...,12); DI_k s are dummies which capture irregularities such as sudden shifts in the series or outlier observations and assumes 1 for the relevant dates and 0 otherwise, hence the λ_k coefficients capture the corresponding shifts thus dampening their impact; and □ is a random disturbance term which, in general, can be allowed to follow an ARIMA process.
The full model still requires some improvement but the main findings are provided in results.
To simplify the presentation of databases and their trends for this report, we have provided scatter diagrams and slopes of regression lines for all variables. Nonetheless, we found that providing the table of trends (slopes of regression lines) still is not the best way to compare the trends between hospitals. In order to scale the changes and find a way to compare the trends between hospitals we calculated the percentage of change/ year according the following formula:
Δ Variable = [(*Slope* * 12)/ *Intercept*] * 100

Point Prevalence Study

The STRAMA (Swedish Strategic Programme for the Rational Use of Antimicrobial Agents and Surveillance of Resistance) web based system for recording national Swedish point prevalence surveys was used for the ESAC point prevalence survey. Mats Erntell worked with Neotide, the Finnish company that maintains the software to produce an English language version. The software was customized for each hospital that used it based on their specialties and drug list. Therefore the pilot was confined to one hospital per country.
A workshop for training on the methods for the Point Prevalence Survey and use of the web based software was organised in January 2006 in Prague. It was agreed that the hospital selected for the longitudinal study should also participate in the cross sectional point prevalence survey.

- Participating hospitals provided:

- List of specialties and subspecialties by administrative units
- List of available antibacterials (ATC class J01, J04AB, A07A, P01AB) in the hospital, with ATC codes and route of administration. There were two columns for entering drug names. The generic name of the drug was entered in English in Column 1 (e.g. amoxicillin, ciprofloxacin). The second Column was used for the name that hospitals wanted to appear in the pull down menu for their web page when they entered data. Hospitals were allowed to enter one or more trade names for the drug or a translation of the generic name into their language. Hospitals were also asked to provide the maximum prescribed daily dose for each product.

- When was the survey done?

The survey was completed during two calendar weeks between 1st April and 31st May 2006. Surgical wards were surveyed on Tuesday, Wednesday or Thursday in order to capture information about prophylaxis in the previous 24h. Medical wards were surveyed on Monday, Tuesday, Wednesday or Thursday. Depending on the number of beds hospitals could decide to complete the survey over one or more days. However, all beds in each administrative unit (e.g. Internal Medicine, General Surgery) should have been completed in a single day.

-Who completed the survey?

Hospitals were asked to identify survey staff familiar with reading patients notes (e.g. ID specialist, microbiologist, pharmacist, infection control nurse). Hospitals could decide to have the survey completed by a single person or a team of people with specialist expertise in microbiology or infectious diseases. The HC Hospital lead was responsible for training other members of the team.

- Which patients were included?

All patients who are in the hospital at 8 am on the days of survey were included in the study. The number of admitted patients at 8 am at the departments was entered in the special form. Patients who were receiving antibiotics at 8am on the day of the survey were identified and the details of prophylaxis or therapy recorded on the data sheet. For surgical patients administration of prophylactic antibiotics was recorded in the previous 24h. The reason for this was to code the duration of prophylaxis as either C1 (one dose), C2 (one day) or C3(>1 day). This information was recorded in the “Indication” field on the data entry form and website.

- *What is the anatomical site of infection or prophylaxis?*
The diagnosise and indication for prophylaxis used the same diagnosis group, which was anatomically related to an organ e.g. skin, lungs etc. The aim was to find out what the physicians thought they were treating. In addition to looking at all patient records, staff could request additional information from nurses, pharmacists or doctors. However, there was no discussion about the appropriateness of prescribing. We did not want staff to have the feeling that we weare checking them and there was no intention to change prescribing.

- *Which drugs to include?:*
All systemic antibacterials in J01, J04AB, A07A and P01AB classes were included. Actual prescribed dose were recorded both for adults and children for single and combination antibiotics (e.g. 960mg of co-trimoxazole).

- *Technical support*
Prof Mats Erntell kindly accepted to be the "help desk" for software problems during the PPS. The software was hosted on the STRAMA server. Core and optional fields were contructed. All of the fields (core and optional) were on the web based data record. For a hospital’s data to be included in the PPS all of the core fields must had to be completed for all patients in the survey. The decision about optional fields was entirely at the discretion of each participating hospitals and was left until the time of the survey. If a hospital found that it did not have the resources to complete an optional field for all patients in the survey then this field was not included in the analysis for that hospital.
The training meeting reviewed pilot data from each of the participating hospitals and also used specimen cases for data entry at the meeting.

Dissemination

The study team in Dundee and the STRAMA website provided concurrent feedback to the participants.
The study will be published by the ESAC hospital subproject principle investigators with ESAC Subproject Group as co-authors. Three papers will be submitted: longitudinal surveillance, point prevalence survey and hospital questionnaire. Feedback of the results for each hospital will be given to the country participants and they can publish their own individual hospital results with themselves as lead authors when the main papers have been accepted for publication. At the same time the overall results will be published on the ESAC website.

Achievements

Hospital Questionnaire

The total number of beds in the 22 participating hospitals was 17,107. Completed questionnaires were returned from 20 hospitals with 15,854 beds. Two hospitals were infectious disease hospitals with 747 beds. Some hospitals were unable to provide any historical data and this was incomplete for most hospitals. We have therefore only presented data from 2005 (Table 1).

Of the 22 hospitals, 16 completed both the longitudinal and point prevalence survey. Two hospitals completed the PPS but only provided drug use data for 2005. Two hospitals only completed the longitudinal survey and two hospitals only completed the PPS. Therefore 18 hospitals completed the longitudinal survey and 20 hospitals completed the PPS.

Longitudinal Study

The longitudinal survey revealed four distinct patterns of antibiotic use. Antibiotic use increased over time in 14 hospitals and decreased over time in 4 hospitals. Increases in use were not explained by changes in clinical activity in 5 hospitals whereas in the remaining 9 hospitals the increasing use was partially (6 hospitals) or completely explained by increases in clinical activity. Antibiotic use decreased over time in four hospitals but in one this was explained by reduction in clinical activity whereas in the other three decreases in antibiotic use had occurred despite stable or reducing clinical activity.

There was an underlying trend of reducing length of stay in 16 of the 18 hospitals. Consequently annual changes in DBD were also greater than annual changes in DAD in 16 of the 18 hospitals. In two hospitals the reduction in length of stay was so extreme that DAD decreased significantly whereas DBD increased significantly.

In conclusion, the key findings are:

1. Antibiotic use measured in DDD increased over time in 14 of the 18 hospitals.
2. The results support the hypothesis that adjustment by occupied bed days (DBD) results in larger changes over time than adjustment by admissions (DAD). For 16 of the 18 hospitals Annual Change in DBD was > Annual Change in DAD. Note that when Annual Change is negative smaller numbers are > larger numbers (e.g. -3% > -5%). The two exceptions were hospitals 12 and 13, where Annual Change in DBD was slightly less than Annual Change in DAD.
3. Adjustment of DDD by clinical activity (DBD or DAD) generally resulted in smaller Annual Changes in antibiotic use. The most extreme example was Hospital 12, where a 3.6% annual increase in use measured in DDD became a 10% decrease in use when measured by DBD or DAD. However, there were some important exceptions.
    a. In hospitals 7, 5, 15 and 10 Annual Change in DDD was magnified by adjustment. In these hospitals both OBD and AD were decreasing over time, meaning that increases in DDD were occurring despite reduction in clinical activity.
    b. In hospital 16 there was a marked increase (13.95%) in admissions combined with a small (-1.19%) decrease in OBD. The combined effect of these changes was that adjustment by AD or OBD produced divergent results. A 2.5% increase in DDD became a 3.56% increase in DBD but a -7.02 decrease in DAD. Hospital 4 had similar results although the Annual Changes were not so marked.

The underlying trends in Occupied Bed Days, Admissions and Length of Stay can also be seen most clearly when presented graphically. Admissions increased over time in 10 of the 18 hospitals. Length of stay increased over time in only two hospitals (12 and 13). Hospitals with increasing admissions but reducing occupied bed days have reducing length of stay, the most extreme example being Hospital 16. However hospitals with similar trends over time in OBD and Admissions can have quite different trends in DBD and DAD (e.g. Hospitals 4 and 9).

Point Prevalence Study

A total of 20 hospitals participated in the study with 11,571 admitted patients, of whom 3,496 (30.2%) admitted were treated with antimicrobials. The highest proportion of treated patients (59%) occurred in one of the two specialist, infectious diseases hospitals. Excluding these two specialist hospitals, between 19-40% of patients in the remaining 18 hospitals were treated with antimicrobials as. A total of 3,655 treatments was recorded. 1,733 were given to women (47.4%) and 388 (10.6%) to children (<17 years). The indication for treatment was community acquired infection in 47.5%, hospital acquired infection in 28.9%, preoperative prophylaxis in 16.6%, and medical prophylaxis in 7.1%. For adults cultures were taken before oral treatment in 40.8% and before parenteral treatment in 42.5%. The most commonly used antimicrobial subgroups for adults in DDDs for treatment and prophylaxis were Penicillins with betalactamase inhibitor (J01CR) 23%, Fluoroquinolones (J01MA) 13.7%, Extended-spectrum Penicillins (J01CA) 8.1% (Table 6). The total amount of antimicrobials used for adults was 52 DDD/100 admitted patients (33 - 88). In total 160 different antibacterials were prescribed. The most commonly prescribed antibacterials for adults were oral Amoxicillin & enzyme inhibitor (9.3%), parenteral Ampicillin & enzyme inhibitor (6.4%), oral

Ciprofloxacin (5.9%), parenteral Cefuroxime (5.4%), parenteral Ciprofloxacin 5.2%, and parenteral Metronidazole (4.7%).
Two diagnosis groups accounted for >30% of all treatments: pneumonia (19.2%) and skin and soft tissue infections (12.6%). In assessment of therapy, 45.5% of therapies were empirical and 36.8% was directed therapy.
The duration of antibiotic prophylaxis for surgery was >1 day in >50% of all patients. The figures for surgical specialties were orthopedic surgery 52%, general surgery 59%, , urology 76% and in ENT 89%. The use of single dose pre-operative prophylaxis ranged from 2 to 27%. Thus, a key target for quality improvement was duration of antibiotic prophylaxis for surgery.
A WHO DDD was available for 15 of the oral formulations and 31 of the parenteral formulations that were used in the Point Prevalence Survey. There was no difference in reported PDDs and WHO DDDs for 4 oral formulations and 6 parenteral formulations. The PDD exceeded the WHO DDD for 7 oral formulations and 12 parenteral formulations. The most extreme examples were oral amoxicillin plus clavulanate (PDD 1.76G *vs* DDD 1.0G) and parenteral doxycycline (PDD 0.4G *vs* DDD 0.1G). The.PDD was less than WHO DDD for 4 oral formulations and 31 parenteral formulations. The most extreme examples were oral metronidazole (PDD 1.19G *vs* DDD 2.0G) and parenteral flucloxacillin (PDD 0.5G *vs* DDD 2.0G). Thus, a WHO DDD was available for 15 of the oral formulations and 31 of the parenteral formulations that were used in the Point Prevalence Survey. There was no difference in reported PDDs and WHO DDDs for 4 oral formulations and 6 parenteral formulations. The PDD exceeded the WHO DDD for 7 oral formulations and 12 parenteral formulations, whereas the PDD was less than WHO DDD for 4 oral formulations and 31 parenteral formulations.

Table 6.2.1 Information collected from the hospital questionnaire

Number of beds	17,107 in 22 hospitals. Completed questionnaire from 20 hospitals with 15,854 beds.
Teaching hospital	15 hospitals with 14,360 beds, 91% from total beds.
Primary hospital	1 hospital with 243 beds, 1.5% from total beds.
Secondary hospital	12 hospitals with 9,688, 61% from total beds.
Tertiary hospital	10 hospitals with 10,422 beds, 66% from total beds.
ICU	In 20 hospitals, 518 beds (7.8- 110), 3.3% from total beds.
Pediatric ICU	In 9 hospitals, 158 beds (2-45), 1% from total beds. NA: 4.
Pediatric unit	In 16 hospitals 1,924 beds (20- 545) 12.1% from total.
Infectious diseases department	In12 hospitals, 542 beds. 7- 247 beds: including infectious disease hospitals. 7-31 beds: excluding infectious diseases hospitals. 3.4% in total.
Hematology	In 12 hospitals, 335 beds (7-58), 2% from total. In 3 hospitals specialty exists but number of allocated beds is not fixed.
Renal dialysis	In 12 hospitals, 190 beds (2- 65), 1.2% from total. In 4 hospitals specialty exists but number of allocated beds is not fixed.
Organ transplant	In 3 hospitals, 46 beds in 3 (0.3-6.4%). In 6 hospitals specialty exists but number of allocated beds is not fixed.
Pharmacist	218 FTE, 0.2- 37.5. 1.38 FTE/100 beds (0.05- 4.4). NA: 1.
Infectious diseases consultant	133 FTE, 0-52 including infectious disease hospitals and 0-23.3 excluding. 0.84 FTE/100 beds, 0 – 21 including infectious disease hospitals and 0-1.2 excluding.
Microbiologist	75 FTE. 1- 11 including infectious disease hospitals and 1-11 excluding. 0.4 7 FTE/ 100 beds, 0.05-2.4 including infectious disease hospitals and 0.05- 1.2 excluding.
Infection control nurse	57 FTE (1-8). 0.36 FTE/100 beds, 0.1- 0.7 including infectious disease hospitals and 0.1-0.7 excluding.
Drug expenses from national budget	Yes: 18, Mainly: 1, No: 1.

Patients pay for drug	No: 19, Yes: 1.
Financial incentives for antibiotic	No: 20.
Hospital pharmacy supply	Yes: 17, No:1, Y/N changed over time: 1, NA: 1.
Prescriptions at discharge excluded	Yes: 15, No: 4, NA: 1.

6.3 Economic/Regional subproject

This subproject has been coordinated by Giuliano Masiero from Switzerland and the ESAC MT liaison person is Matus Ferech.
Participating countries are Austria, Belgium, Denmark, Germany, Italy, Switzerland and the United Kingdom

Background

Regional variations in outpatient antibiotic consumption can be investigated by looking at associations with potential socioeconomic determinants of use. The empirical literature on the demand for pharmaceuticals helps to identify some of them.
A specific approach to antibiotic use in ambulatory care has been previously applied by Filippini, Masiero and Moschetti (2006) to analyse regional variations of antibiotic use in Switzerland. The Economic/Regional subproject applied a similar approach to investigate variations in outpatient antibiotic use across European countries and regional variations within other countries (Italy). The approach has also been extended to include a further level of detail: small geographic areas.
The total use of antibiotics can be disaggregated into main groups of components. The subproject investigated determinants of the demand structure, the impact of prices on different antibiotic categories and some economic incentives related to the characteristics of antibiotic prescribers.

Objectives

The two main objectives of the subproject were:

A) To investigate regional and local variations in outpatient antibiotic use within European countries and their components;

B) To investigate the determinants of differences in outpatient antibiotic use between European countries.

The analysis would eventually allow drawing a regional map of antibiotic use in Europe and identifying important determinants of regional antibiotic consumption in ambulatory care for a range of European countries. Effective health policies to induce appropriate antibiotic use could benefit from the development of this methodology which could later be applied to other countries.

Achievements

Questionnaire on regional data

The availability of data in different European countries was assessed through a short questionnaire. All ESAC participating countries was asked to provide information on the level of detail of their outpatient antibiotic consumption data and the availability of defined determinants.

Regional variations

An analysis was conducted on regional variations in outpatient antibiotic use in Italy (see document attached). Data on antibiotic use between 2000 and 2003 were provided by ESAC. The University of Bergamo constructed a dataset of potential determinants of use.

Methodology

Variations in antibiotic use in Italy were investigated by means of descriptive statistics. An anova analysis was performed to disentangle different components of regional variations: regional component, seasonal component and annual trend. We calculated simple correlations between regional variations and potential determinants. This was the first step to identify an appropriate econometric model of antibiotic use for Italy.

Results

Antibiotic use in Italy slighly increased over time. Seasonal variations were remarkable. Northern regions exhibited lower levels of use per capita compared to central and southern regions. Apparently, regional differentials seemed to be smaller for Italy (a relatively large country) than for Switzerland (a relatively small country). This would suggest that the characteristics of the health care system are important to explain the magnitude of variations in different countries (Switzerland is a federal state made of cantons with different health care systems whereas Italy is a regional state with a National Health Service).

Regional differences not explained by seasonal fluctuations and annual trends account for around 50% of total variations. Correlations identified some potential determinants that could be tested in an econometric specification. Moreover, the negative correlation between antibiotic use and the per capita income suggested that determinants may not have the same impact in different European countries (a positive impact was found by Filippini, Masiero and Moschetti, 2006). This called for the specification of an appropriate econometric model to investigate causes of variations in antibiotic use across regions in Italy.

Reference

Masiero G., Ferech M. *Variations in outpatient antibiotic use in Italy and preliminary associations with socioeconomic determinants*. summary report, 2007

Local variations

The regional analysis was extended to local (small areas) variations in the case of Switzerland (see working paper attached). Significant differences were observed in the per capita antibiotic consumption measured in defined daily doses per 1000 inhabitants (DID) across small geographic areas in Switzerland.

Methodology

An econometric model was proposed in which, antibiotic use varied according to the socioeconomic characteristics of the population, the incidence of infections, antibiotic price and local supply of health care.

Results

The most important determinants of variations in outpatient antibiotics use in the community were income, demographic structure of the population and local supply and price of antibiotic treatment. The analysis also allowed assessing the welfare loss due to heterogeneous attitudes towards the risk of bacterial infections and resistance at local level. We estimated that unexplained variations may account for 11% of the total antibiotic spending in the community, thus leading to a €6ml loss per year in Switzerland.

Dissemination

The analysis was presented at the 6th European Conference on Health Economics, Budapest, July 6-9, 2006.

References

Filippini M., Masiero G., Moschetti K., *Small area variations and welfare loss in the use of antibiotic in the community*. Working paper N. 06-07, University of Lugano, 2006.

Filippini M., Masiero G., Moschetti K. *Small area variations and welfare loss in the use of antibiotic in the community*, 6th European Conference on Health Economics, Budapest, July 6-9, 2006.

Variation components

The analysis focused on the use of different classes of antibiotics for respiratory infections in outpatient care. We investigated economic incentives for physicians to prescribe different types of antibiotics locally and analyses substitution and complementary effects between alternative groups of substances.

Methodology

We modeled the use of antibiotics in outpatient care by looking at the allocation of the expenditure to different groups of substances (classic penicillins, penicillins amoxi/clav and 1st and 2nd generations of cephalosporins, 3rd generation of cephalosporins and quinolones, and macrolides), aggregated according to doctor's perception of alternatives in the treatment of respiratory infections. The methodology applied was based upon the Almost Ideal Demand System (AIDS) specification, using shares of expenditure and prices for different categories of antibiotics from small geographic areas in Switzerland. The model included demographic and cultural characteristics of the population and the dispensing status of practices. We calculated compensated and uncompensated own- and cross- price and expenditure elasticities for antibiotic categories and Allen's elasticities of substitution.

Results

We found evidence that the shares of different therapeutic substitutes in the treatment of respiratory infections are quite responsive to price changes and affected by the status of practices. This suggested that health authorities have a margin to adjust economic incentives on self-dispensing behaviour in order to reduce antibiotic misuse.

Dissemination
The analysis will be presented at the 6th World Congress of the International Health Economics Association in July 2007.

Reference
Filippini M., Masiero G., Moschetti K. *Characteristics of demand for antibiotics in primary care: an almost ideal model*. Working paper N. 07-01, University of Lugano, 2007.

Determinants of variations across Europe
The collaboration between ESAC and the University of Lugano and Bergamo led to the investigation of socioeconomic determinants of variations in outpatient antibiotic use across European countries and the impact of bacterial resistance. Comparable data on antibiotic use measured in the defined daily doses per 1000 inhabitants (DID) was provided by the ESAC project together with a list of potential determinants.

Methodology
The University of Lugano and the University of Bergamo constructed a parsimonious dataset of determinants and specified some econometric models to explain antibiotic use.

Results
Results from applied econometric estimations for panel data revealed a link between antibiotic use and the per capita income, the demographic structure of the population, the level of education and cultural aspects. Supply-side factors, such as the density of providers and their remuneration methods, were also taken into account. The interaction between bacterial resistance and antibiotic consumption was tested simultaneously with other determinants. Therefore, we provided an improved estimate of the impact of resistance compared to previous studies based on univarate analysis.

Reference
Masiero G., Filippini M., Ferech M., Goossens H. for the ESAC Project Group. *Determinants of outpatient antibiotic consumption in Europe: bacterial resistance and drug prescribers*, Working paper, University of Lugano, 2007.

6.4 Nursing home subproject

The project is led by Pawel Grzesiowski (Poland) and the ESAC MT liaison person is Carl Suetens (Belgium).
Contributors: Maria Luisa Moro (IT), Bea Jans (BE), Peter Davey (UK)

EUROPEAN SURVEILLANCE OF ANTIBIOTIC CONSUMPTION IN NURSING HOMES ACROSS EUROPE

<u>Introduction</u>

Optimizing the use of antibiotics in the nursing home population is an important priority of quality of care. In the last 10 years many studies in the US, Canada and selected European countries were undertaken in order to describe antibiotic use in NHs. It is already clear, that an antibiotic prescribing policy similar to the one recommended for acute care facilities should be developed. Guidelines for the clinical diagnosis of specific infections commonly found in long-term care facilities are also necessary.
In order to better understand the antimicrobial utilization and its indications in NHs across EU, the ESAC-2 Project carried out pilot subproject in close collaboration with the nursing home workpackage 7 of the IPSE Project on infection control (WP Leader Maria Luisa Moro, Agenzia Sanitaria Regionale, Emilia-Romagna, IT).

<u>Objectives and methods</u>

The objectives of the subproject were to identify mechanisms that regulate antibiotic use in nursing homes across Europe (feasibility phase), to assess the availability of AB use data at the nursing home level and to test a methodology to compare antibiotic use in several NHs in selected countries (Point Prevalence Survey pilot pretest).

Phase I: Identification of NH types and feasibility study

The first questionnaire has been addressed to the national contact points and had following objectives:

- to establish an inventory of different types of NH and characteristics in the EU member states;
- to assess availability list of institutions at the national or sub-national level to draw random sample, AB use data at national/regional level and to assess the assignment of antibiotic use data in nursing homes to either ambulatory care data or hospital care data;
- to describe mechanisms of antibiotic prescribing, sale and delivery in NHs.

The parts of the questionnaire aimed for identifying the different NH types and the availability of institution lists were identical for ESAC and IPSE projects.

Phase II: Data collection at nursing home level – pilot point prevalence survey (PPS)

As a function of the results of the first questionnaire, a pilot PPS survey was designed and tested in a limited number of nursing homes. The second questionnaire has been sent to 4 countries (Belgium, Scotland, Poland and Lithuania).
The objectives of this part of the project were to test the feasibility to perform a large scale PPS in a later phase and to evaluate the capacity of the PPS methodology to provide an answer to following questions:

- detailed description of mechanisms of AB prescribing, sale and delivery at the nursing home level;
- estimation and comparison patterns of AB use between selected countries and NH types across the EU;
- identification of institutional determinants of AB use in nursing homes

<u>Results</u>

Identification of NH types and feasibility study

Participation to the country survey

In collaboration with the IPSE workpackage 7 (WP leader Maria Luisa Moro, IT) on nursing homes, 33 survey questionnaires including questions on nursing home characteristics and antibiotic use was sent to the national contact points in June 2006. Parts of these results are common for the IPSE and ESAC subprojects. Non respondents were contacted several times, by e-mail, to increase the response rate. 26 (78.8%) questionnaires were returned.

Table 6.4.1 European countries answering to the survey

Austria	Latvia
Belgium	Lithuania
Bulgaria	Luxembourg
Cekia	Netherlands
Croatia	Norway
Denmark	Portugal
England	Republic of Ireland
Estonia	Scotland
Finland	Slovak republic
France	Spain
Germany	Sweden
Hungary	Switzerland
Italy	Turkey

Long-term care organisation in different countries

National and regional programmes

A plan/policy, defining the services to be provided, the population eligible, and the sources for funding, for long-term care (LTC) was defined in 16 European countries (48,5% of the 33 countries; 61,5% of the 26 respondents1). Four countries (Croatia, Denmark, Sweden and Turkey) claimed not to have a national programme, but to have implemented regional ones. In Austria the federal government is not responsible for these health care institutions, while federal province (Lander) are in charge and they have their own local programmes.

Several national LTC programmes only started recently (after the year 2000). The LTC programme includes all age classes in fifteen countries (in France, LTC services are provided to older than 60 years of age only). The HC programme includes all age classes in eleven countries (in Slovak Republic, HC services are provided to older than 65 years of age only).

Due to the lack of national or regional programmes, 9/26 countries provided very incomplete answers to the questionnaire.

Long-term care information systems

Sixteen countries claimed to have data available regarding the number and characteristics of LTC facilities (76,2% of the 21 respondents2). Of those, fourteen declared to have a routine national information system in place, while one (Sweden) declared to collect data through ad hoc surveys and another one (France) did not specify if data available were obtained through a routine information system or ad hoc surveys. Two countries (Denmark and Hungary) declared that data were not available, but a routine information system was in place at local and national level, respectively.

Routine information systems included in most of the cases information related to the type of facility, the ownership, number of beds, and number of employed staff (Table 6.4.2).

Table 6.4.2. Type of data available in routine information systems

Denomination	15
Address	17
Type of facility	17
Ownership	16
N° of beds	16
Average LOS	10
Mean occupancy %	13
Employed staff	15
Resident characteristics	13

[1] data for Finland were missing

[2] data for Croatia, Estonia, Finland, Luxembourg, Spain, Switzerland were missing

Few countries claimed to use specific scales to take into account the need of the residents. The Katz scale, or an adaptation of it, was used in Belgium, and in Portugal. All the other countries used different scales (Table 6.4.3).

Table 6.4.3. Systems used to classify residents according to their conditions and needs

Country	Long term care	Home care
Belgium	An adaptation of the Katz-scale is used to classify the care need in 5 categories (O, A, B, C, CD-category) which determine the financial intervention (fixed rate) provided by the national insurance system	
France	AGGIR score	Karnofsky score
Germany	Pflegestufe I-III	Pflegestufe I-III
Lithuania	classification of need	classification of need
Netherlands	not used yet, will most probably start in 2008	
Norway	You get information on most aspect of care needs, but reports are available at local level and not easy to get hold on a national level	Reports are available at local level and not easy to get hold on a national level
Portugal	KATZ Index; Mini Mental State	
Republic of Ireland	Long stay activity statistics collated nationally 31/12/05 for all older person services. Residential Public + Private submission to the Department of Health	
Wales	categorized as elderly nursing/dementia, residential or nursing	Broadly categorized as to care requirements

Type of long-term care residential facilities

Long-term care facilities in different European countries are called in different ways, accommodate different type of residents (Table 6.4.4) and even when the apparently same type of facilities are selected (nursing homes) the proportions of residents for each category is highly variable.

Table 6.4.4. Type of long.term care facilities and type of residents

Country	Type of long-term care facilities	Rehabilitation	Custodial/supportiv e care	Mental disorders	Dependency	Medical/nursing care	Dementia
		(% of residents)					
Belgium	Maisons de repos et de soins					100	
	Maison de repos		100				
Czeck Republic	Nursing home	20	30	10	-	30	10
	Residential homes	-	80	.	-	20	-
	Psychogeriatric - mental health	-	20	80	-	-	-
Denmark	Nursing homes	No	No	No	No	Yes	Yes
	Home care within nursing homes	No	Yes	No	No	Yes	No
	Residential homes / "Communes"	No	Yes	No	No	No	No
	Rehabilitation	100	-	-	-	-	-
	Terminal care (hospice)	No	Yes	No	No	Yes	No
England	Care home with nursing	-	49	7	1	18	25
	Care home - non medical	-	47	15	-	6	32
	Care home only	-	50	8	1	11	30

France	Unités de soins de longue durée (ULSD) - long term care units Etablissement d'hébergement pour PA dépendante (EHPAD) - nursing homes Maison de retraite - residential homes	Yes Yes No	No No Yes	No No No	No No No	Yes Yes Yes	No No No
Germany	Nursing + residential Home care	- -	38 56	- -	- -	62 44	- -
Hungary	Nursing homes Residential homes						
Italy	Nursing homes Residential homes	10 2	15 50	- -	- -	70 40	5 8
Latvia	Long-term social care and social rehabilitation institutions	-	52	-	-	-	48
Lithuania	Country nursing homes	No	Yes	Yes	No	Yes	Yes
Netherlands	Nursing homes Residential home	40 -	- -	- -	- -	60 100	- -
Norway	Nursing homes	11	-	-	-	75	14
Portugal	Social Institutions as Residential homes	No	Yes	No	No	Yes	No
Republic of Ireland	Private nursing home Public comm. hosp. elderly	No Yes	Yes No	No No	No No	Yes Yes	No Yes
Scotland	Care homes Care at home Independent hosp./specialist clinic Hospice care	Yes	Yes	Yes	Yes	Yes	Yes
Slovak rep.	LTC for elderly LTC for handicapped	- 55	75 -	- -	- -	25 45	- -
Wales	Nursing Residential	Yes No	Yes Yes	Yes No	No No	No No	Yes Yes

The reported percentages in Table 4 (if any) should be interpreted with caution as they may reflect theoretical situations at the national level on the one hand to situations in one or a limited number of facilities on the other.

Antibiotic use in nursing homes
Data on antimicrobial use were rarely available in EU member states (4/17 countries). DDDs were only available in one country (Norway). Three other countries reported the availability of relative frequencies of antimicrobials from survey data.

In the majority of countries, general practitioners (GPs) were responsible for the prescription of antibiotics in the LTC facilities. In 4 countries, specialists (infectious disease physician, specialized ambulatory care physicians…) also prescribed antimicrobials, either alone or sometimes in addition to the GPs.

Table 6.4.5. Availibility of antimicrobial use data and identity of AB prescribers

Information system exists	4 (2 nat)
Data available DDDs % antimicrobials	- 1 3
Who prescribes antibiotics in the LTC facilities ? no data GP (GP+)Specialist	- 3 13 4

In only 3/11 countries (27%) there was a limitation of the type of antibiotics that could be prescribed by the GP (or in some cases the specialist) in the nursing home (Table 6.4.6).

Table 6.4.6. Is there a limited list of antibiotics? (E.g. special procedure to prescribe vancomycin?)

	N of countries
Limited list of antibiotics	-
no data	6
all AB can be prescribed without limitation	8
yes	3

Table 6.4.7. How are antimicrobial drugs provided?

Antimicrobial drug provision	-
no data	4
From a single pharmacy	9
From several pharmacies	8
Wholesales	2

In approximately half of the countries antibiotics for the nursing home patients or residents were provided by several pharmacies (Table 6.4.7), indicating that it would be difficult if not impossible to organize a centralized routine surveillance of antimicrobial use at the nursing home level from a single data source.

Point prevalence survey pilot

Introduction and Methodology

Given the lack of available data on antibiotic use at the national or regional level in the EU member states, a protocol for a point prevalence survey at the nursing home level was developed and pretested. The protocol consisted of two questionnaires:

- *Institutional questionnaire*, including questions on characteristics of the LTC institution, denominator data (total number of residents on the day of the survey and subtotals stratified by NH resident classification, if available, see table 3), availability and type of an infection prevention expert, availability and specialty of a designated physician in the nursing home, type of antibiotic prescribers in the facility, existence of a restrictive list of antibiotics and of guidelines for antibiotic use.
- *Resident questionnaire*: for each resident receiving antibiotics at the day of the survey, a questionnaire had to be filled in including characteristics of the resident, the name of the antibiotic(s), start date, where it was prescribed, total dose per day, administration route, indications (code list) and names of isolated micro-organisms (code list) if a culture was taken.

The questionnaires were prepared as scanning forms using the Teleform software at the Scientific Institute of Public Health in Brussels (IPH).

For the purpose of the pilot PPS pretest, the forms together with an accompanying letter for the nursing home contact person and for the national coordinator were sent to 4 countries (Belgium, UK-Scotland, Poland, Lithuania). Data from Poland and Lithuania were not available yet at the time of the present analysis.

The forms of 12 institutions (11 Belgian and 1 Scottish) were received and scanned at the IPH. Data were collected between 26 March and 24 April 2007. The results presented below are only given to illustrate the type of information that can be drawn from the survey.

Characteristics of the institutions

The mean number of beds per institution was 97 beds (min 47, max 181). There were 5 private and 7 public institutions. At the day of the survey, 1119 of the 1166 beds were occupied. The mean occupancy rate was 98.3% (Scottish institution 95%). All institutions had a mean length of stay of more than 1 year.

While the Belgian institutions were facilities for residential care for the elderly, the Scottish institution was in fact a LTC department of a hospital. Furthermore, some of the Belgian institutions also had beds for day care, rehabilitation, palliative care, psychogeriatrics or short stay beds. On average, 43% of the Belgian

residents belonged to 2 most care-depended out of 5 case-mix categories (based on the Katz-scale, see tabel 3). In the Scottish institution there was no categorization of patients available.
Infection control expert(s) were only available in the Scottish institution (one IC physician and one IC coordinator). Designated physicians were present in 11 of the 12 nursing homes. In Belgian, these were coordinating physicians (general practitioners with additional training, defined by a law from 2004 and one specialist in gerontology), in Scotland it was a geriatric specialist who worked 48 hours per month in the department. The Belgian coordinating physicians worked on average 11 hours per month in the institution.
On average GP's prescribed 91.2% of the antibiotics in Belgium and 10% in the Scottish institution. Specialists (geriatrics, infectious diseases, internal medicine, surgeons, dermatologists etc.) accounted for 8.8% in Belgium and 90% (designated physician) in Scotland. Although the number of antibiotics that can be prescribed by GP's in Belgium is limited by the health insurance system (no reimbursment for reserve antimicrobials), only 2 institutions reported the existence of a limitative list of antibiotics, indicating that this question should be reformulated since it only detects limitative lists in addition to any existing national system. Eight institutions reported the availability of antibiotic use guidelines. In Scotland these guidelines were also available through the intranet of the institution. The use of the guidelines by the antibiotic prescribers was reported to be low in Belgium (score 2=sometimes on a 5-item scale in 71%) but high (score 4=very often) in the Scottish institution.

Resident questionnaire: antibiotic use
On the day of the point prevalence survey, 85 of the 1119 residents received antibiotics, giving a one-day estimate of overall antibiotic use prevalence of 7.6% (95% confidence interval 6.1%-9.3%). On average, a single institution had 7 out of 98 residents receiving an antibiotic on the survey day, yielding an individual prevalence estimate of 7.1% with a rather broad 95% confidence interval of 2.9% to 14.2%.
In total, 93 different molecules were used (1.1 molecule per resident), of which 82 were systemic antibiotics (Table 6.4.8) and 13 were for topical use.

Table 6.4.8. Systemic antibiotics used at the day of the point prevalence survey in 12 nursing homes, ESAC antibiotic use PPS pilot pretest, March-April 2007

Antibiotic	N BE	N UK-SC	Total
Nitrofurantoine	14	0	14 (17.3%)
Fosfomycine	11	0	11 (13.6%)
Ciprofloxacine	10	0	10 (12.3%)
Amoxi + clavul. acid	7	2	9 (11.1%)
Amoxi	7	0	7 (8.6%)
co-trimoxazole	5	0	5 (6.2%)
Cefuroxime (C2)	5	0	5 (6.2%)
Macrolides	5	0	5 (6.2%)
Moxifloxacine	3	0	3 (3.7%)
Fluconazole/miconazole	3	0	3 (3.7%)
Ofloxacine	2	0	2 (2.5%)
Metronidazole	1	1	2 (2.5%)
Tuberculostatics	2	0	2 (2.5%)
Norfloxacine	1	0	1 (1.2%)
Cefalexine (C1)	0	1	1 (1.2%)
BL-R SS peni (flucloxacilline)	1	0	1 (1.2%)

The route of administration was oral in 81.7%. In the Belgian institutions, 88.6% of the antibiotics were prescribed in the institution, 11.4% in the hospital. 21.4% of the residents receiving an antibiotic had been hospitalised in an acute care department in the 3 months prior to the PPS. Of 90 antibiotic prescriptions were the indication was given, 22% of the antibiotics were used for prophylactic purposes, 51% for empirical (non documented) therapy and 27% for documented therapy. Half of the antibiotics (50.5%) were prescribed for urinary tract infections and 31.9% for respiratory tract infections. A sample result was reported to be available for 37 infections, but 5 institutions did not report the micro-organism. Consistent with the predominant type of infections, enterobacteriaceae were the most frequently reported (Table 6.4.9). The mean duration of treatment at the time of the survey was 6 days (min 2, max 16 days).
Complementary analyses such as the analysis of the prescribed molecule according to the isolated micro-organism, the types of prophylactic AB use, the stratified analysis of antibiotic use according to the nursing home characteristics (risk factor analysis) etc. are not presented here because of the limited sample size and the pilot test setting.

Table 6.4.9. Micro-organisms isolated in 12 nursing homes, ESAC antibiotic use PPS pilot pretest, March-April 2007

	BE	SC	N (%)
Escherichia coli	8 (32%)	2 (66.7%)	10 (35.7%)
Klebsiella species	2 (8%)	0 (0%)	4 (7.1%)
Pseudomonas aeruginosa	3 (12%)	0 (0%)	3 (10.7%)
Providentia species	2 (8%)	0 (0%)	2 (7.1%)
Proteus mirabils	2 (8%)	0 (0%)	2 (7.1%)
S. aureus	2 (8%)	0 (0%)	2 (7.1%)
Clostridium difficile	0 (0%)	1 (33.3%)	1 (3.6%)
Enterococcus species	1 (4%)	0 (0%)	1 (3.6%)
Morganella species	1 (4%)	0 (0%)	1 (3.6%)
Mycobacterium tuberculosis	1 (4%)	0 (0%)	1 (3.6%)
Klebsiella oxytoca	1 (4%)	0 (0%)	1 (3.6%)

Conclusion

The PPS methodology proved to be a useful, non labour-intensive tool for the comparative analysis of antibiotic use in nursing homes. It allows comparing antibiotic use patterns and indications between countries as well as, to some extent, to assess its (institutional) determinants.

Some of the questions need to be reformulated or explained to avoid misinterpretation. Moreover, since GP's are unfamiliar with ATC coding, molecules were asked instead. But often commercial names were given by the person who fills the questionnaire at the NH level. In order to recode these names to ATC codes an international conversion table for antimicrobials (specialty-ATC code), wich is already partially available, will be needed to preform a point prevalence survey at the European level. An additional field should be added on the optical forms to make coding of the ATC code by the national coordination team possible before processing (scanning) the forms.

In summary, the methodology of the point prevalence survey of antibiotic use in nursing homes was tested successfully and mids some minor adaptations of the questionnaire, it is ready to be used for a large scale EU-wide PPS in nursing homes in ESAC-3.

7 DISSEMINATION OF RESULTS

7.1 Papers published in peer reviewed journals

List of papers published in peer reviewed journals

2007

- Coenen S, Ferech M, Haaijer-Ruskamp FM, Butler CC, Vander Stichele RH, Verheij TJM, Monnet DL, Little P, Goossens H and the ESAC Project Group. European Surveillance of Antimicrobial Consumption (ESAC): Quality indicators for outpatient antibiotic use in Europe. Qual Saf Health Care. In press.
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- Coenen S, Ferech M, Malhotra-Kumar S, Hendrickx E, Suetens C, Goossens H and the ESAC project group. European Surveillance of Antimicrobial Consumption (ESAC): quality indicators of outpatient antibiotic use [Abstract]. European Journal of Public Health 2006;16 (Suppl. 1):S79-80.
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7.2 Abstracts accepted for presentation

List of abstracts accepted for presentation:

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7.3 Newsletters

MEDFLASH Thema antibiotica (Theme antibiotics) Mei (May) 2004
http://www.riziv.fgov.be/care/nl/doctors/promotion-quality/feedbacks/feedback-antibiotics/pdf/medflash200405.pdf

MEDFLASH Thema antibiotica (Theme antibiotics) Januari (January) 2005
http://www.riziv.fgov.be/care/nl/doctors/promotion-quality/feedbacks/feedback-antibiotics/pdf/medflash200501.pdf

7.4 Website

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

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, 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.

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

Furthermore, a new section was created for the National Representatives. After the login, they had access to confidential documents and the interactive database.

The interactive ESAC database

The interactive ESAC database was introduced at the ESAC website and all data are publicly available to download from here. On behalf of the University of Antwerp, ESAC maintains this database to enhance public access to information about antibiotic use in Europe. Our goal is to keep this information timely and accurate.

This database contains the validated and comparable administrative outpatient data from 26 participating countries from 1997-2004 (2005 data will be made available in September 2007), which are classified according to ATC/DDD classification.

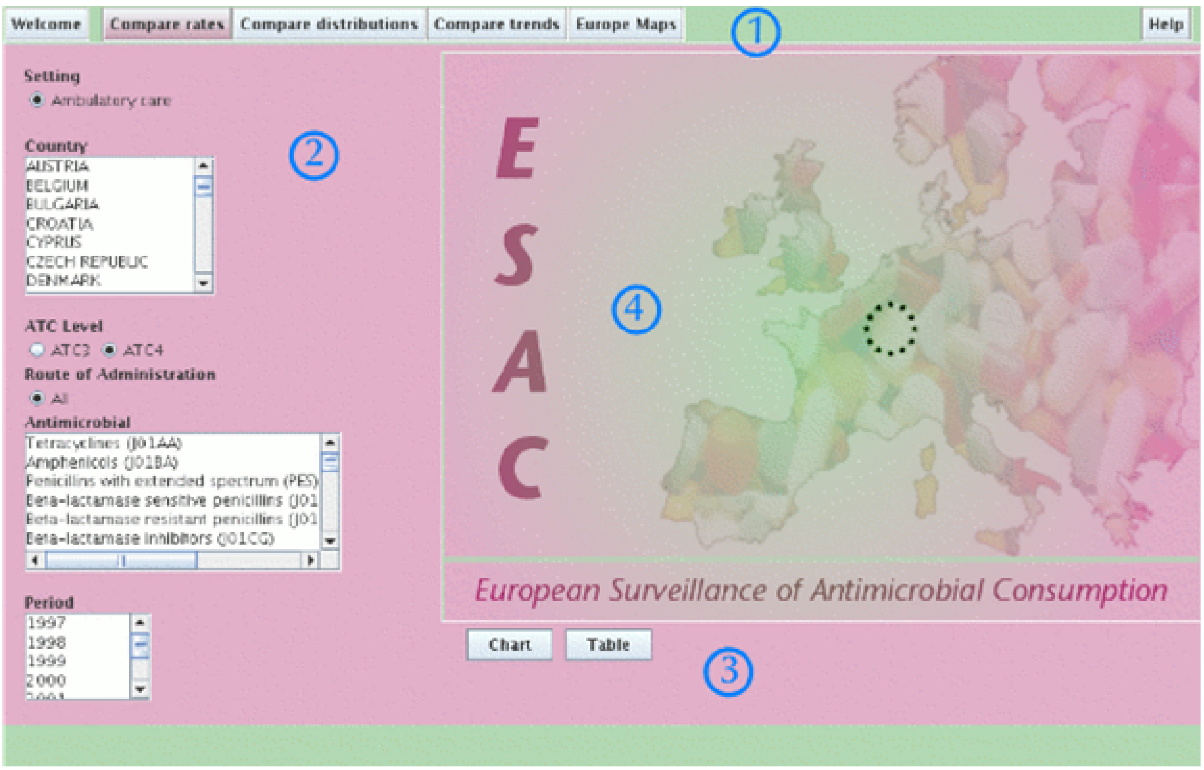
The ESAC interactive database has been developed to provide convenient access to the ESAC data on antibiotic use in Europe by means of charts, tables and maps. It allows you to obtain the data by the following 3 main parameters:

- The country where the antibiotics were utilised;
- The kind of antimicrobials that were utilised; and
- The time period in which the antibiotic were utilised.

How to use the ESAC interactive database?

Figure 7.1 presents the key features of the application:
1 *Menus*: Allow switching between different types of comparisons (see below).
2 *Parameter scroll menus:* Allow the selection of countries, antimicrobials and years.
3 *Output buttons*: Allow the selection of the output format (chart, table or map).
4 *Result area*: The chart, table or map will be drawn here.

Figure 7.1 Screenshot of the ESAC website



How to obtain data?

<u>Step 1: Selection of the type of comparison</u>

The ESAC interactive database provides four types of comparisons:
1. <u>Compare rates</u>: Allows comparing the use of one antimicrobial class in one year between six countries by means of a bar plot or a table.
2. <u>Compare distributions</u>: Allows comparing the relative proportion of the use of all subclasses within a defined antimicrobial class (at ATC-2 or ATC-3) in one year between four countries by means of a pie chart, a bar plot or a table.
3. <u>Compare trends</u>: Allows comparing (A) the use of different antimicrobial classes within one country over time or (B) the use of one antimicrobial class in all countries by means of a line chart or table.
4. <u>Europe maps</u>: Allows comparing the use of one antimicrobial class in one year between countries participating in ESAC by means of a map.

<u>Step 2: Selection of the parameters</u>

The four types of comparisons are based on the same three key parameters:
1. The country where the antibiotics were utilised;

All ESAC participating countries are listed. Depending of the query, the user can select one or more countries. Data for some countries and years are missing.

2. The kind of antimicrobials that were utilised; and
   Depending of the ATC level selection, a list of ATC-3 or ATC-4 antimicrobials is displayed. It is possible to choose one or multiple antibiotic classes following the selected query.

3. The time period in which the antibiotic were utilised.
   The user can select one or multiple years depending of the query. Data for some countries and years are missing.

Step 3: Choice of the output format

The available output formats are charts, tables or maps. The output is generated by clicking the output button.

Further comments:

Hospital setting:
For the hospital care setting (with a number of countries able to provide only sample data), the ESAC interactive database allows only the comparison of relative distributions ("Compare distribution"). In this case countries providing only a sample data can be selected are typed in italic. The user is recommended to consult "ESAC data collection methodology" prior to the data interpretation.

ATC level:
Data are available at ATC-3 and ATC-4 levels of aggregation within J01 group. When the ATC-3 level is selected, the list of ATC-3 subgroups will appear on the scroll menu below, while after selection of the ATC-4 level, the list of ATC-4 subgroups will appear on the scroll menu.
For the "comparison of distribution" query, selection of the ATC-3 level will show their relative distribution within J01 group in the selected country. When ATC-4 is selected, the user will be asked to choose one of ATC-3 groups, for which the distribution of ATC-4 subgroups will be shown.
The *route of administration* is currently not available. Nevertheless ESAC data have been collected at the level of the "route of administration" since 2004.

8 FINAL CONCLUSIONS

In 2001, the European Commission (Directorate-General SANCO – Health Monitoring Program) funded the European Surveillance of Antimicrobial Consumption (ESAC) project. A pilot project was established from 2001 to 2003 (referred to as ESAC-1). The aim of the project was to collect comparable and reliable data on antibiotic use in Europe in ambulatory and hospital care from publicly available sources, and to assess the time trends in human exposure to antibiotics. In this project a 'network of networks' approach was taken. A multidisciplinary management team based at the University of Antwerp, Belgium, established a network of dedicated national representatives (NR), collaborating on a voluntary basis. In each country, the national representative was to contact potential data providers. Data collection was 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 (WHO). The original data collection was limited to the ATC class J01. Consumption was expressed in defined daily doses (DDD).

In 2004, the European Commission (Directorate-General SANCO – Health Monitoring Program) decided to continue funding ESAC from 2004 to 2007 (referred to as ESAC-2). The main objective of the second phase of the ESAC project was to consolidate the continuous collection of comprehensive antibiotic consumption data. In addition, use data (i) on antibiotics not included in ATC class J01 (combinations for eradication of *Helicobacter pylori*, oral metronidazole, ornidazol, vancomycin, and colistin), (ii) at the package level, and (iii) of antimycotics for systemic use, were collected. In-depth consumption data for ambulatory care, hospital care, and nursing homes were investigated, and a pharmaco-economic evaluation was carried out. Finally, a set of twelve quality indicators for outpatient antibiotic use, which can be derived from ESAC data, were developed.

Six years after the ESAC launch meeting in Brussels in November 2001, the ESAC project represents the first and only set of publicly available standardised and validated supranational data on antibiotic use in Europe.

The ESAC 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.

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. These indicator values allow individual countries to position themselves and to define their own benchmark, based on the epidemiology of infectious diseases and national guidelines.

These 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 should study and implement effective professional and public strategies to encourage appropriate prescribing of antibiotics.

The hospital care subproject showed that interpretation of longitudinal data about antibiotic use is facilitated by presentation of changes in DDD without adjustment for clinical activity in addition to adjusted data. Antibiotic use is influenced by number of admissions and by length of stay, consequently adjustment for clinical activity should be done with both admissions and occupied bed days. Point prevalence surveys provide important detail about management of individual patients and should be used to produce quality indicators. Reduction in unnecessary prolongation of surgical antibiotic prophylaxis is a key target for quality improvement.

The ambulatory care subproject showed that more detailed data linking antibiotic use to the patients' age and gender, the prescribers' speciality and the indication. Such data are mandatory to be used to validate further indicators developed in ESAC-2 to assess the quality of antibiotic use in ambulatory care. However, indicators that are equally relevant across countries in Europe, i.e. corrected for case-mix, resistance patterns and other contextual factors should be developed

The nursing home subproject showed that point prevalence survey methodology proved to be a useful, non labour-intensive tool for the comparative analysis of antibiotic use in nursing homes. It allows comparing antibiotic use patterns and indications between countries as well as, to some extent, to assess its (institutional) determinants. Mids some minor adaptations of the questionnaire, it is ready to be used for a large scale EU-wide PPS in nursing homes.

The economic subproject showed that antibiotic consumption is characterized by multiple market imperfections. The investigation of determinants of antibiotic use may represent an important contribution for discussion of effective government interventions to induce efficient use of drugs. We have shown that differences in outpatient antibiotic use across countries can hardly be explained by epidemiological, demographic and cultural factors only. Supply-side factors such as the density of doctors and economic incentives attached to the remuneration system may contribute to the explanation of variations in antibiotic consumption. Econometric estimations indicate that the per capita income, the proportion of children and the elderly, and cultural attitudes in southern and eastern countries induce higher levels of antibiotic use. On the other hand, higher levels of education reduces consumption. Increasing antibiotic use is also associated with higher density of doctors and fee-for-service and salary remuneration.

A wealth of scientific papers was published in top peer-reviewed journals, such as the Lancet and the Journal of Antimicrobial Chemotherapy. Scientific papers will continue to be published, focusing on the development of health indicators, the linkage of consumption to antibiotic resistance, consumption patterns in specific groups in ambulatory care and hospitals, and the pharmaco-economic evaluation of antibiotic consumption.