Antibiotic Use in Europe

Herman Goossens
Project Leader ESAC
ESAC Project

Mission Statement

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

ESAC I (2001-2004)
Agreement Number – SI2.325736
Duration:
from 01/11/2001 to 31/01/2004

ESAC II (2004-2007)
Agreement Number – 2003211
Duration:
from 01/02/2004 to 31/01/2007

ESAC III (2007 – 2010) ?
ESAC Participating countries in 2007

34 participating countries

All 25 EU countries

4 applicant countries
Bulgaria, Romania
Turkey, Croatia

5 Others
Norway, Iceland
Switzerland
Russia, Israel
Data Collection Methodology of ESAC

A quest for the greatest common denominator in data collection: between desirable and feasible

1. Country data (not county data)
2. Aggregated at the substance level (ATC-5)
3. Years: ongoing starting 1997
4. Separated for Ambulatory and Hospital Care
5. Quarterly for AC and Yearly for HC
6. Classified according to ATC classification (WHO)
7. Expressed in Defined Daily Doses


www.ua.ac.be/ESAC
The Defined Daily Dose (DDD) is the assumed average maintenance dose per day for a drug used for its main indication in adults. The DDD is a unit of measurement and does not necessarily reflect the recommended or prescribed daily dose.

Packages of different brands with the same active ingredient but with different strength and pack size can be aggregated.
The **Number of Defined Daily Doses per 1000 inhabitants per day (DID)**

is a method to express exposure to a given drug or a given class of drugs for a given area and a given period, independent of the population size of the catchment area.
J Antiinfectives for systemic use (1st level, anatomical main group)
J01 Antibacterials for systemic use (2nd level, therapeutic subgroup)
J01C Beta-lactam antibacterials, penicillins (3rd level, pharmacological subgroup)
J01C A Penicillins with extended spectrum (4th level, chemical subgroup)
J01CA04 Amoxicillin (5th level, chemical substance)

DDD = 1000mg
Sources of Antibiotic Use Data

**Sales (distribution) data**

based on reports from the distribution chain: from companies, wholesalers or pharmacies

**Reimbursement data**

collected from the third party payer: from insurance companies or health care services
Outpatient Antibiotic Use
Total Outpatient Antibiotic Use in 25 European Countries in 2003

TOTAL ANTIBIOTIC USE IN AC
- Others
- Sulfonamides (J01E)
- Quinolones (J01M)
- Macrolides (J01F)
- Tetracyclines (J01A)
- Cephalosporins (J01D)
- Penicillins (J01C)

Total use in DDD/1000 inh./day
Outpatient Use of Penicillins in 25 European Countries in 2003

DDD / 1000 inhabitants/day

- Green = Beta-lactamase sensitive penicillins (narrow spectrum penicillins J01CE),
- Yellow = Penicillins with extended spectrum (broad spectrum pen. J01CA),
- Red = Combinations of penicillins, incl. beta-lactamase inhibitors (J01CR),
- Blue = Beta-lactamase resistant penicillins (J01CF)
Outpatient Use of Cephalosporins in 25 European Countries in 2003

- First-generation (J01DB) cephalosporin use.
- Second-generation (J01DC) cephalosporin use.
- Third-generation (J01 DD) cephalosporin use.

The use of fourth-generation cephalosporins is marginal.
Outpatient Use of MLS in 25 European Countries in 2003

Green = short-acting macrolide, Yellow = intermediate-acting macrolide, including telithromycin, Orange = long-acting macrolide, Red = lincosamide, Blue = streptogramin use.
Outpatient Use of Quinolones in 25 European Countries in 2003

Total national quinolone use according to the ATC/DDD 2003 version

- Green = First generation
- Yellow = Second generation
- Red = Third generation

Graph showing the use of quinolones in 25 European countries, with a legend indicating the generations of quinolones used.
Total Outpatient Antibiotic Use in 25 European Countries in 2004
Trends of Outpatient Antibiotic Consumption in 15 Countries July 2002-June 2005

<table>
<thead>
<tr>
<th>Year</th>
<th>2003</th>
<th>2004</th>
<th>2005</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total use</strong></td>
<td>426.15</td>
<td>407.66</td>
<td>426.28</td>
</tr>
</tbody>
</table>

**TOTAL ANTIBIOTIC USE IN AC**
- Others (J01E)
- Sulfonamides (J01E)
- Quinolones (J01M)
- Macrolides (J01F)
- Tetracyclines (J01A)
- Cephalosporins (J01D)
- Penicillins (J01C)

Graph showing trends over three years with countries listed horizontally.
Influenza morbidity rates

www.EISS.org
Seasonality of use, 2003-2005

DDD per 1000 inh. per day

Austria
Belgium
Croatia
Czech Rep.
Denmark
Estonia
Finland
Hungary
Iceland
Ireland
Netherlands
Slovakia
Slovenia
Spain
Sweden
Outpatient Antibiotic Use
Regional Variation
Regional Variation of Outpatient Antibiotic Use in Italy

Total use in DID

Compania
Sicilia
Calabria
Puglia
Abruzzo
Basilicata
Molise
Umbria
Lazio
Italy
Marche
Toscana
Emilia Romagna
Lombardia
Piemonte
Liguria
Sardegna
Veneto
Valle d’Aosta
Prov Aut Trento
Friuli Venezia Giulia
Prov Aut Bolzano

J01X
J01R
J01M
J01G
J01F
J01E
J01D
J01C
J01B
J01A
Caveats of DDDs...
Calculation scheme

Antibiotic use in DDDs

- DDD per prescription
- Number of prescriptions

- DDD per unit of administration
- Number of units administered daily

- Treatment duration
- Daily dose
## Amoxicillin

<table>
<thead>
<tr>
<th>Country</th>
<th>France</th>
<th>Italy</th>
<th>Spain</th>
<th>UK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescr. per 1000 inh. per day</td>
<td>0.33</td>
<td>0.19</td>
<td>0.52</td>
<td>0.50</td>
</tr>
<tr>
<td>Prescriptions (% of total)</td>
<td>18.6%</td>
<td>9.3%</td>
<td>17.6%</td>
<td>28.5%</td>
</tr>
<tr>
<td>DDD per day</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment in days</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total DDD per course</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

18.4% of all prescriptions
<table>
<thead>
<tr>
<th>Country</th>
<th>France</th>
<th>Italy</th>
<th>Spain</th>
<th>UK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescr. per 1000 inh. per day</td>
<td>0.33</td>
<td>0.19</td>
<td>0.52</td>
<td>0.50</td>
</tr>
<tr>
<td>Prescriptions (% of total)</td>
<td>18.6%</td>
<td>9.3%</td>
<td>17.6%</td>
<td>28.5%</td>
</tr>
<tr>
<td>DDD per day</td>
<td>1.65</td>
<td>1.90</td>
<td>1.61</td>
<td>0.93</td>
</tr>
<tr>
<td>Treatment in days</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total DDD per course</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Amoxicillin J01CA04

<table>
<thead>
<tr>
<th>Country</th>
<th>France</th>
<th>Italy</th>
<th>Spain</th>
<th>UK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescr. per 1000 inh. per day</td>
<td>0.33</td>
<td>0.19</td>
<td>0.52</td>
<td>0.50</td>
</tr>
<tr>
<td>Prescriptions (% of total)</td>
<td>18.6%</td>
<td>9.3%</td>
<td>17.6%</td>
<td>28.5%</td>
</tr>
<tr>
<td>DDD per day</td>
<td>1.65</td>
<td>1.90</td>
<td>1.61</td>
<td>0.93</td>
</tr>
<tr>
<td>Treatment in days</td>
<td>7.00</td>
<td>7.19</td>
<td>8.89</td>
<td>6.69</td>
</tr>
<tr>
<td>Total DDD per course</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Country</td>
<td>France</td>
<td>Italy</td>
<td>Spain</td>
<td>UK</td>
</tr>
<tr>
<td>-------------------------</td>
<td>--------</td>
<td>-------</td>
<td>-------</td>
<td>-----</td>
</tr>
<tr>
<td>Prescr. per 1000 inh. per day</td>
<td>0.33</td>
<td>0.19</td>
<td>0.52</td>
<td>0.50</td>
</tr>
<tr>
<td>Prescriptions (% of total)</td>
<td>18.6%</td>
<td>9.3%</td>
<td>17.6%</td>
<td>28.5%</td>
</tr>
<tr>
<td>DDD per day</td>
<td>1.65</td>
<td>1.90</td>
<td>1.61</td>
<td>0.93</td>
</tr>
<tr>
<td>Treatment in days</td>
<td>7.00</td>
<td>7.19</td>
<td>8.89</td>
<td>6.69</td>
</tr>
<tr>
<td>Total DDD per course</td>
<td>11.49</td>
<td>13.52</td>
<td>14.29</td>
<td>6.18</td>
</tr>
<tr>
<td>Country</td>
<td>France</td>
<td>Italy</td>
<td>Spain</td>
<td>UK</td>
</tr>
<tr>
<td>-------------------------</td>
<td>--------</td>
<td>-------</td>
<td>-------</td>
<td>-----</td>
</tr>
<tr>
<td>Prescr. per 1000 inh. per day</td>
<td>0.17</td>
<td>0.31</td>
<td>0.68</td>
<td>0.09</td>
</tr>
<tr>
<td>Prescriptions (% of total)</td>
<td>9.2%</td>
<td>15.4%</td>
<td>24.0%</td>
<td>5.3%</td>
</tr>
<tr>
<td>DDD per day</td>
<td>1.09</td>
<td>1.54</td>
<td>1.50</td>
<td>0.85</td>
</tr>
<tr>
<td>Treatment in days</td>
<td>7.80</td>
<td>6.99</td>
<td>9.23</td>
<td>7.75</td>
</tr>
<tr>
<td>Total DDD per course</td>
<td>8.78</td>
<td>10.62</td>
<td>13.26</td>
<td>6.56</td>
</tr>
<tr>
<td>Country</td>
<td>France</td>
<td>Italy</td>
<td>Spain</td>
<td>UK</td>
</tr>
<tr>
<td>--------------------------</td>
<td>--------</td>
<td>-------</td>
<td>-------</td>
<td>-----</td>
</tr>
<tr>
<td>Prescr. per 1000 inh. per day</td>
<td>0.12</td>
<td>0.18</td>
<td>0.21</td>
<td>0.05</td>
</tr>
<tr>
<td>Prescriptions (% of total)</td>
<td>6.7%</td>
<td>9.2%</td>
<td>7.3%</td>
<td>2.7%</td>
</tr>
<tr>
<td>DDD per day</td>
<td>1.04</td>
<td>1.40</td>
<td>1.32</td>
<td>1.31</td>
</tr>
<tr>
<td>Treatment in days</td>
<td>7.73</td>
<td>8.56</td>
<td>8.28</td>
<td>10.78</td>
</tr>
<tr>
<td>Total DDD per course</td>
<td>8.04</td>
<td>11.76</td>
<td>11.01</td>
<td>12.25</td>
</tr>
</tbody>
</table>
Caveats of Data Sources...
Sales vs. Reimbursement Data

Total AC Consumption 2001

Greece
Spain

Total use in DID

0 5 10 15 20 25 30 35

GR ES
Sales vs. Reimbursement Data

10% overestimated due to: Parallel exports
Private hospitals in AC

30% underestimated due to: OTC sales exclusion
Sales vs. Reimbursement Data

Total AC Consumption 2001

Greece
Spain
Assessment of OTC sales in Spain

Ferech M, Campos J et al.
Analysis of Sales Data (SD) and Reimbursement Data (RD) as a Tool to Assess OTC Antibiotic Dispensing. 45th ICAAC, Washington 2005
Assessment of variability in the number of routinely used antibiotics to treat outpatients using the DU90% method
Antibiotic therapeutic arsenal in 2003
Correlation between countries – DU 99%

Cluster Dendrogram

A hierarchical cluster analysis

dist.d99
hclust(*, "complete")
Correlation between countries – DU 90%

Dissimilarity of antibiotics in DU90% (index)

0 0.1 0.2 0.3

Denmark

Finland
Norway
Sweden

Ireland
UK

France
Italy
Bulgaria
US
Austria
Germany

Israel

Estonia
Latvia
Netherlands

Portugal
Spain
Belgium

Luxembourg
Iceland
Slovenia

Croatia

Czech Rep.
Slovakia

Hungary
Poland

Greece
Outpatient Antibiotic Use

DDD versus Packages
Co-amoxiclav use in Croatia 2001-2002

<table>
<thead>
<tr>
<th>Packages/1000inh./day</th>
<th>500+125mg TID</th>
<th>875+125mg BID</th>
</tr>
</thead>
<tbody>
<tr>
<td>DDD/1000inh./day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>6.21</td>
<td>9.03</td>
</tr>
<tr>
<td>II</td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DDD/pack</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

DDD/pack
Antibiotic Use in Packages/1000 Inhabitants/day, 1997-2005, Januari - December

- Sulphonamides (J01E)
- Tetracyclines (J01A)
- Quinolones (J01M)
- Macrolides (J01F)
- Cephalosporins (J01D)
- Penicillins (J01C)

- Others

Percentage changes:
- +0.2% 0% 1997
- -3.4% 0% 1998
- -5.1% 0% 1999
- -9.3% -4.0% 2000
- -7.1% 0% 2001
- -13.4% -2.9% 2002
- -4.0% 0% 2003
- +2.9% 0% 2004
- +2.9% 0% 2005

- Sulphonamides - J01E
- Tetracyclines - J01A
- Quinolones - J01M
- Macrolides - J01F
- Cephalosporins - J01D
- Penicillins - J01C

Others

-0.7% -2.8% -7.0% -7.3% -7.0% -9.3% -7.0% -3.8%
Antibiotic Use in Packages/1000 Inwoners/Day, per Province, 2000 vs 2005

- Sulphonamides - J01E
- Tetracyclines - J01A
- Quinolones - J01M
- Macrolides - J01F
- Cephalosporins - J01D
- Penicillins - J01C

Packs per 1000 inhabitants per day
Proportionel Use of the Penicillins, in Packages/1000 Inhabitants/Day, 1997 - 2005

- Others
- Amoxiclav - J01CR02
- Amoxi - J01CA04
Outpatient Antibiotic Use:
as an indicator of appropriate and inappropriate antibiotic prescribing
Seasonal Variation of Outpatient Antibiotic Use in Europe

![Graph showing seasonal variation of outpatient antibiotic use in Europe. The graph displays data for various countries over the years 1997 to 2003, with the y-axis representing DDD per 1000 inhabitants per day and the x-axis representing the years. Each country is represented by a different line color or marker.

Key:
- Austria
- Belgium
- Croatia
- Czech Rep.
- Denmark
- Estonia
- Finland
- Greece
- Germany
- Hungary
- Iceland
- Ireland
- Italy
- Netherlands
- Poland
- Portugal
- Slovakia
- Slovenia
- Spain
- Sweden
- UK]
Seasonal Variation of Outpatient Tetracyclines Use

![Seasonal Variation of Outpatient Tetracyclines Use](image-url)

- Belgium
- Denmark
- Finland
- Greece
- Ireland
- Iceland
- Netherlands
- Portugal
- Sweden
- Slovenia
- UK
Seasonal Variation of Outpatient Ciprofloxacin Use with Quarterly Data for 1997-2003.
Seasonal Variation of Outpatient Ofloxacin Use with Quarterly Data for 1997-2003.
Outpatient Antibiotic Use:

*link with resistance*
<table>
<thead>
<tr>
<th>Organism year of isolation [source of information]</th>
<th>Antibiotic resistance</th>
<th>Antibiotic use - ATC group (year of data)</th>
<th>No. of countries</th>
<th>Spearman correlation (r) (confidence interval)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>S. pneumoniae 2001 [7]</strong></td>
<td><em>Penicillin</em></td>
<td><em>Penicillins - J01C (2000)</em></td>
<td>19</td>
<td>0.84 (0.62-0.94)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

**Graph:**
- X-axis: Consumption of penicillins (J01C) in DID, AC 2000
- Y-axis: Penicillin resistant S. pneumoniae (%)
- Country codes: UK, DK, SE, NL, AT, DE, CZ, HU, HR, SI, IT, FR, ES, FI

**Legend:**
- Penicillin resistant S. pneumoniae (%) vs Consumption of penicillins (J01C) in DID, AC 2000

**Note:**
- Goossens et al, Lancet, February 2005
<table>
<thead>
<tr>
<th>Organism</th>
<th>year of isolation [source of information]</th>
<th>Antibiotic resistance</th>
<th>Antibiotic use - ATC group (year of data)</th>
<th>No. of countries</th>
<th>Spearman correlation (r) (confidence interval)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>S. pneumoniae</strong></td>
<td>1999/2000 [8]</td>
<td>Erythromycin</td>
<td>Macrolides - J01FA (1998)</td>
<td>16</td>
<td>0.83 (0.67-0.94)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Consumption of macrolides (J01FA) in DID, AC 1998

Goossens et al, Lancet, February 2005
<table>
<thead>
<tr>
<th>Organism year of isolation [source of information]</th>
<th>Antibiotic resistance</th>
<th>Antibiotic use - ATC group (year of data)</th>
<th>No. of countries</th>
<th>Spearman correlation (r) (confidence interval)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>S. pyogenes</em> 1999/2000 [8]</td>
<td><em>Erythromycin</em></td>
<td><em>Macrolides - J01FA and lincosamides - J01FF (1998)</em></td>
<td>21</td>
<td>0.65 (0.25-0.86)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Consumption of MLS (J01F) in DID, AC 1998

Goossens et al, Lancet, February 2005
Resistence of *S. pneumoniae* in Belgium

National Reference Centre of *S. pneumoniae* (KULeuven)
Resistence of S. pyogenes in Belgium

National Reference Cente of S. pyogenes (UA)
Semi-quantitative Analysis: Temporal Changes in Proportion of Macrolide-resistant Oral Streptococci

Qualitative Analysis: Temporal Changes in Proportion of Macrolide-resistant Genes in Oral strept.

Quality indicators of outpatient antibiotic use
Background

- Increasing development and use of indicators to measure the quality of health care by health care professionals and policy makers.

- Antibiotic resistance as a major European and global public health problem, antibiotic consumption as the main driver for resistance, and the largest volumes of antibiotic prescriptions in ambulatory care. *Lancet* 2005;365:579-87

Objectives

To develop valid antibiotic prescribing quality indicators* for ambulatory care, which can be derived from ESAC data.

* APQI = explicitly defined measurable items of antibiotic prescribing giving a possible indication of the level of prescribing quality focussing on different aspects of prescribing quality, and relevant for clinical practice
Methods

Developing a proposed set of quality indicators

- ESF workshop with 27 experts (15 countries) from
  - GRIN/ESPRIT (ESCMID Study Group on Primary Care Topics)
  - Euro DURG (European Drug Utilisation Research Group)
  - WHO (World Health Organisation)
  - ESAC
  - Other experts
- Discussion of APQI development (plenary sessions/small workgroups)
- From the perspective of professionals and policy makers
- Based on 1997-2003 ESAC data
- Set of proposed indicators
Methods

Assessing a proposed set of quality indicators

- All participants to score the relevance to 4 dimensions:
  1. reducing antimicrobial resistance,
  2. patient health benefit,
  3. cost-effectiveness, and
  4. public health policy

- Scale: 1-9 (= completely disagree - agree)

- Analysis: UCLA-RAND appropriateness method and taking into account the participants’ comments

- Proposed indicator = relevant if median score not within 1-6 interval and if number of scores within 1-3 interval < 1/3 of panel
Methods

Defining a final set of quality indicators
- From relevant indicators with overlapping info ➔ highest scoring one

Applying a final set of quality indicators
- Indicator values of final set updated with 2004 ESAC data
- ESAC countries categorised into five groups,
  i.e. four group ~ four quartiles of the distribution of the indicator values
  one group for ESAC countries for which no data were available
Results

A set of 24 proposed indicators

Consumption of ... expressed in DDD per 1000 inhabitants per day (DID)

1 [J01_DID] = antibacterials for systemic use
2 [J01A_DID] = tetracyclines
3 [J01C_DID] = penicillins
4 [J01D_DID] = cephalosporins
5 [J01E_DID] = sulfonamides and trimethoprim
6 [J01F_DID] = macrolides, lincosamides and streptogramins
7 [J01M_DID] = quinolones
Results

Consumption of ... expressed as percentage of the total consumption (J01)

8  [J01A_ %] = tetracyclines
9  [J01C_ %] = penicillins
10 [J01D_ %] = cephalosporins
11 [J01E_ %] = sulfonamides and trimethoprim
12 [J01F_ %] = macrolides, lincosamides and streptogramins
13 [J01M_ %] = quinolones
14 [J01CE_ %] = β-lactamase sensitive penicillins
15 [J01CR_ %] = combinations of penicillins
16 [J01DD+DE_ %] = 3\textsuperscript{rd} and 4\textsuperscript{th} generation of cephalosporins
18 [J01MA_ %] = fluoroquinolones
Results

Seasonal variation of ... consumption
19 [J01_SV] = antibacterials for systemic use
20 [J01M_SV] = quinolone
21 [J01M_SVDID] = quinolone * use in DID

17 [J01_B/N] = Ratio of the consumption of broad to that of narrow spectrum penicillins, cephalosporins and macrolides
{J01(CR+DC+DD+(F-FA01))/ J01(CE+DB+FA01) }

22 [J01_TT] = Index of longitudinal trends of antibiotic consumption

Structural indicators
23 [J01_DU99] = No of substances representing 99% of J01 use in DID
24 [J01_NR] = No of items in the national register of available J01
Results

General format of the indicators

- Indicator number: Title [Label]
- Definition
- Public health objective
- Calculation formula:
- Benchmark and recommended action
- Limitations
- ESAC boxplot
Results

A final set of quality indicators

- Experts from 11 countries scored (♂/♀: 16/6)
- Relevant indicators:
  - on all 4 dimensions: n=9.
  - on reducing resistance and public health policy: n=14.
- [J01MA_%] overlapped with and scored higher than [J01M_%]
- [J01MSV] overlapped with and scored higher than [J01MSVDID]
- Indicator values for the final set of 12 quality indicators for 28 countries in 2004 (box plots & maps)
Narrow spectrum penicillins (J01CE) in %

- 4th quartile
- 3rd quartile
- 2nd quartile
- 1st quartile

(n = 28)
Combinations of penicillins (J01CR) in %

- 4th quartile
- 3rd quartile
- 2nd quartile
- 1st quartile
(n = 28)

= other ESAC country
Fluoroquinolones (J01MA) in % of total

4th quartile
3rd quartile
2nd quartile
1st quartile
(n = 28)
Seasonal variation of antibiotic use in %
From a set of 24 proposed ESAC based quality indicators for outpatient antibiotic use in Europe a final set of 12 indicators seems to be relevant, i.e. have content and face validity, and is potentially applicable:

- [J01_DID]; [J01C_DID]; [J01D_DID]; [J01F_DID]; [J01M_DID]
- [J01CE_%]; [J01CR_%]; [J01DD+DE_%]; [J01MA_%];
- [J01_B/N]; [J01_SV]; [J01M_SV]

Link with indication? Concurrent and construct validity?

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

In line with the main objectives of antimicrobial surveillance at the European level, this subset can be used to describe antibiotic use in ambulatory care in order to assess the quality of antibiotic prescribing.
## ESAC II Subprojects

<table>
<thead>
<tr>
<th>AMBULATORY CARE</th>
<th>SEX AND AGE</th>
<th>PRESCRIBER</th>
<th>INDICATION</th>
<th>NURSING HOMES</th>
<th>HOSPITAL CARE</th>
<th>ECONOMICS/REGIONAL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Leader</strong></td>
<td></td>
<td></td>
<td></td>
<td>Pawel Grzesiowski (PL)</td>
<td>Peter Davey (UK)</td>
<td>Giuliano Masiero (CH)</td>
</tr>
<tr>
<td><strong>ESAC MT</strong></td>
<td></td>
<td></td>
<td></td>
<td>Sigvard Mölstad (SE)</td>
<td>Carl Suetens</td>
<td>Herman Goossens</td>
</tr>
<tr>
<td><strong>Core group</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Matus Ferech</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td></td>
<td></td>
<td></td>
<td>CZ DK EE FI GR NL NO PT SE SK UK</td>
<td>FI NO PL IL LT</td>
<td>AT CH DE DK IT UK</td>
</tr>
</tbody>
</table>

Participants: BE CZ DK ES FR IE IS LU NL NO RO SE SK UK

Participants: AT BE CZ DK ES FR IS LU NL NO PT RO SK UK

Participants: DK NL RO SE SK UK

Participants: BE FI IL IT LT NO PL PT TR

Participants: AT BE BG DE DK ES FI FR GR HU IE IS LU LV LT MT NL NO PL RO SE SI SK UK

Participants: AT BE CH DE DK FI FR HR IE IS LU NL MT NO PT RO SE SK UK
Objectives:

1. Standardise a measure for longitudinal analysis of antibiotic use by hospitals
   - Numerator: Defined Daily Doses
   - Denominator: comparison of bed days versus admissions
2. Standardise a method for point prevalence survey (cross sectional analysis) of antibiotic use
3. To develop methods that can be applied in all participating countries in ESAC III.

Why?

1. Calculation of DDDs is not as easy as it seems
2. Data from the Netherlands has shown increase in antibiotic use over time with DDD/100 bed days but not with DDD/100 admissions
3. Point prevalence surveys have the potential to provide added value (prescribed doses, documentation, clinical indication)
What We Wanted to Achieve

- Standardised data from one hospital in each participating country
- A practical method that can be rolled out
  - To other hospitals in each participating country
  - To other countries in ESAC III
- A platform for statistical analysis:
  - Trends within hospitals
  - Comparison between hospitals or countries
Composition Hospital Subproject

- **Members**: 23 countries (including England, Northern Ireland, Scotland, Wales)
  - **Present in Prague**: 20 countries: Austria (Sigrid Metz), Belgium (Hilde Jansens), Croatia (Arjana Tambić Andrašević), Denmark (Birgit Molstad), England (Conor Jamieson), Estonia (Piret Mitt), Finland (Outi Lyytikainen), France (Isabelle Patry, Xavier Bertrand), Germany (Michaela Steib-Bauert), Latvia (Elina Pujate), Lithuania (Ilma Bertulyte), Malta (Peter Zarb), Netherlands (Margreet Filius, Claire van Nispen tot Pennerden), Northern Ireland (Sheila Maltby), Norway (Cecile Syrrist), Poland (Pawel Grzesiowski), Slovenia (Milan Cizman), Sweden (Mats Erntell), Scotland (Faranak Ansari), Czech Republic (Jiri Vlcek)
  - **Apologies**: Greece (Anastasia Antoniadou), Turkey (Denis Gür) and Wales (Maggie Heginbotham)

- **Structure**
  - **Lead**: Peter Davey and team (Faranak Ansari!) in Tayside
  - **ESAC co-ordinator**: Herman Goossens and team (Matus Ferech) in Antwerp
  - **Software support**: Mats Erntell (STRAMA), Johan Kullas (Neotide, Finland)
Methods Longitudinal Survey

- Monthly data from 1/2000 - 12/2005

- J01 + oral metronidazole and oral vancomycin

- Dispensed from hospital pharmacy to inpatient destinations

- For every dosage form

- Convertible to DDD

- OBDs and admissions
Data set and software based on STRAMA annual PPS

English language version written by NEOTIDE

All patients who were receiving systemic (not topical) antibacterials (not antifungals or antivirals or TB treatment)
- Treatment – on day of survey
- Prophylaxis – on day before survey

Completed during two calendar weeks in April or 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 survey over one or more days. However, all beds in each administrative unit (e.g. Internal Medicine, General Surgery) were completed in a single day.
Data Point Prevalence Study

- Drug
- Unit dose
- Doses per day
- Route
- Diagnosis (site of infection or operation)
- Indication (CAI, HAI, surgical prophylaxis, medical proph)
- Immunosuppression
- Foreign material
- Culture pre-therapy
- Reason for antibiotics in case notes
- Assessment of concordance with local antibiotic policy
<table>
<thead>
<tr>
<th>Country Code</th>
<th>DDD/100 bed-days</th>
<th>DDD/100 admissions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>▲▲</td>
<td>▲▲</td>
</tr>
<tr>
<td>2</td>
<td>▲▲</td>
<td>▲▲</td>
</tr>
<tr>
<td>3</td>
<td>▲▲</td>
<td>▲▲</td>
</tr>
<tr>
<td>4</td>
<td>▲</td>
<td>▲</td>
</tr>
<tr>
<td>5</td>
<td>▲</td>
<td>▲</td>
</tr>
<tr>
<td>6</td>
<td>▲▲</td>
<td>▲</td>
</tr>
<tr>
<td>7</td>
<td>▲▲</td>
<td>▲</td>
</tr>
<tr>
<td>8</td>
<td>▲▲</td>
<td>▲</td>
</tr>
<tr>
<td>9</td>
<td>▲▲</td>
<td>▼▼</td>
</tr>
<tr>
<td>10</td>
<td>▲</td>
<td>▼▼</td>
</tr>
<tr>
<td>11</td>
<td>▼▼</td>
<td>▼▼</td>
</tr>
<tr>
<td>12</td>
<td>▼▼</td>
<td>▼▼</td>
</tr>
<tr>
<td>13</td>
<td>▼▼</td>
<td>▼▼</td>
</tr>
</tbody>
</table>
Total Use of Antibacterials in 2005

Use DDD/100 bed-days

Oral
Parenteral

Country Code

6 4 13 3 9 2 1 5 8 7 10 11 12
ESAC Ambulatory Care Subproject
ESAC NRs to ask the data provider(s) in your country for data for 2005 on

A. antibiotic dispensing by prescriber (GP, paediatrician and others), age and gender;

B. GPs’ antibiotic prescribing by age, gender and diagnosis.
**A: Link to specialism, age and gender**

Samples of the data files for 2004 from the Belgian pilot for A:

<table>
<thead>
<tr>
<th>ATC_7</th>
<th>Age</th>
<th>Gender</th>
<th>Speciality</th>
<th>Packages</th>
<th>DDD</th>
</tr>
</thead>
<tbody>
<tr>
<td>J01AA02</td>
<td>1</td>
<td>M</td>
<td>?</td>
<td>2</td>
<td>20.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>1</td>
<td>M</td>
<td>GP</td>
<td>8</td>
<td>96.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>1</td>
<td>M</td>
<td>OT</td>
<td>1</td>
<td>10.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>1</td>
<td>M</td>
<td>PE</td>
<td>1</td>
<td>10.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>1</td>
<td>F</td>
<td>GP</td>
<td>3</td>
<td>30.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>1</td>
<td>F</td>
<td>OT</td>
<td>1</td>
<td>10.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>1</td>
<td>F</td>
<td>PE</td>
<td>1</td>
<td>6.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>2</td>
<td>M</td>
<td>GP</td>
<td>21</td>
<td>226.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>2</td>
<td>F</td>
<td>?</td>
<td>2</td>
<td>20.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>2</td>
<td>F</td>
<td>GP</td>
<td>7</td>
<td>76.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>2</td>
<td>F</td>
<td>OT</td>
<td>4</td>
<td>40.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>2</td>
<td>F</td>
<td>PE</td>
<td>1</td>
<td>10.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>3</td>
<td>M</td>
<td>GP</td>
<td>24</td>
<td>240.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>3</td>
<td>M</td>
<td>PE</td>
<td>1</td>
<td>6.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>3</td>
<td>F</td>
<td>GP</td>
<td>13</td>
<td>146.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>3</td>
<td>F</td>
<td>OT</td>
<td>12</td>
<td>130.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>4</td>
<td>M</td>
<td>GP</td>
<td>22</td>
<td>270.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>4</td>
<td>M</td>
<td>OT</td>
<td>6</td>
<td>36.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>4</td>
<td>M</td>
<td>PE</td>
<td>1</td>
<td>10.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>4</td>
<td>F</td>
<td>GP</td>
<td>6</td>
<td>72.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>4</td>
<td>F</td>
<td>OT</td>
<td>4</td>
<td>36.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>4</td>
<td>F</td>
<td>PE</td>
<td>3</td>
<td>22.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>5</td>
<td>M</td>
<td>GP</td>
<td>19</td>
<td>162.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>5</td>
<td>M</td>
<td>OT</td>
<td>2</td>
<td>20.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>5</td>
<td>M</td>
<td>PE</td>
<td>3</td>
<td>18.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>5</td>
<td>F</td>
<td>GP</td>
<td>21</td>
<td>174.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>5</td>
<td>F</td>
<td>OT</td>
<td>2</td>
<td>20.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>5</td>
<td>F</td>
<td>PE</td>
<td>6</td>
<td>40.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>6</td>
<td>M</td>
<td>?</td>
<td>1</td>
<td>10.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>6</td>
<td>M</td>
<td>GP</td>
<td>23</td>
<td>228.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>6</td>
<td>M</td>
<td>OT</td>
<td>11</td>
<td>110.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>6</td>
<td>M</td>
<td>PE</td>
<td>6</td>
<td>40.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>6</td>
<td>F</td>
<td>GP</td>
<td>16</td>
<td>124.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>6</td>
<td>F</td>
<td>OT</td>
<td>3</td>
<td>30.00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>6</td>
<td>F</td>
<td>PE</td>
<td>3</td>
<td>22.00</td>
</tr>
</tbody>
</table>

**Variable description:**
- **ATC_7:** 7 digit ATC code (ATC version 2005, or mention version) (see Annex 1);
- **Age:** in years;
- **Gender:** M (=male); F (=female);
- **Speciality:** GP (=general practitioner); PE (=paediatrician); OT (=others);
- **Packages:** number of ATC J01 packages dispensed (ATC version 2005, or mention version);
- **DDD:** number of ATC J01 DDD dispensed (ATC version 2005, or mention version);
- **Population:** number of ‘population at risk’ covered*
Data provided for A

- **National** data from BE, DK, FI, IL, NL & SE
  - not yet from IS, LU, SL; ? UK
  - sample LV, not available for ES

- **2005** for DK, FI, IL (IS; July-June LU; ? SL & UK)
  **2004** for BE, NL, SE

- **DID** for all;
  **PID** and/or **R\ID** for BE, DK, SE (IS, LU, NL; ? SL & UK)

- **Gender** for all

- **Age** BE, DK, IL (IS, LU, SL & UK)
  **100+** for FI, SE; **age groups** for NL

- **Specialism** for BE, DK, SE (only for prescriptions)
  (LU, NL & UK; ? SL)

⇒ GP vs other vs ?
ESAC vs ESAC AC Subproject data
Use by age
Use by prescriber
Use by age & gender

Country
Finland

Denmark

Belgium
Use by age & gender

Gender
- F
- M

Sweden

Israel
### Sample of the Data Files for 2004 from the Belgian Pilot for B:

<table>
<thead>
<tr>
<th>ATC_7</th>
<th>Age</th>
<th>Gender</th>
<th>ICPC2</th>
<th>Packages</th>
<th>DDD</th>
</tr>
</thead>
<tbody>
<tr>
<td>J01AA02</td>
<td>11</td>
<td>M</td>
<td>A78</td>
<td>1.00</td>
<td>10,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>11</td>
<td>M</td>
<td>S06</td>
<td>1.00</td>
<td>10,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>13</td>
<td>M</td>
<td>R74</td>
<td>1.00</td>
<td>10,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>14</td>
<td>F</td>
<td>S94</td>
<td>1.00</td>
<td>10,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>14</td>
<td>M</td>
<td>A86</td>
<td>1.00</td>
<td>10,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>15</td>
<td>F</td>
<td>H71</td>
<td>1.00</td>
<td>10,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>15</td>
<td>F</td>
<td>R81</td>
<td>1.00</td>
<td>20,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>15</td>
<td>M</td>
<td>A86</td>
<td>1.00</td>
<td>10,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>15</td>
<td>M</td>
<td>R74</td>
<td>1.00</td>
<td>20,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>16</td>
<td>F</td>
<td>S12</td>
<td>1.00</td>
<td>20,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>16</td>
<td>M</td>
<td>A75</td>
<td>1.00</td>
<td>10,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>16</td>
<td>M</td>
<td>R74</td>
<td>1.00</td>
<td>10,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>17</td>
<td>F</td>
<td>R77</td>
<td>1.00</td>
<td>10,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>17</td>
<td>F</td>
<td>R78</td>
<td>1.00</td>
<td>10,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>17</td>
<td>F</td>
<td>S09</td>
<td>1.00</td>
<td>20,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>17</td>
<td>F</td>
<td>S76</td>
<td>1.00</td>
<td>20,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>17</td>
<td>M</td>
<td>R07</td>
<td>1.00</td>
<td>20,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>17</td>
<td>M</td>
<td>R74</td>
<td>1.00</td>
<td>20,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>17</td>
<td>M</td>
<td>R75</td>
<td>1.00</td>
<td>20,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>17</td>
<td>M</td>
<td>S12</td>
<td>1.00</td>
<td>20,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>18</td>
<td>F</td>
<td>R75</td>
<td>2.00</td>
<td>20,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>18</td>
<td>F</td>
<td>R76</td>
<td>1.00</td>
<td>20,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>18</td>
<td>M</td>
<td>H71</td>
<td>1.00</td>
<td>10,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>18</td>
<td>M</td>
<td>R74</td>
<td>1.00</td>
<td>10,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>18</td>
<td>M</td>
<td>R74</td>
<td>1.00</td>
<td>20,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>18</td>
<td>M</td>
<td>R77</td>
<td>1.00</td>
<td>20,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>19</td>
<td>F</td>
<td>R77</td>
<td>1.00</td>
<td>10,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>19</td>
<td>M</td>
<td>A86</td>
<td>1.00</td>
<td>20,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>19</td>
<td>M</td>
<td>S76</td>
<td>1.00</td>
<td>10,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>20</td>
<td>F</td>
<td>R74</td>
<td>1.00</td>
<td>10,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>21</td>
<td>F</td>
<td>R78</td>
<td>1.00</td>
<td>10,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>21</td>
<td>F</td>
<td>U71</td>
<td>1.00</td>
<td>10,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>21</td>
<td>M</td>
<td>A78</td>
<td>1.00</td>
<td>20,00</td>
</tr>
<tr>
<td>J01AA02</td>
<td>21</td>
<td>M</td>
<td>R75</td>
<td>2.00</td>
<td>30,00</td>
</tr>
</tbody>
</table>

**Variable description:**
- **ID:** anonymous identification of each individual patient;
- **Date:** date of the prescription;
- **ATC_7:** 7 digit ATC code (= substance level) (ATC version 2005, or mention version);
- **Age:** in years;
- **Gender:** M (= male); F (= female);
- **ICPC2:** ICPC2-R codes (rather than ICD10 of ICD 9 codes)* for diagnosis (see Annex 1);
- **Packages:** number of ATC J01 packages prescribed (ATC version 2005, or mention version);
- **DDD:** number of ATC J01 DDD prescribed (ATC version 2005, or mention version);
- **Population:** number of ‘population at risk’ covered**
Data provided for B

- **National** 2005 data from DK (not just GPs)
- Sample 2004 data from BE & 2005 from SE
- **DID** for BE, DK; **PID** for BE; **RID** for DK
- SE population data not yet available
- **Gender** for all
- **Age** BE, DK, SE
- **Indications: ICPC2-R for** BE, DK*, SE
  * link with ICPC2-R?

=> Samples representative for country?
=> Comparable data not yet available…
Conclusions

A: Allows to assess differences in use* by differences in demographics, differences in prescriber characteristics
   * total use and use of different subclasses of antibiotics
   Data from more countries is welcome, and will come!

B: Allows to assess differences in use* by indications
   * total use and use of different subclasses of antibiotics
   More data is needed and is available, but …!
Outpatient Antibiotic Use
Europe versus USA
Total outpatient antibiotic use in 27 European countries and USA in 2004

Goossens et al, CID, April 2007
Total Outpatient MLS Use in the United States and 27 European Countries in 2004

DDD / 1000 inhabitants / day

Others
Telithromycin
Spiramycin
Clindamycin
Roxithromycin
Erythromycin
Clarithromycin
Azithromycin
### Outpatient systemic use of major antibiotic classes in the United States and Europe in 2004

<table>
<thead>
<tr>
<th>Class</th>
<th>USA DID* (%)</th>
<th>Europe DID* (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetracyclines</td>
<td>4.63 (18.60)</td>
<td>2.37 (12.42)</td>
</tr>
<tr>
<td>Penicillines [8]</td>
<td>9.70 (38.93)</td>
<td>8.71 (45.73)</td>
</tr>
<tr>
<td>J01CE Narrow spectrum penicillins</td>
<td>0.68 (2.71)</td>
<td>0.75 (3.92)</td>
</tr>
<tr>
<td>J01CA Broad spectrum penicillins</td>
<td>5.68 (22.81)</td>
<td>4.49 (23.58)</td>
</tr>
<tr>
<td>J01CR Combination of penicillins</td>
<td>3.29 (13.22)</td>
<td>3.20 (16.82)</td>
</tr>
<tr>
<td>J01CF Penicillin resistant penicillins</td>
<td>0.05 (0.19)</td>
<td>0.27 (1.40)</td>
</tr>
<tr>
<td>Cephalosporins, monobactams, carbapenems [9]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>J01DB First generation cephalosporins</td>
<td>1.47 (5.90)</td>
<td>0.31 (1.62)</td>
</tr>
<tr>
<td>J01DC Second generation cephalosporins</td>
<td>0.61 (2.46)</td>
<td>1.12 (5.89)</td>
</tr>
<tr>
<td>J01DD Third generation cephalosporins</td>
<td>0.39 (1.57)</td>
<td>0.59 (3.11)</td>
</tr>
<tr>
<td>Sulphonamides and trimethoprim</td>
<td>1.34 (5.37)</td>
<td>0.77 (4.04)</td>
</tr>
<tr>
<td>Macrolides, lincosamides and streptogramins [10]</td>
<td>3.52 (14.14)</td>
<td>2.98 (15.66)</td>
</tr>
<tr>
<td>J01FF Short-acting macrolides</td>
<td>0.43 (1.73)</td>
<td>0.48 (2.54)</td>
</tr>
<tr>
<td>J01FG Intermediate-acting macrolides</td>
<td>1.16 (4.66)</td>
<td>1.71 (8.96)</td>
</tr>
<tr>
<td>J01FG Long-acting macrolides</td>
<td>1.68 (6.74)</td>
<td>0.53 (2.77)</td>
</tr>
<tr>
<td>J01FF Lincosamides</td>
<td>0.25 (1.02)</td>
<td>0.16 (0.85)</td>
</tr>
<tr>
<td>J01FG Streptogramins</td>
<td>&lt;0.01 (0.00)</td>
<td>0.10 (0.55)</td>
</tr>
<tr>
<td>Quinolones [11]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>J01FF First generation quinolones</td>
<td>0.01 (0.03)</td>
<td>0.41 (2.15)</td>
</tr>
<tr>
<td>J01FF Second generation quinolones</td>
<td>2.07 (8.30)</td>
<td>1.01 (5.31)</td>
</tr>
<tr>
<td>J01FF Third generation quinolones</td>
<td>0.39 (1.58)</td>
<td>0.16 (0.86)</td>
</tr>
<tr>
<td>Others</td>
<td>0.78 (3.11)</td>
<td>0.61 (3.18)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>24.92 (100.00)</strong></td>
<td><strong>19.04 (100.00)</strong></td>
</tr>
</tbody>
</table>
Outpatient systemic use of antibiotic substances in the United States and Europe in 2004.

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>United States</th>
<th>Europe</th>
<th>Range in Europe</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DID** (%)</td>
<td>DID** (%)</td>
<td>Highest DID** (country)</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>5.59 (22.4)</td>
<td>4.26 (22.3)</td>
<td>12.83 (France)</td>
</tr>
<tr>
<td>Co-amoxiclav</td>
<td>3.29 (13.2)</td>
<td>3.16 (16.6)</td>
<td>7.32 (Portugal)</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>2.98 (12)</td>
<td>1.73 (9.1)</td>
<td>5.17 (Iceland)</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>1.68 (6.7)</td>
<td>0.52 (2.7)</td>
<td>1.34 (Croatia)</td>
</tr>
<tr>
<td>Cefalexin</td>
<td>1.39 (5.6)</td>
<td>0.17 (0.9)</td>
<td>1.89 (Finland)</td>
</tr>
<tr>
<td>Co-trimoxazol</td>
<td>1.31 (5.2)</td>
<td>0.56 (2.9)</td>
<td>1.62 (Croatia)</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>1.10 (4.4)</td>
<td>1.23 (6.5)</td>
<td>7.16 (Greece)</td>
</tr>
<tr>
<td>Minocycline</td>
<td>1.07 (4.3)</td>
<td>0.24 (1.3)</td>
<td>1.36 (Ireland)</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>1.06 (4.3)</td>
<td>0.24 (1.3)</td>
<td>1.05 (Italy)</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>0.97 (3.9)</td>
<td>0.59 (3.1)</td>
<td>1.81 (Portugal)</td>
</tr>
<tr>
<td>Phenoxyomethylpenicillin</td>
<td>0.68 (2.7)</td>
<td>0.64 (3.4)</td>
<td>5.23 (Denmark)</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>0.63 (2.5)</td>
<td>0.27 (1.4)</td>
<td>0.8 (Netherlands)</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>0.57 (2.3)</td>
<td>0.08 (0.4)</td>
<td>1.02 (Finland)</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>0.43 (1.7)</td>
<td>0.34 (1.8)</td>
<td>1.72 (UK)</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>0.35 (1.4)</td>
<td>0.70 (3.7)</td>
<td>3.40 (Luxembourg)</td>
</tr>
<tr>
<td>Cefdinir</td>
<td>0.34 (1.4)</td>
<td>No use</td>
<td>No use (Luxembourg)</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>0.25 (1.0)</td>
<td>0.14 (0.8)</td>
<td>0.70 (Hungary)</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>0.25 (1.0)</td>
<td>0.16 (0.9)</td>
<td>0.56 (Belgium)</td>
</tr>
<tr>
<td><strong>Grand Total</strong></td>
<td><strong>24.91 (100)</strong></td>
<td><strong>19.04 (100)</strong></td>
<td><strong>33.37 (Greece)</strong></td>
</tr>
</tbody>
</table>
Outpatient Antimycotic Use in Europe
Total outpatient antimycotic use in 15 European countries in 2004

- Belgium
- Luxembourg
- Portugal
- Hungary
- Netherlands
- Slovenia
- Finland
- Latvia
- Slovakia
- Israel
- Poland
- Iceland
- France
- Sweden
- Bulgaria

DDD/1000 inh./day

- Ketoconazole J02AB02
- Fluconazole J02AC01
- Itraconazole J02AC02

Others
Outpatient use of antimycotics in 15 European countries in 2004

- Belgium
- Luxembourg
- Hungary
- Netherlands
- Slovenia
- Finland
- Latvia
- Slovakia
- Israel
- Poland
- France
- Sweden
- Bulgaria

- Others
- Voriconazole (J02AC03)
- Ketoconazole (J02AB02)
- Fluconazole (J02AC01)
- Itraconazole (J02AC02)
Hospital use of antimycotics in 9 European countries in 2004

- Latvia
- Luxembourg
- France
- Finland
- Slovenia
- Slovakia
- Sweden
- Hungary
- Israel

DDD/1000 inh./day

Others
Amphotericin B J02AA01
Voriconazole J02AC03
Ketoconazole J02AB02
Fluconazole J02AC01
Itraconazole J02AC02
Correlation between outpatient antimycotic use and outpatient antibiotic use in 2004

Outpatient use of antifungals (J02) in 2004 (DID)

Outpatient use of antibiotics (J01) in 2004 (DID)

n = 11
Outpatient antimycotic use in Belgium between 1997 and 2005

- **Others**
- **Ketoconazole** (J02AB02)
- **Fluconazole** (J02AC01)
- **Itraconazole** (J02AC02)
Outpatient antimycotic use in Belgium between 1997 and 2004

Graph showing the trend of DDD per 1000 inh. per day and packs per 1000 inh. per day from 1997 to 2004.
Outpatient antibiotic use in Belgium between 1997 and 2004

Graph showing the trend of outpatient antibiotic use from 1997 to 2004, measured in Defined Daily Doses (DDD) per 1000 inhabitants per day, with data points for J01 DID and J01 PID.
Outpatient itraconazole use in Belgium between 1997 and 2005

Itraconazole 100 mg

DDD per 1000 inh. per day

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