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

Vander Stichele RH, Elseviers M, Ferech M, Blot S, Goossens H and the ESAC Project Group: **European Surveillance of Antimicrobial Consumption: Data Collection Performance and Methodological Approach.** Br J Clin Pharmacol. 2004 Oct; 58(4):419-28

Defined Daily Dose (DDD)

A unit of measurement

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*

DDD per 1000 inhabitants per day

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.

ATC Classification

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

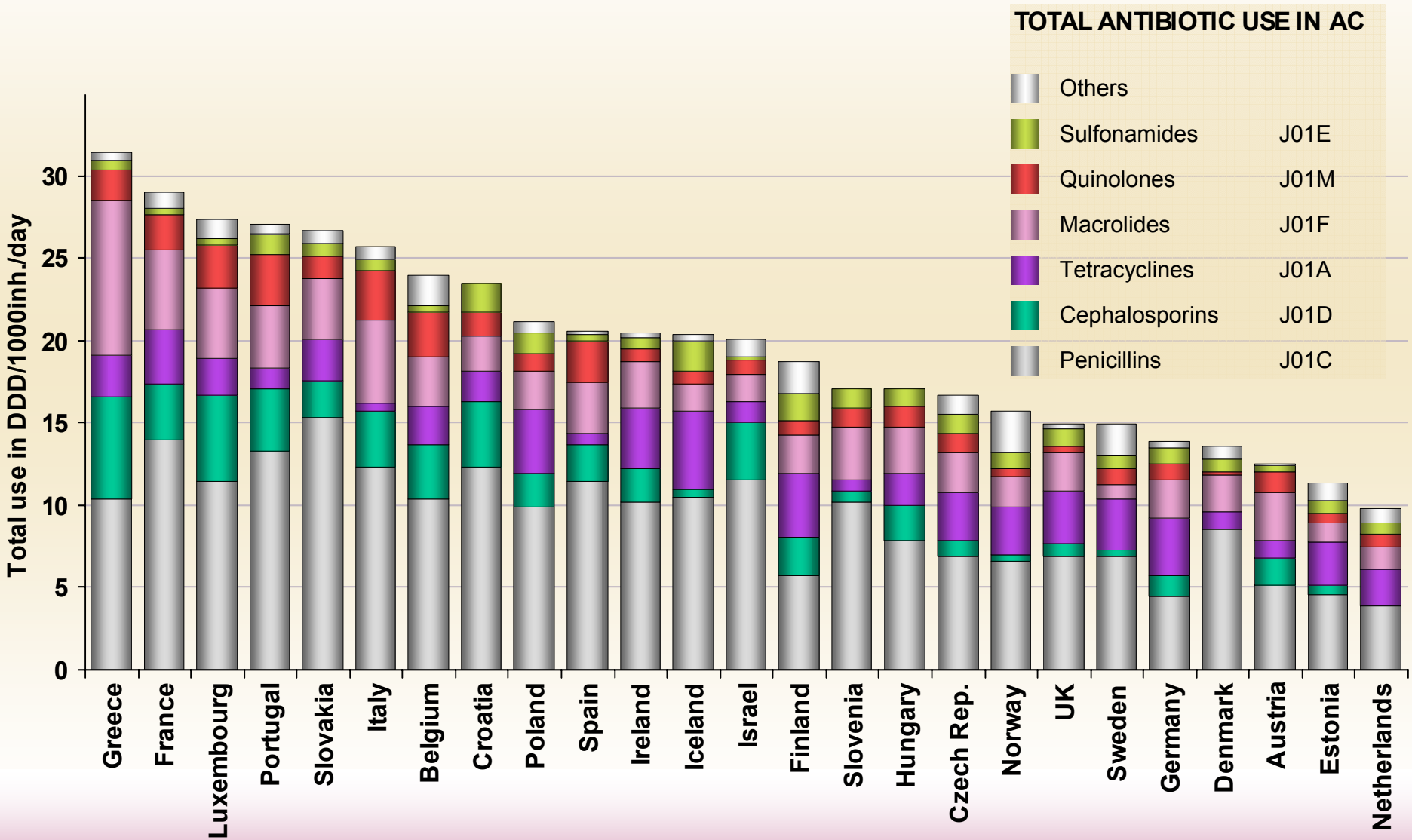
based on reports from the distribution chain:
from companies, wholesalers or pharmacies

Reimbursement data

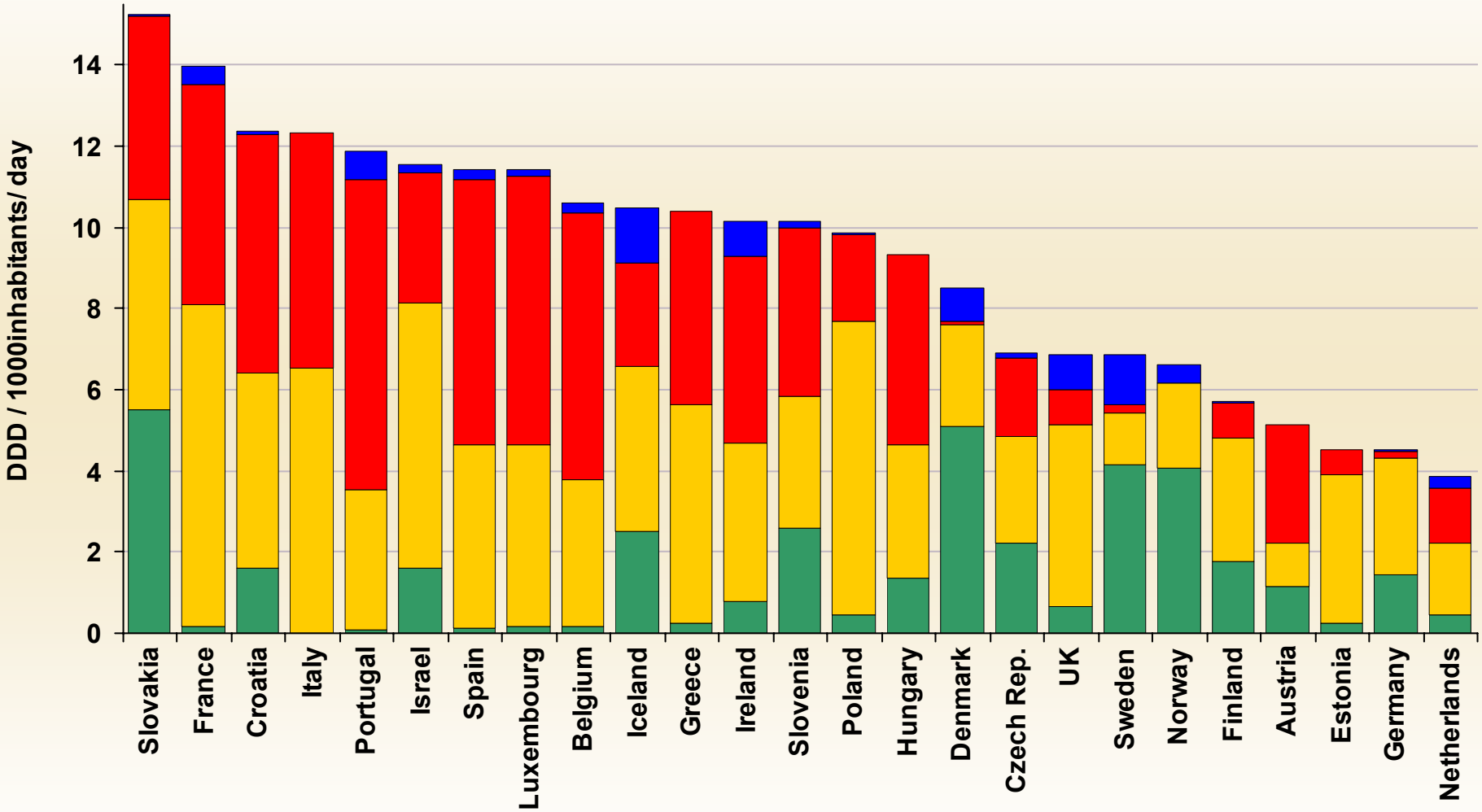
collected from the third party payer:
from insurance companies or health care services

Outpatient Antibiotic Use

Total Outpatient Antibiotic Use in 25 European Countries in 2003

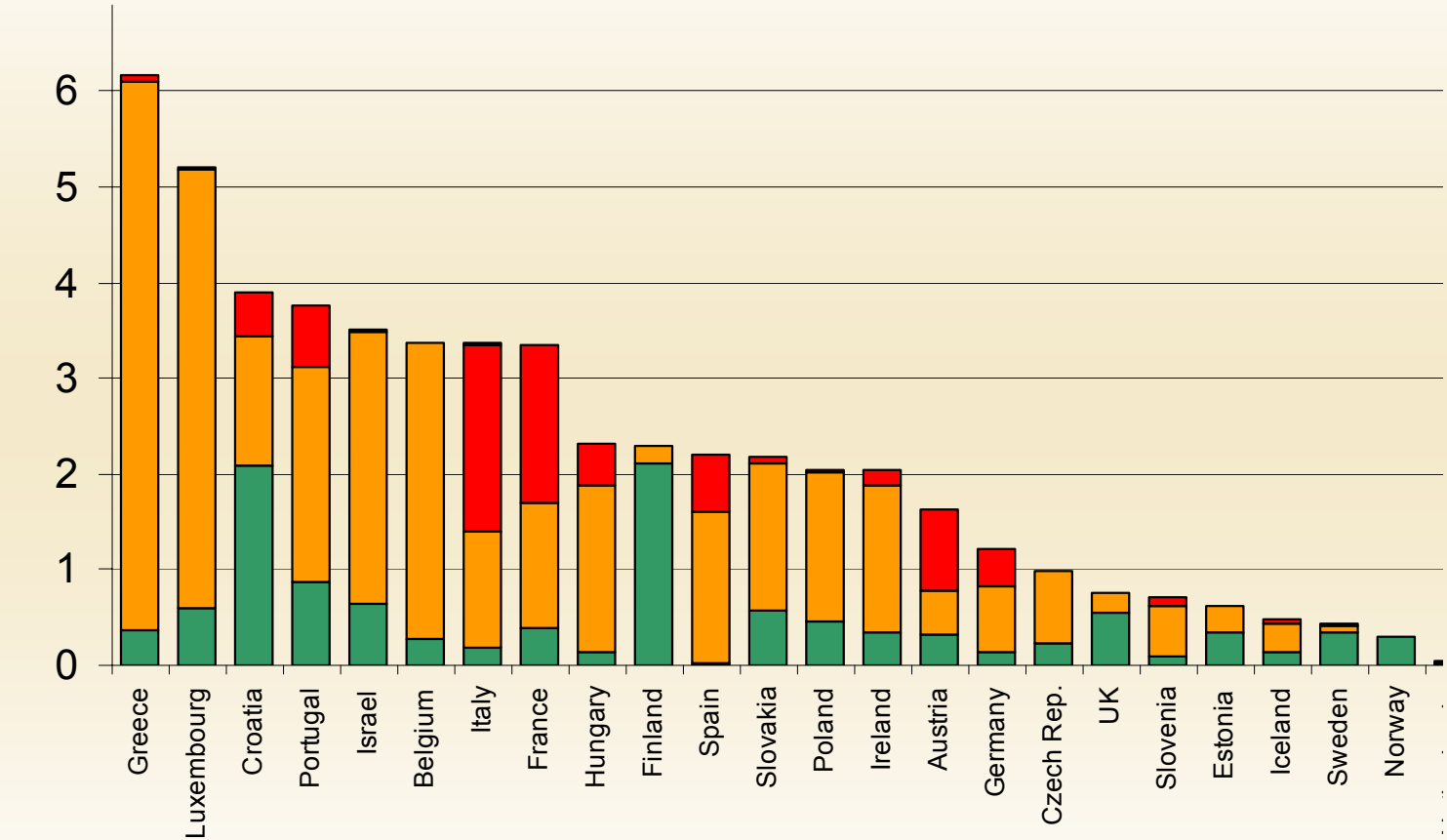


Outpatient Use of Penicillins in 25 European Countries in 2003



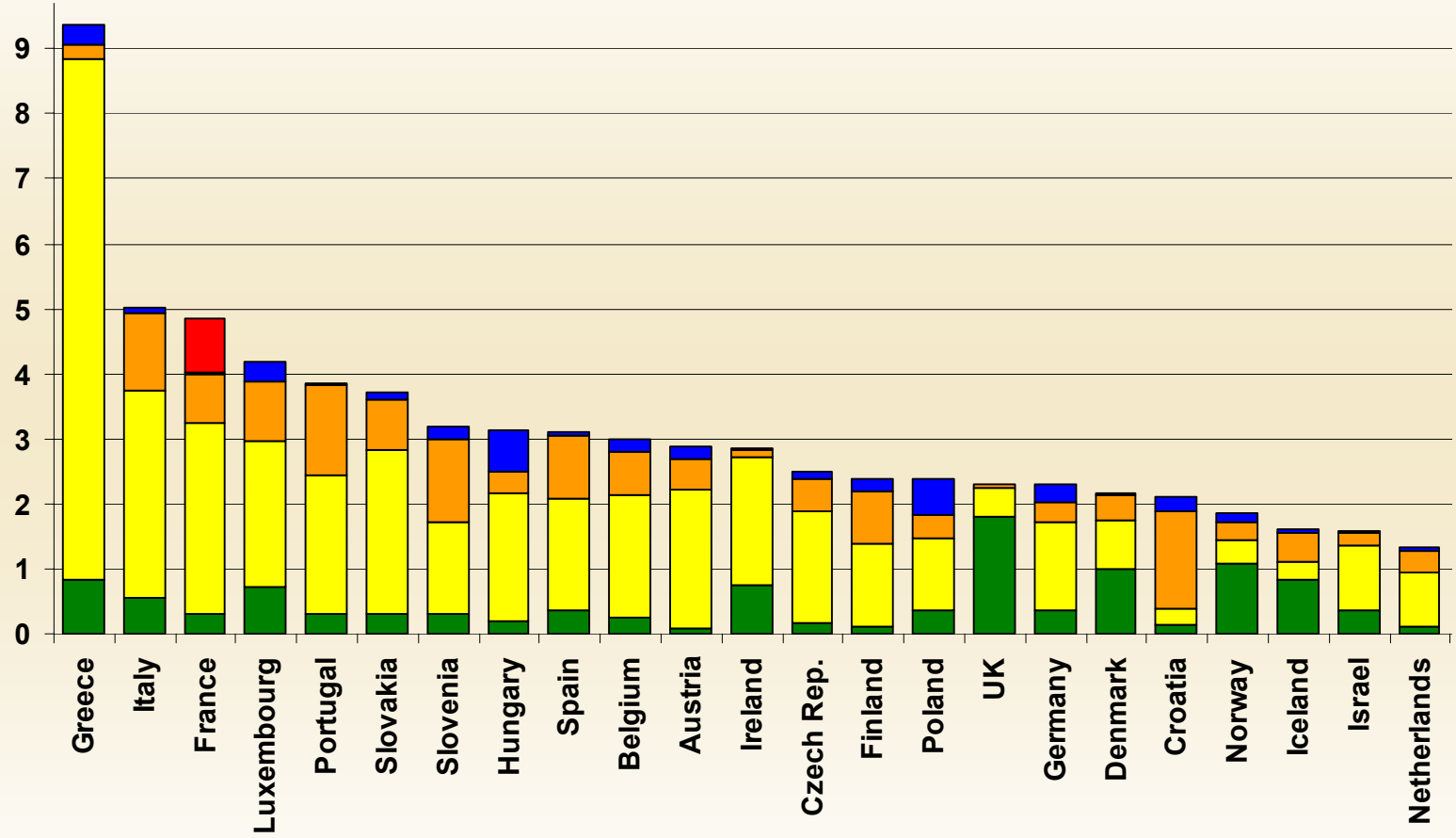
= Beta-lactamase sensitive penicillins (narrow spectrum penicillins J01CE), = Penicillins with extended spectrum (broad spectrum pen. J01CA), = Combinations of penicillins, incl. beta-lactamase inhibitors (J01CR), = Beta-lactamase resistant penicillins (J01CF)

Outpatient Use of Cephalosporins in 25 European Countries in 2003



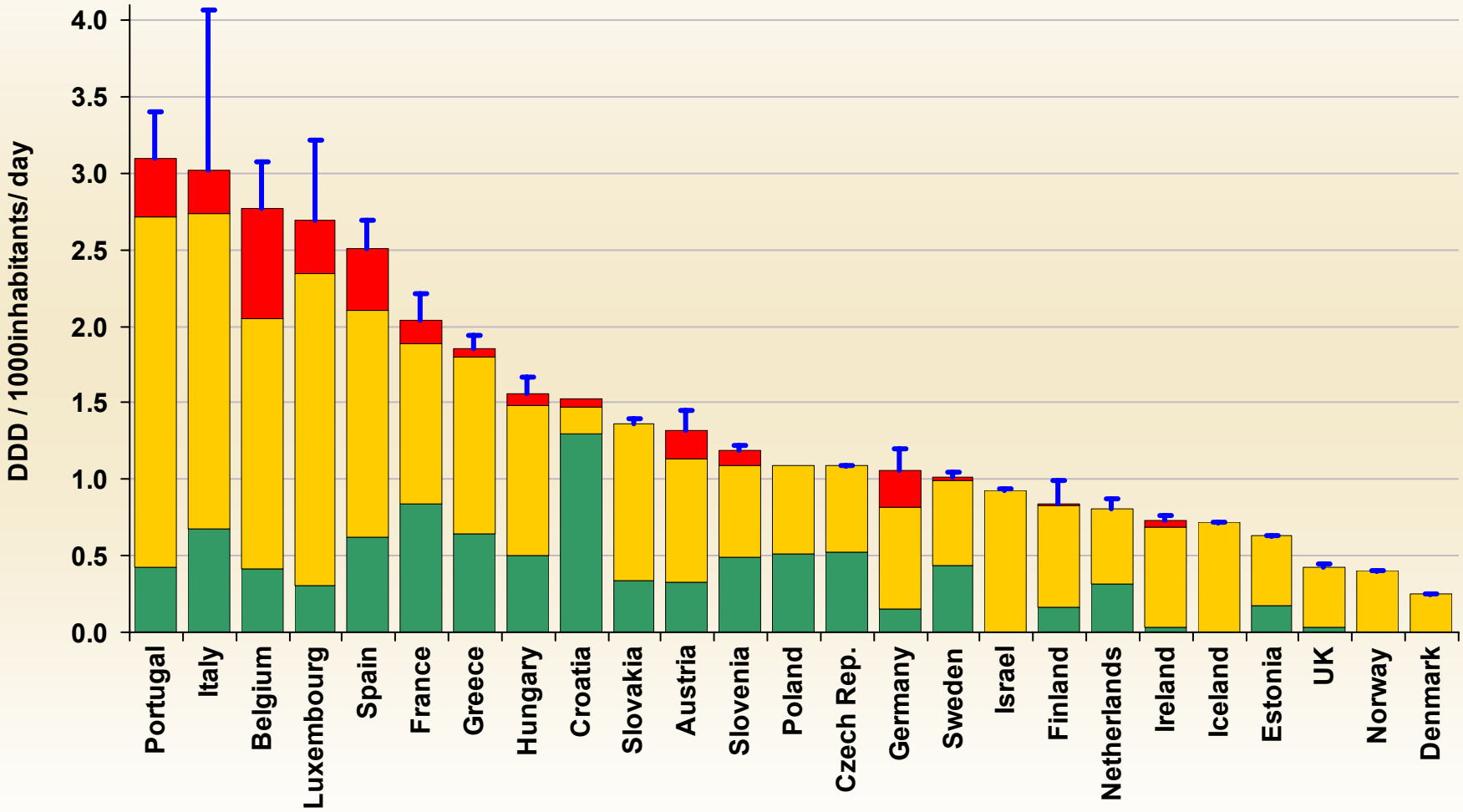
= first- (J01DB), = second- (J01DC), = third-generation (J01 DD) cephalosporin use. The use of fourth-generation cephalosporins is marginal.

Outpatient Use of MLS in 25 European Countries in 2003

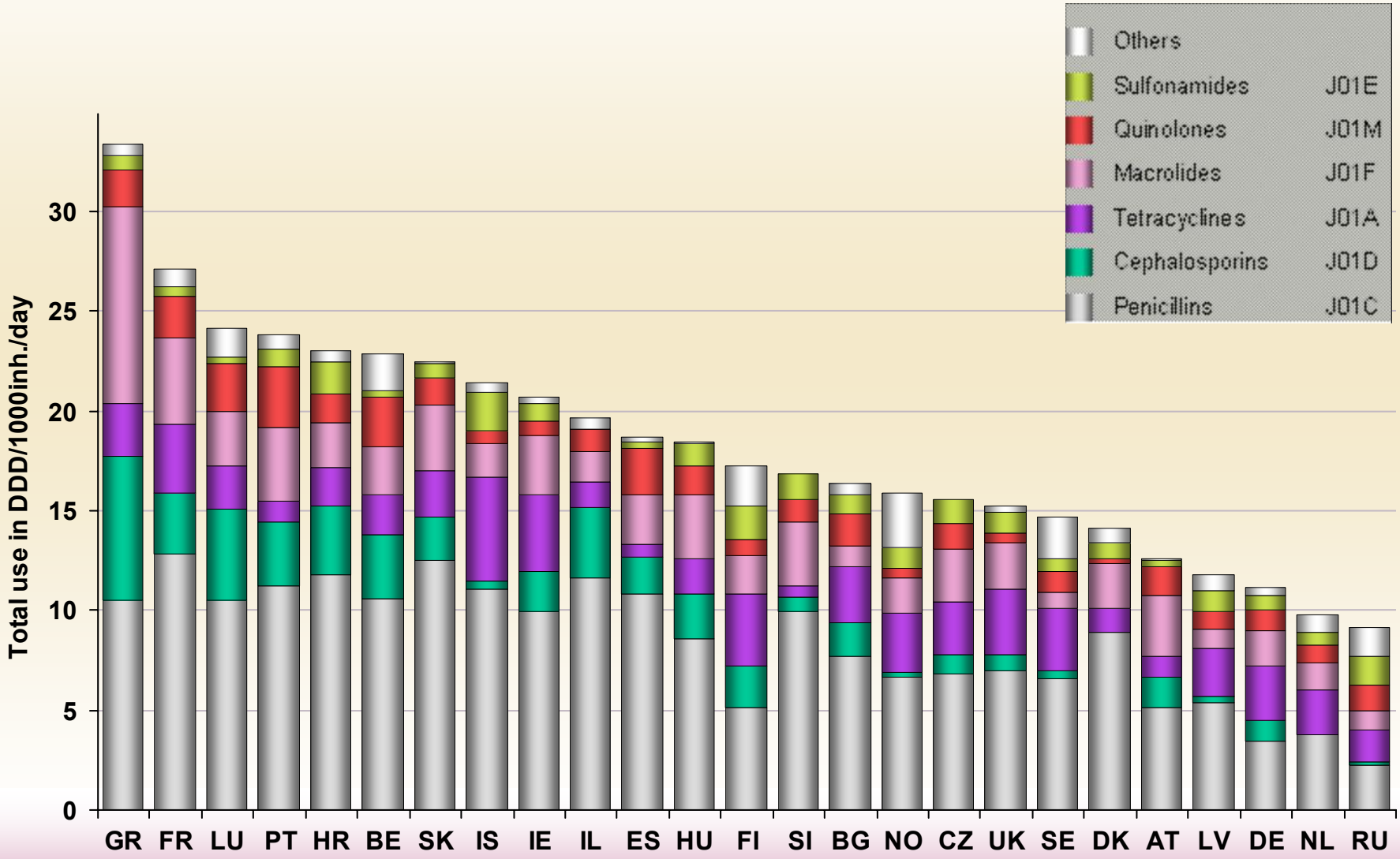


= short-acting macrolide, = intermediate-acting macrolide, including telithromycin, = long-acting macrolide, = lincosamide, = streptogramin use.

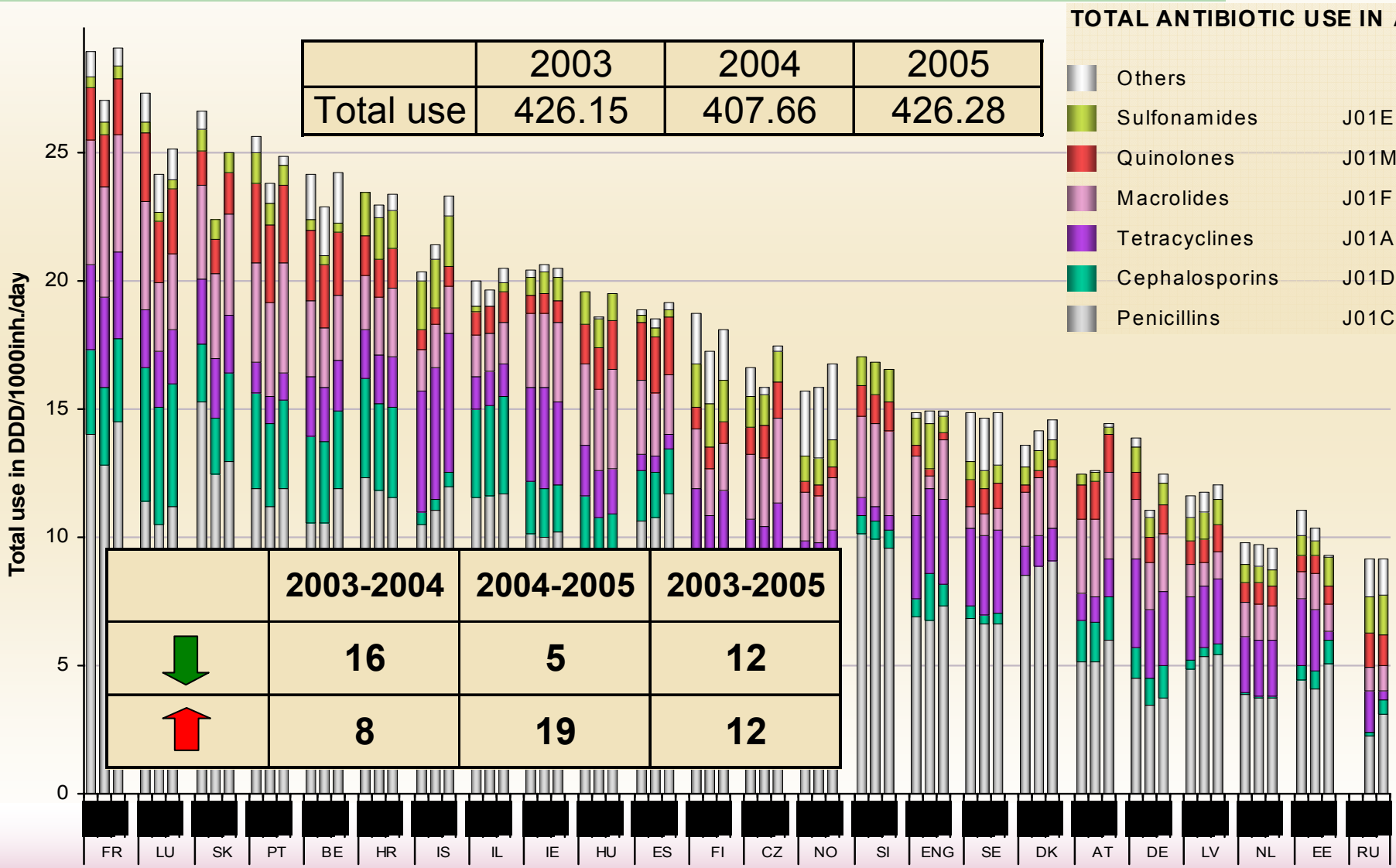
Outpatient Use of Quinolones in 25 European Countries in 2003



Total Outpatient Antibiotic Use in 25 European Countries in 2004



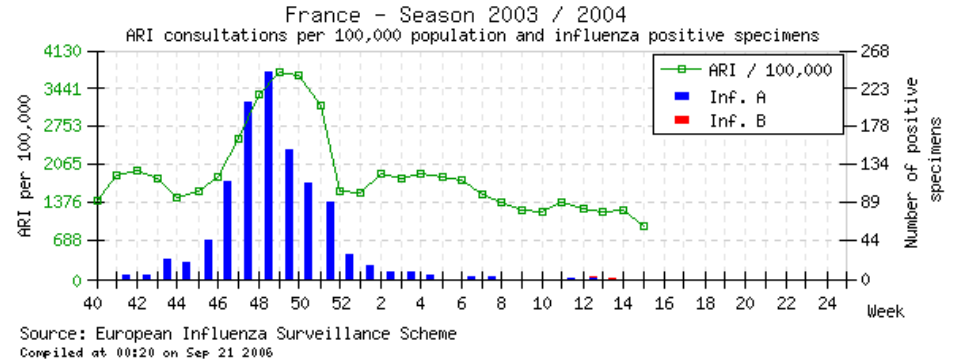
Trends of Outpatient Antibiotic Consumption in 15 Countries July 2002-June 2005

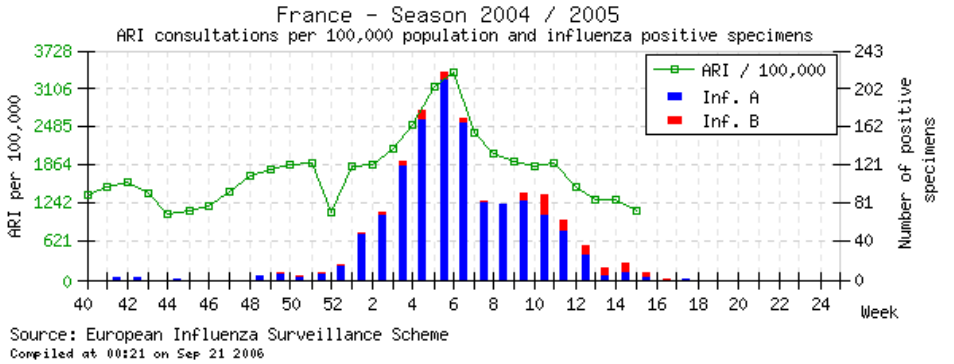


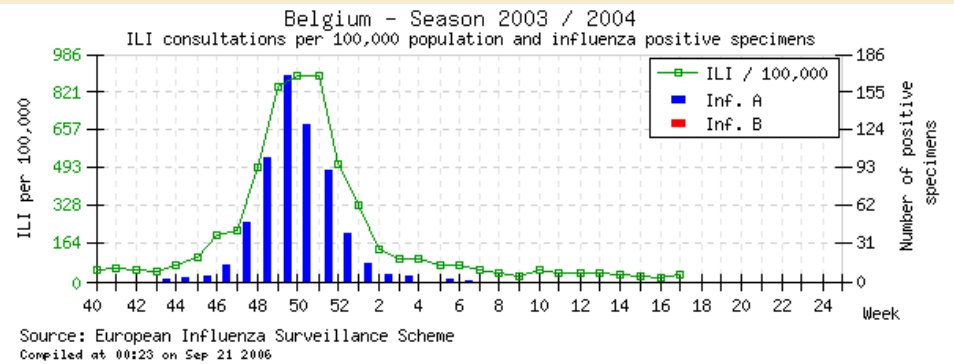
	2003	2004	2005
Total use	426.15	407.66	426.28

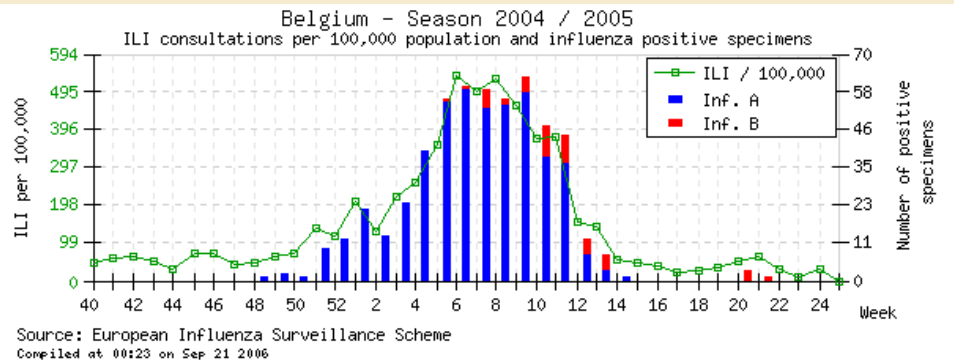
	2003-2004	2004-2005	2003-2005
↓	16	5	12
↑	8	19	12

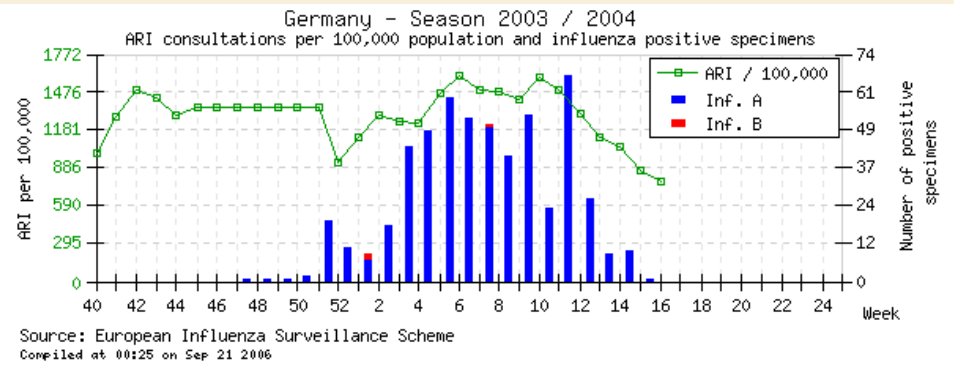
Influenza morbidity rates www.EISS.org

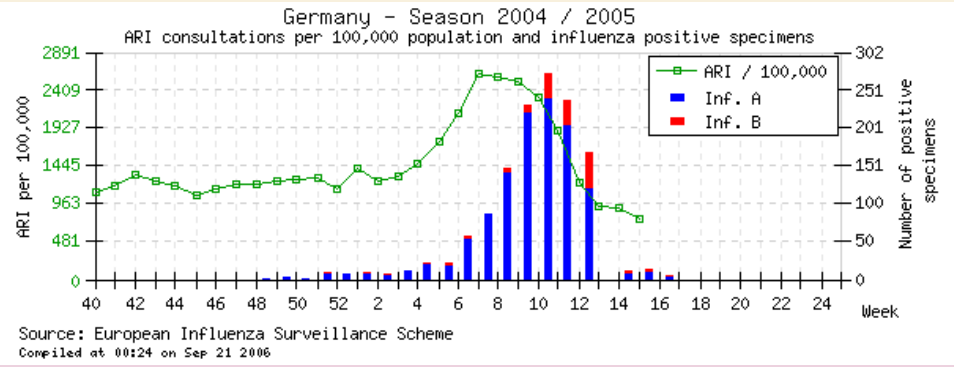




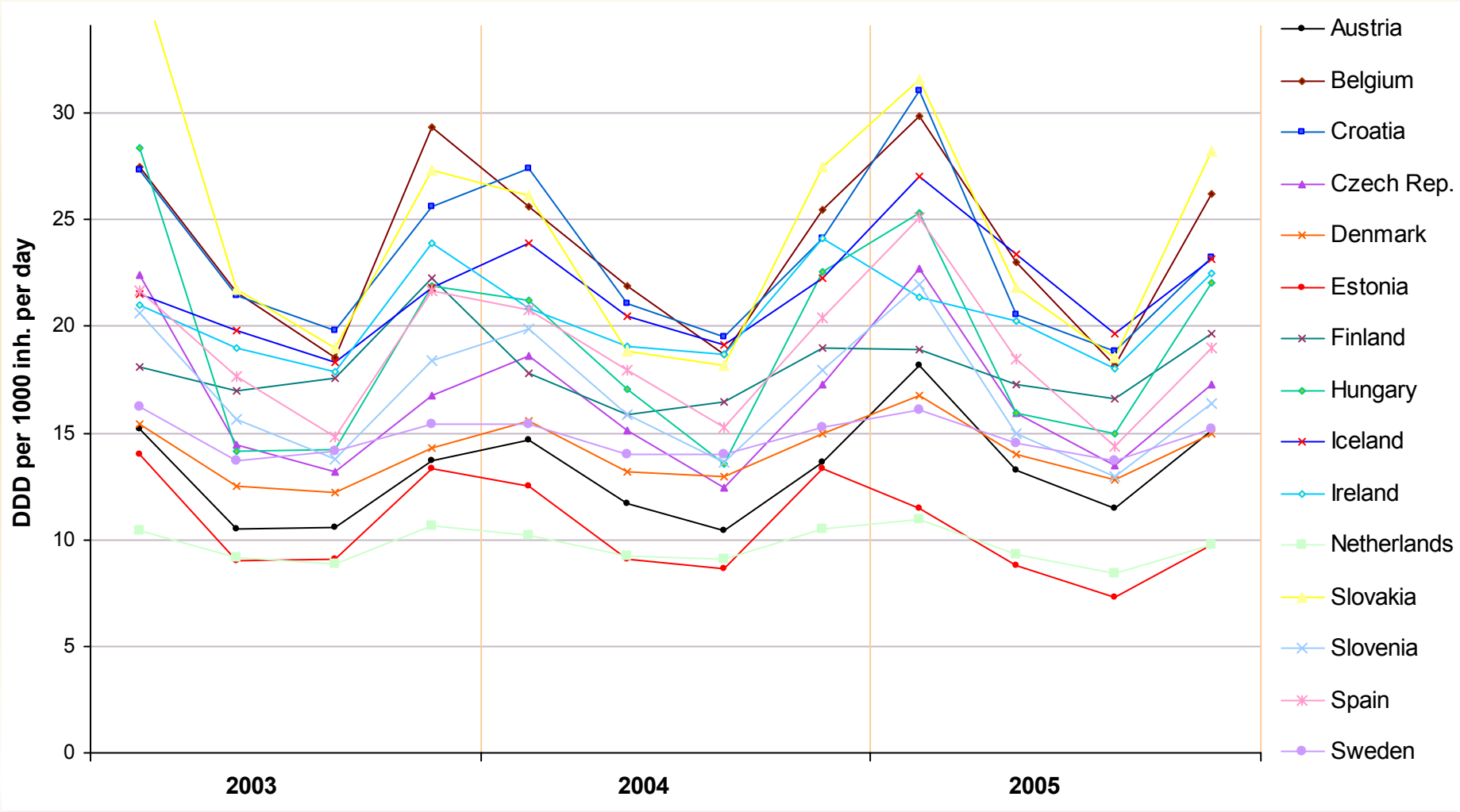




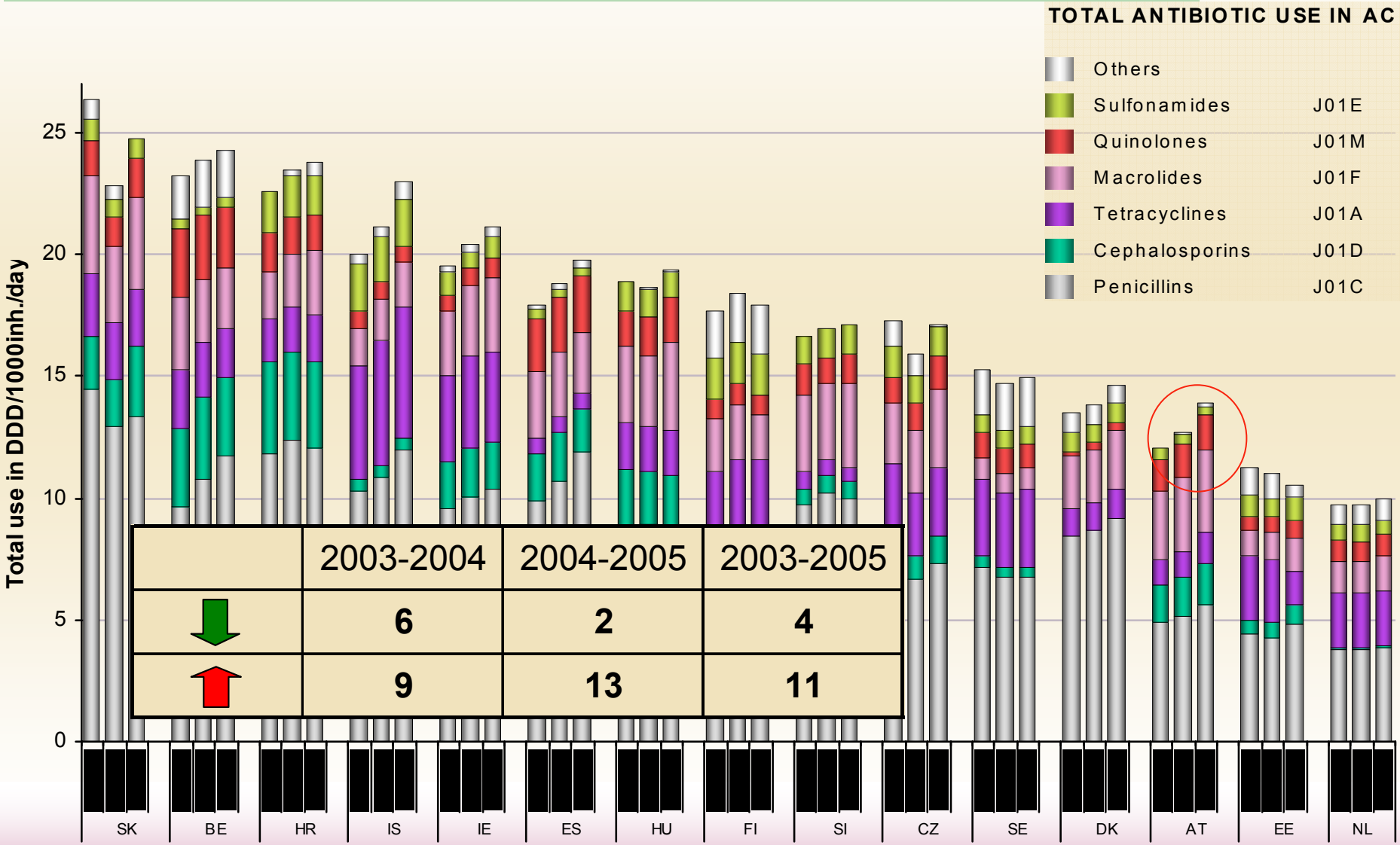




Seasonality of use, 2003-2005



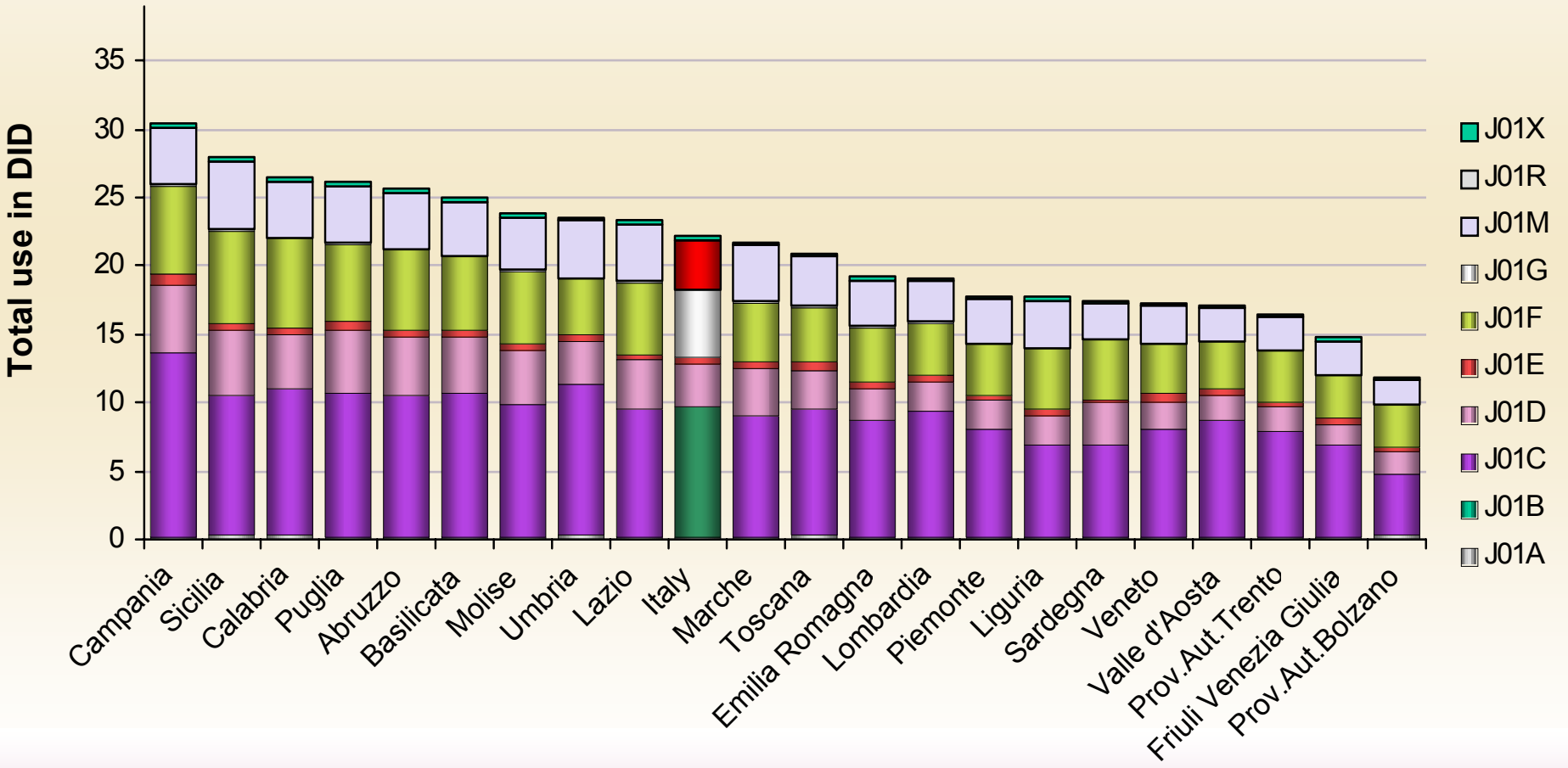
Trends of Outpatient Antibiotic Consumption in 15 Countries - July 2002-June 2005



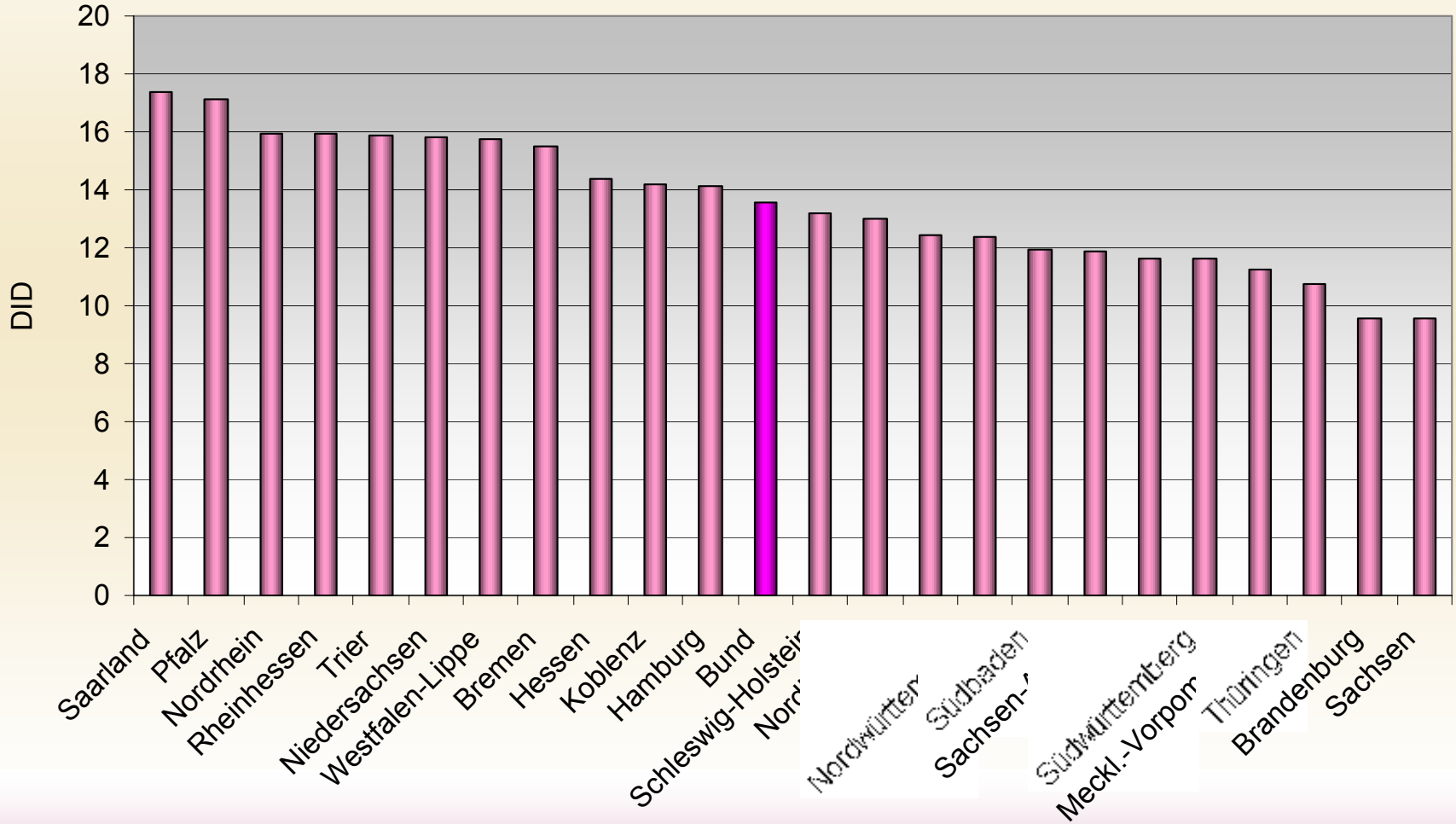
	2003-2004	2004-2005	2003-2005
↓	6	2	4
↑	9	13	11

Outpatient Antibiotic Use
Regional Variation

Regional Variation of Outpatient Antibiotic Use in Italy

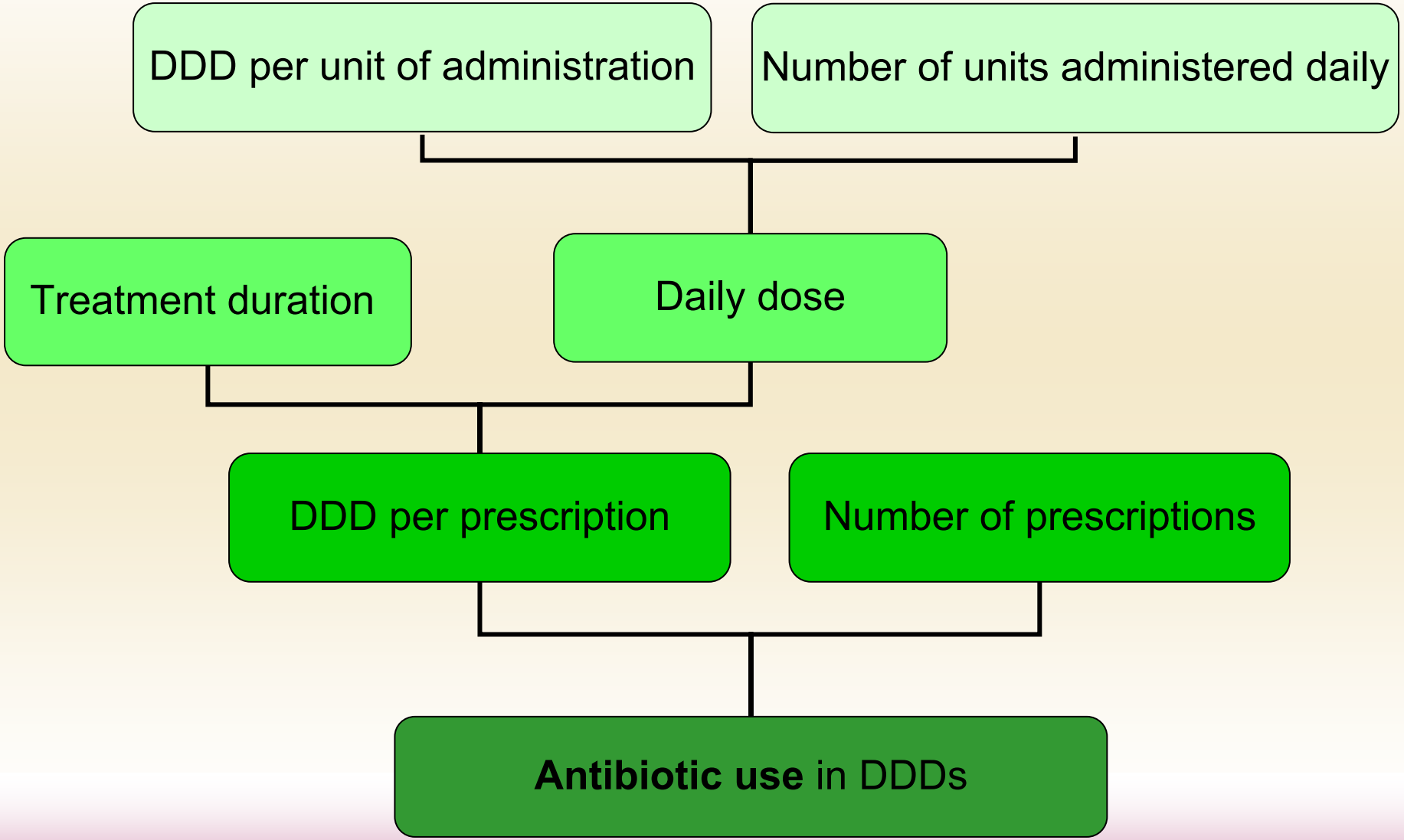


Regional Variation of Outpatient Antibiotic Use in Germany



Caveats of DDDs…

Calculation scheme



Amoxicillin J01CA04

Country	France	Italy	Spain	UK
Prescr. per 1000 inh. per day	0.33	0.19	0.52	0.50
Prescriptions (% of total)	18.6%	9.3%	17.6%	28.5%
DDD per day				
Treatment in days				
Total DDD per course				

18.4% of all prescriptions

Amoxicillin J01CA04

Country	France	Italy	Spain	UK
Prescr. per 1000 inh. per day	0.33	0.19	0.52	0.50
Prescriptions (% of total)	18.6%	9.3%	17.6%	28.5%
DDD per day	1.65	1.90	1.61	0.93
Treatment in days				
Total DDD per course				

Amoxicillin J01CA04

Country	France	Italy	Spain	UK
Prescr. per 1000 inh. per day	0.33	0.19	0.52	0.50
Prescriptions (% of total)	18.6%	9.3%	17.6%	28.5%
DDD per day	1.65	1.90	1.61	0.93
Treatment in days	7.00	7.19	8.89	6.69
Total DDD per course				

Amoxicillin J01CA04

Country	France	Italy	Spain	UK
Prescr. per 1000 inh. per day	0.33	0.19	0.52	0.50
Prescriptions (% of total)	18.6%	9.3%	17.6%	28.5%
DDD per day	1.65	1.90	1.61	0.93
Treatment in days	7.00	7.19	8.89	6.69
Total DDD per course	11.49	13.52	14.29	6.18

Co-amoxiclav J01CR02

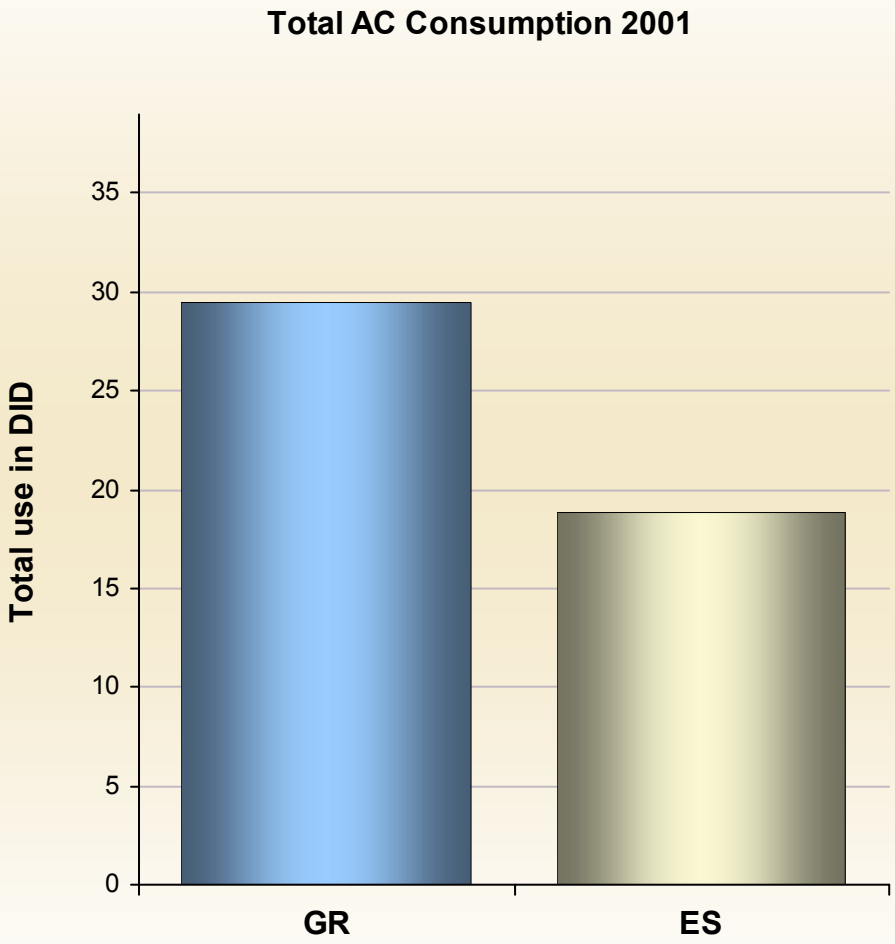
Country	France	Italy	Spain	UK
Prescr. per 1000 inh. per day	0.17	0.31	0.68	0.09
Prescriptions (% of total)	9.2%	15.4%	24.0%	5.3%
DDD per day	1.09	1.54	1.50	0.85
Treatment in days	7.80	6.99	9.23	7.75
Total DDD per course	8.78	10.62	13.26	6.56

Clarithromycin J01FA09

Country	France	Italy	Spain	UK
Prescr. per 1000 inh. per day	0.12	0.18	0.21	0.05
Prescriptions (% of total)	6.7%	9.2%	7.3%	2.7%
DDD per day	1.04	1.40	1.32	1.31
Treatment in days	7.73	8.56	8.28	10.78
Total DDD per course	8.04	11.76	11.01	12.25

Caveats of Data Sources…

Sales vs. Reimbursement Data

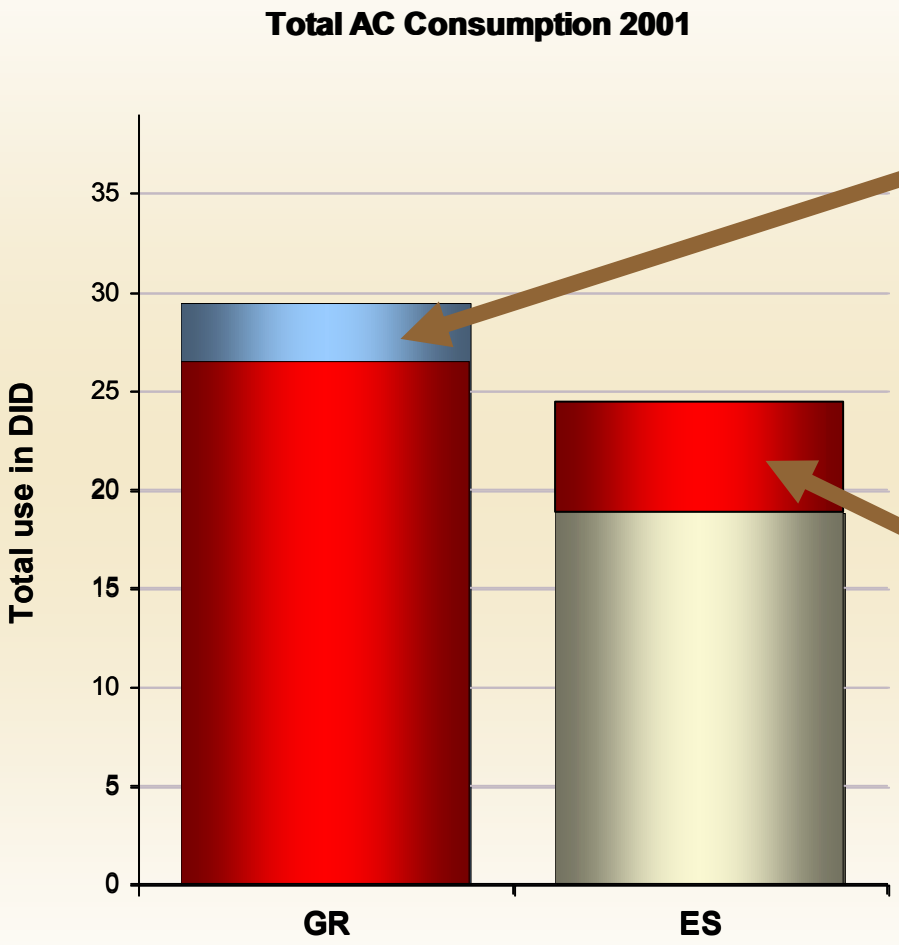


Greece

✖

Spain

Sales vs. Reimbursement Data



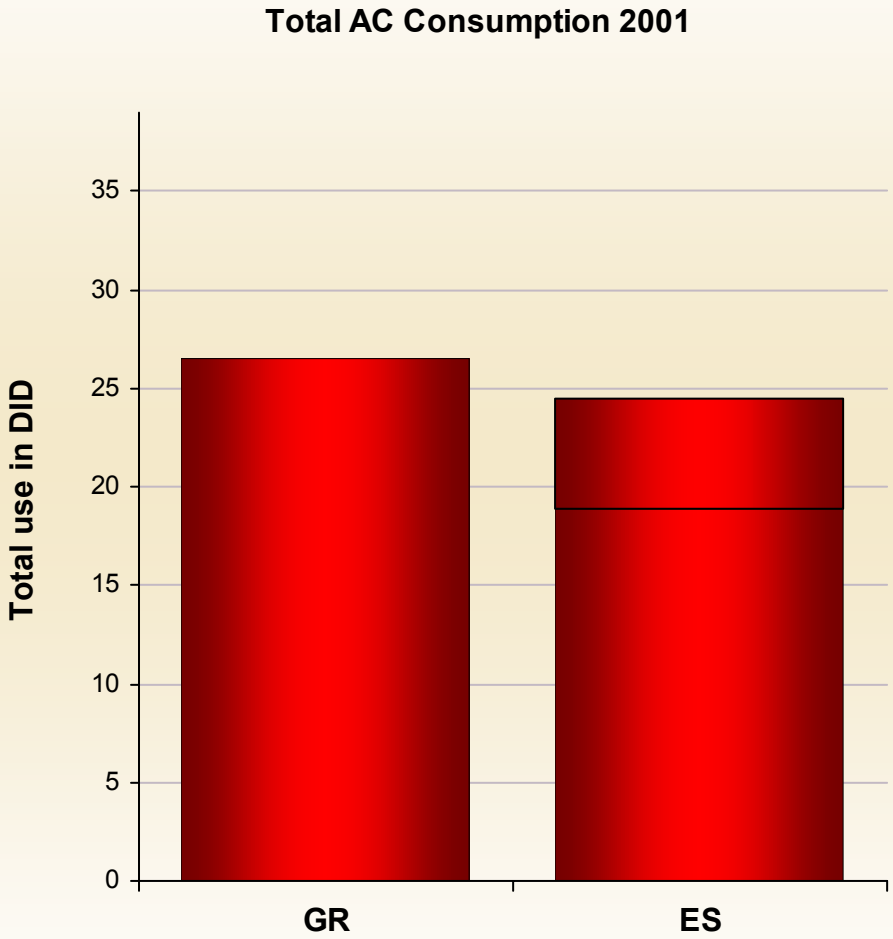
10% overestimated due to: Parallel exports

Private hospitals in AC

30% underestimated due to:

OTC sales exclusion

Sales vs. Reimbursement Data

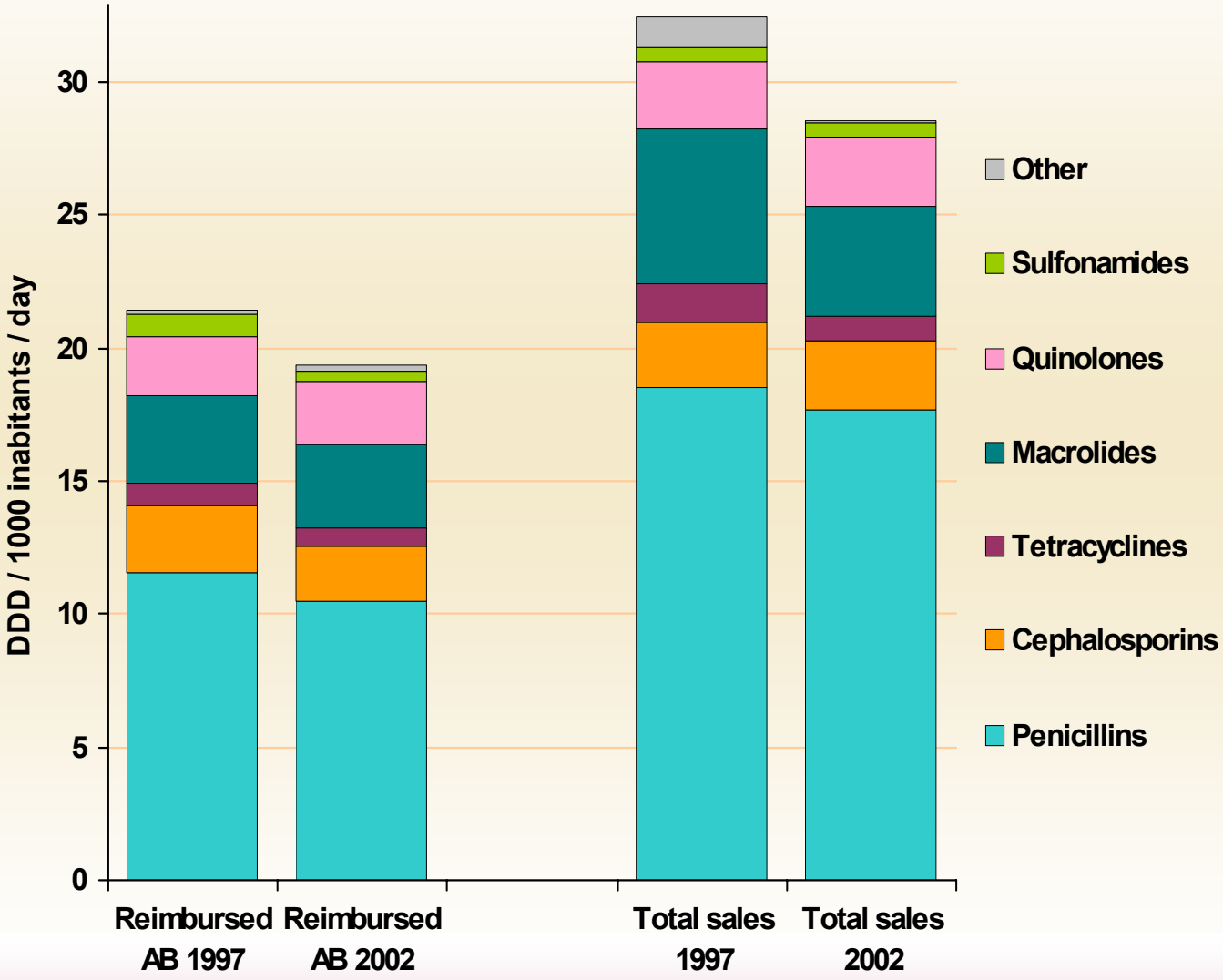


Greece

✖

Spain

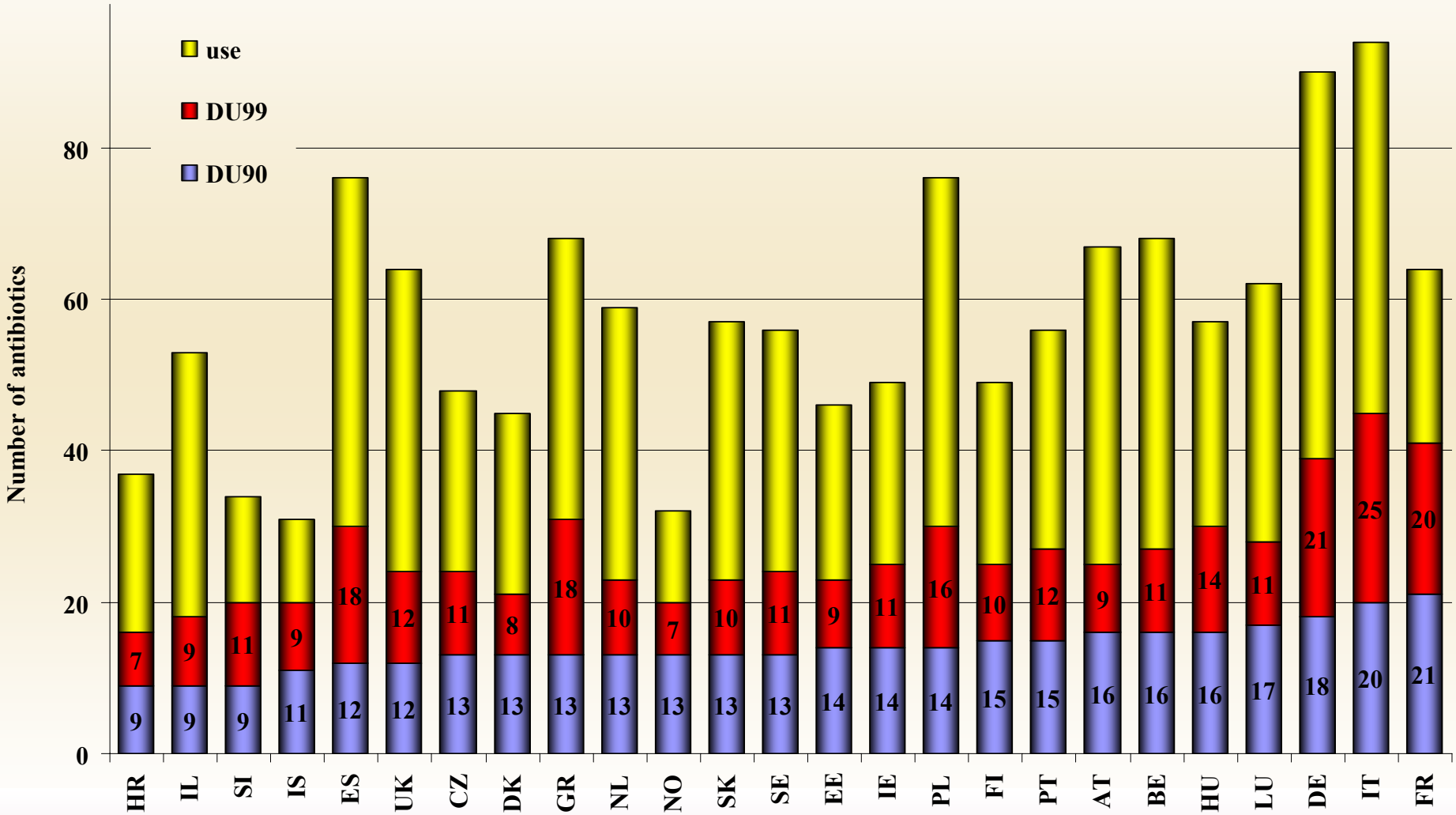
Assessment of OTC sales in Spain



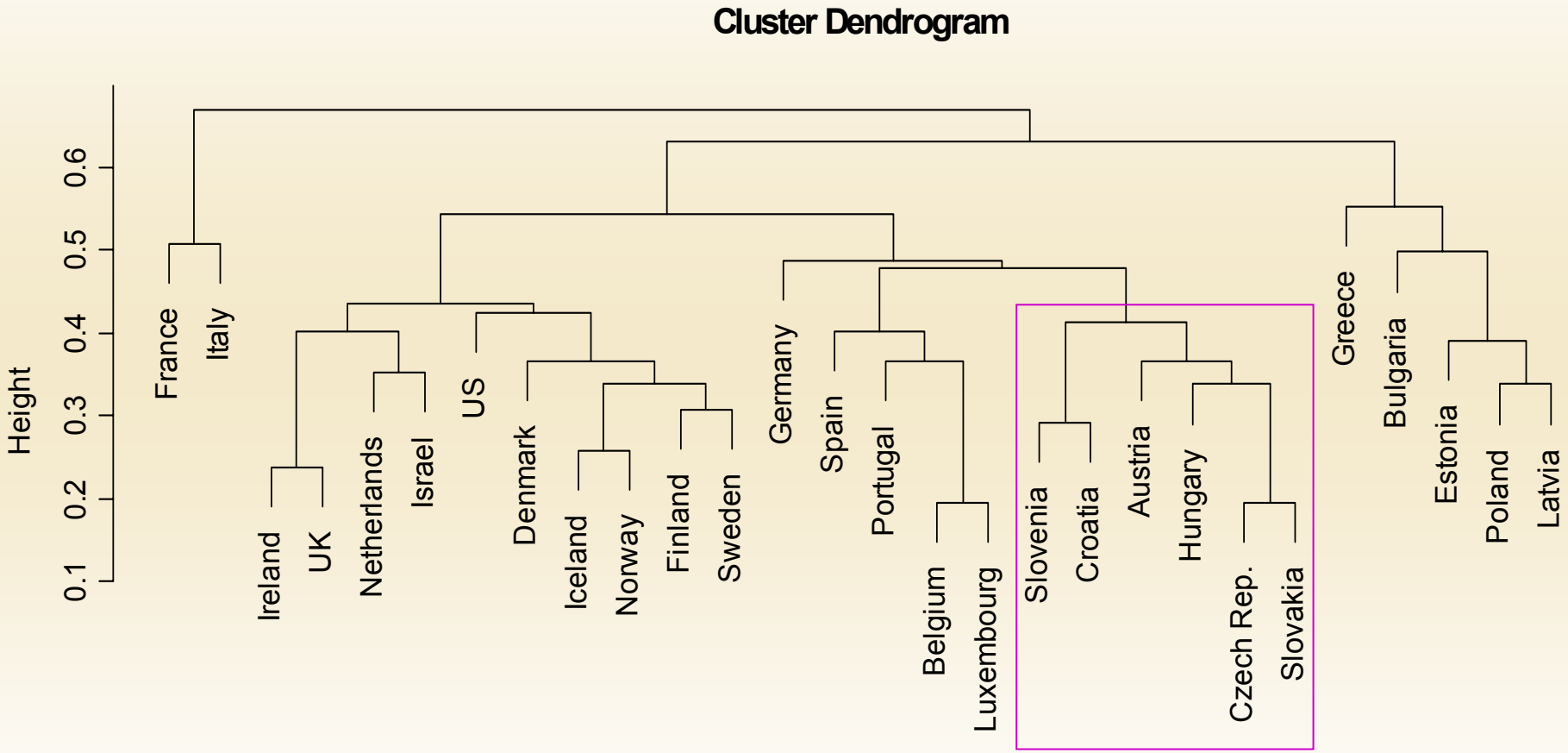
Ferech M, Campos J et al.
Analysis of Sales Data (SD) and Reimbursement Data (RD) as a Tool to Assess OTC Antibiotic Dispensing. 45th ICAAC, Washington2005

Assessment of variability in the number of routinely used antibiotics to treat outpatients using the DU90% method

Antibiotic therapeutic arsenal in 2003

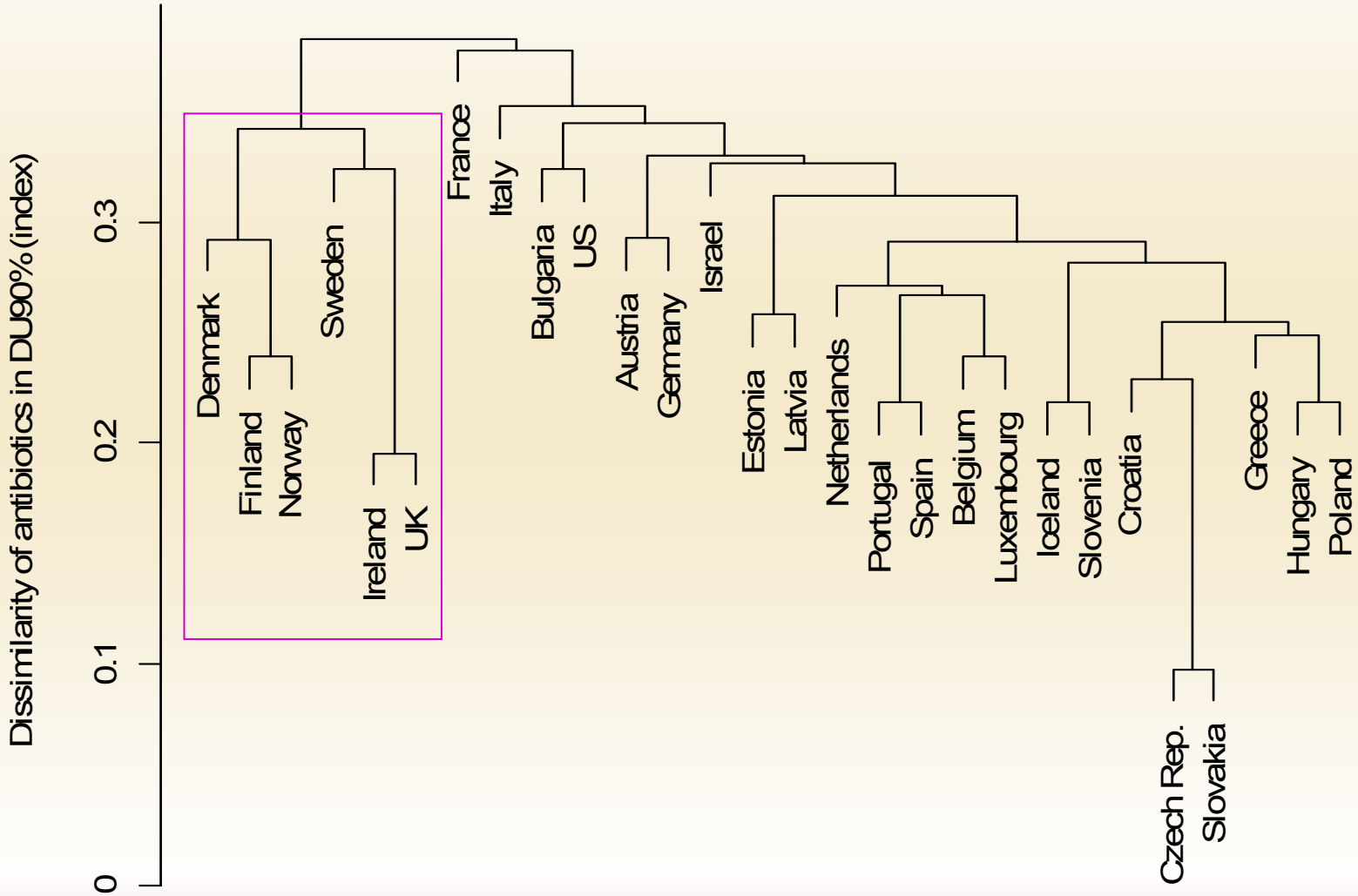


Correlation between countries – DU 99%



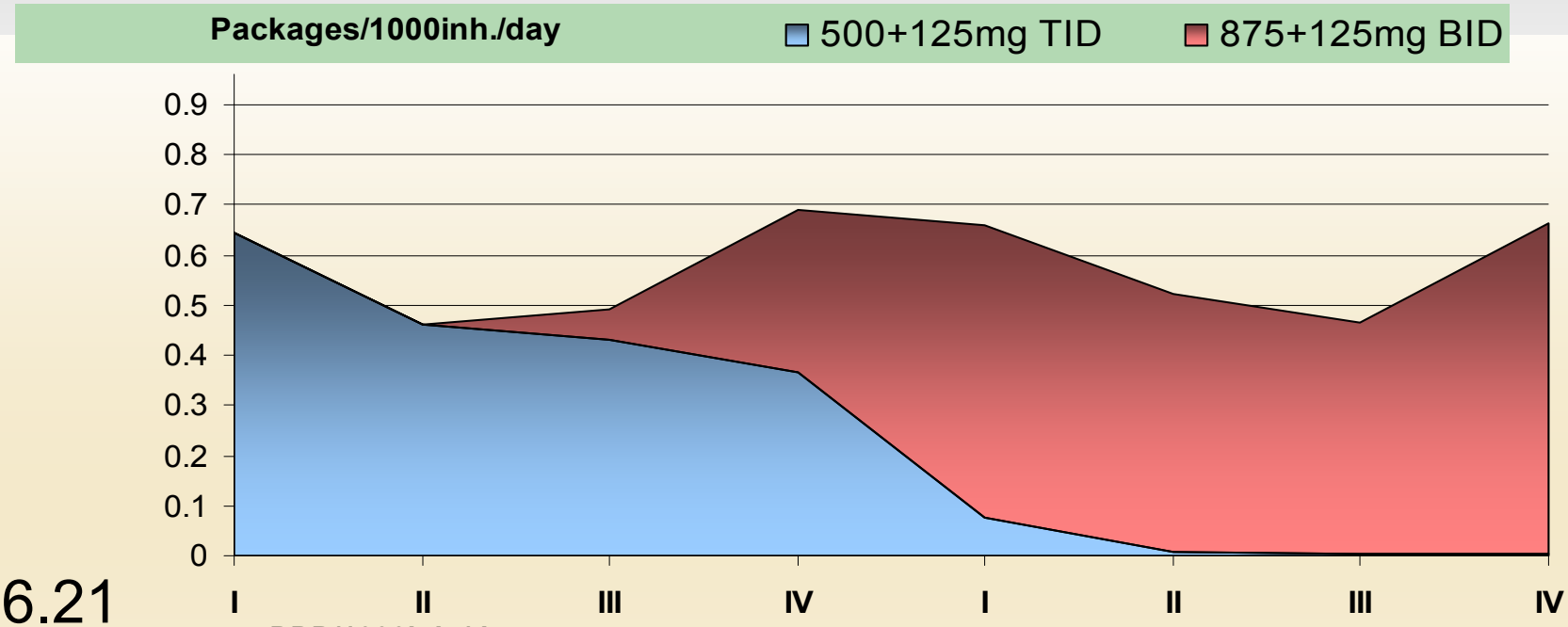
A hierarchical cluster analysis

Correlation between countries – DU 90%



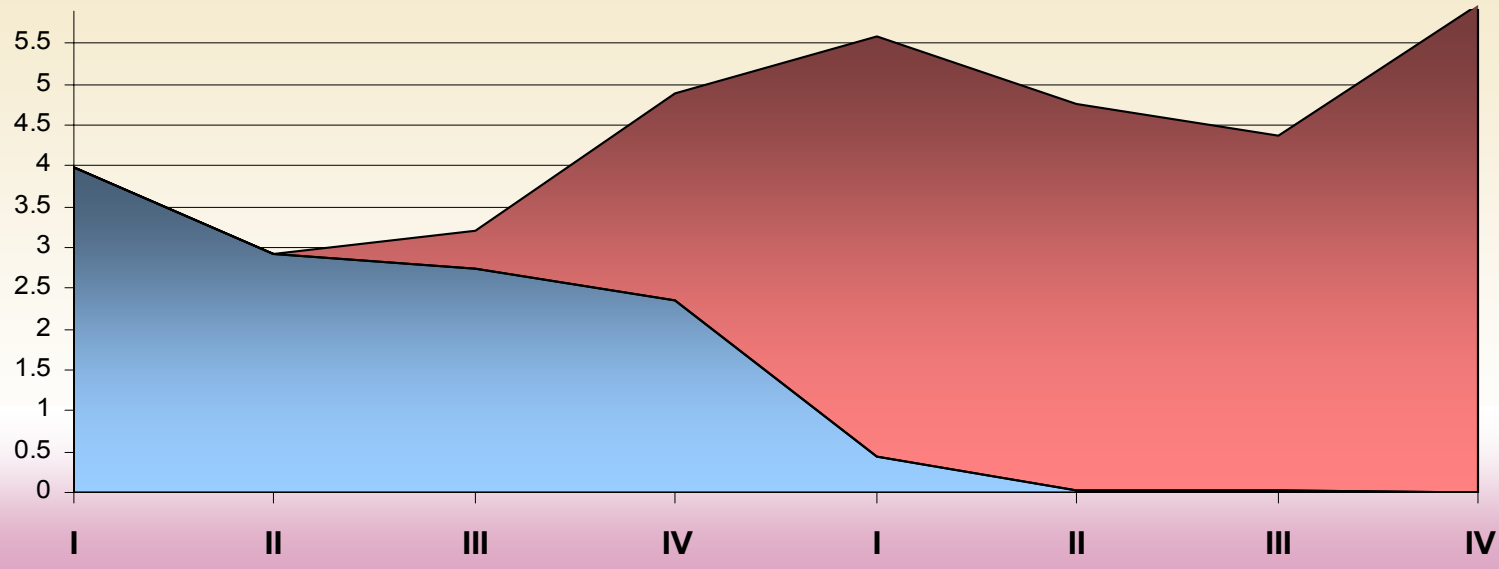
Outpatient Antibiotic Use
DDD versus Packages

Co-amoxiclav use in Croatia 2001-2002

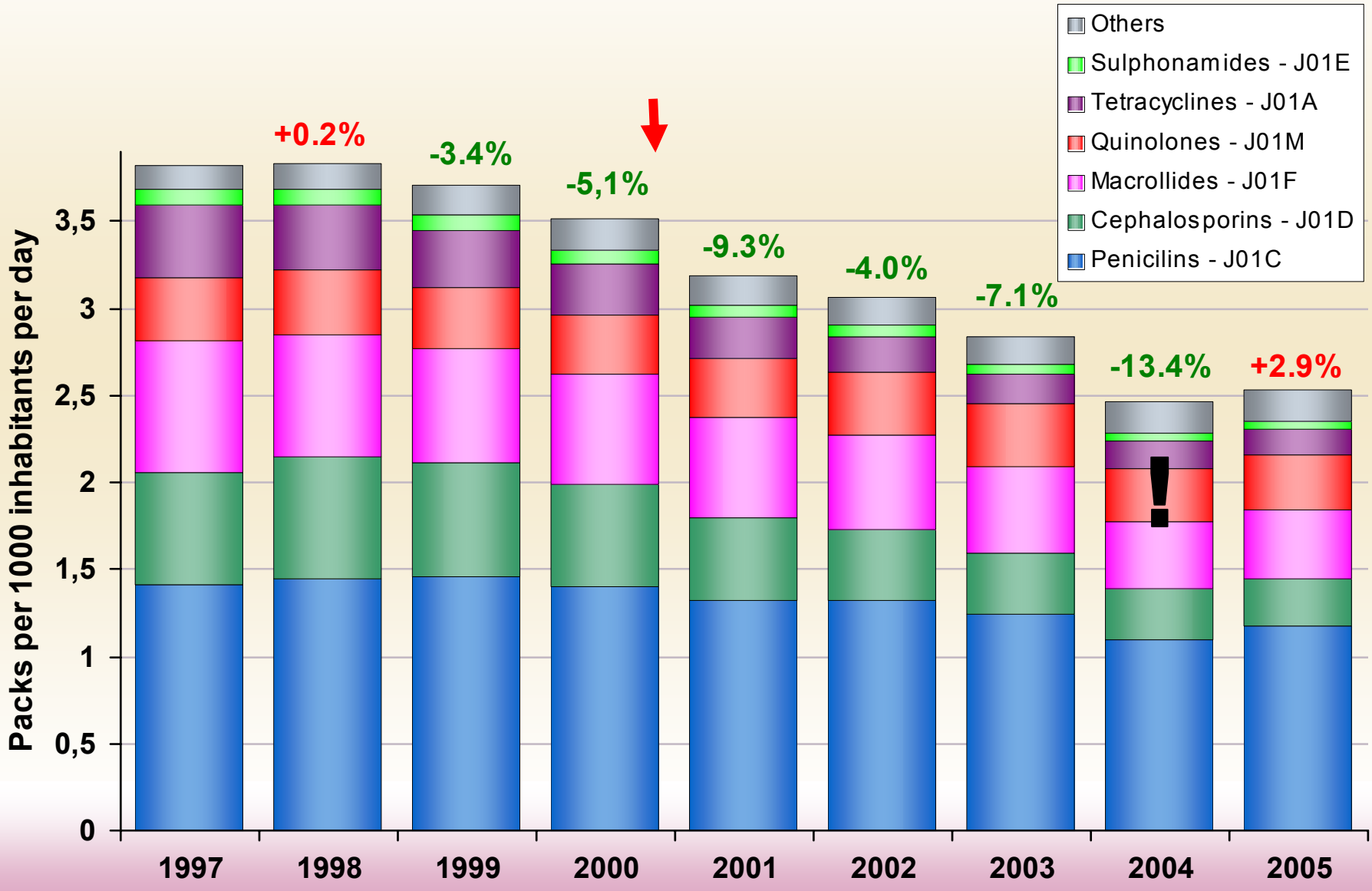


6.21 DDD/ pack

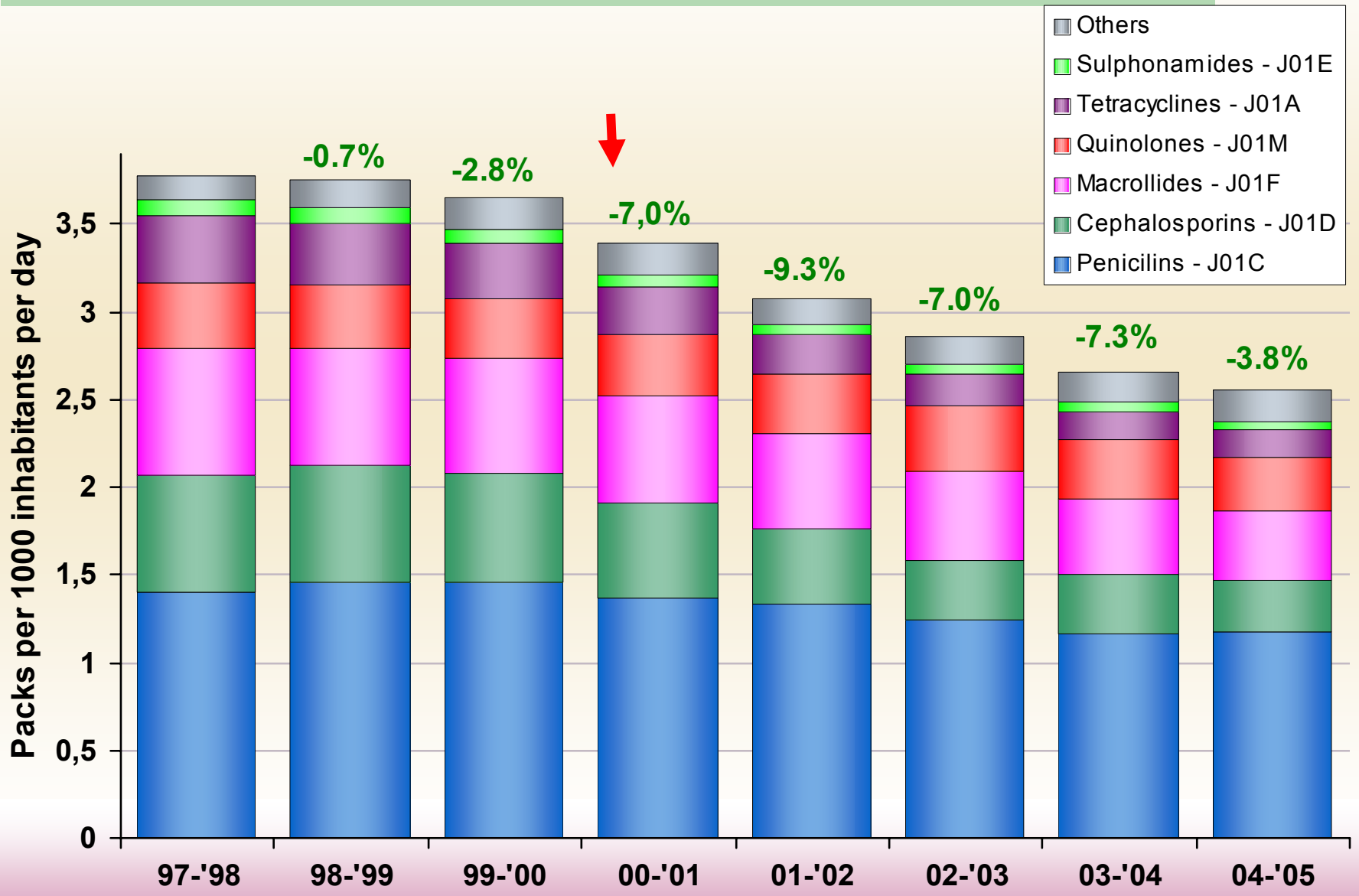
9.03 DDD/ pack



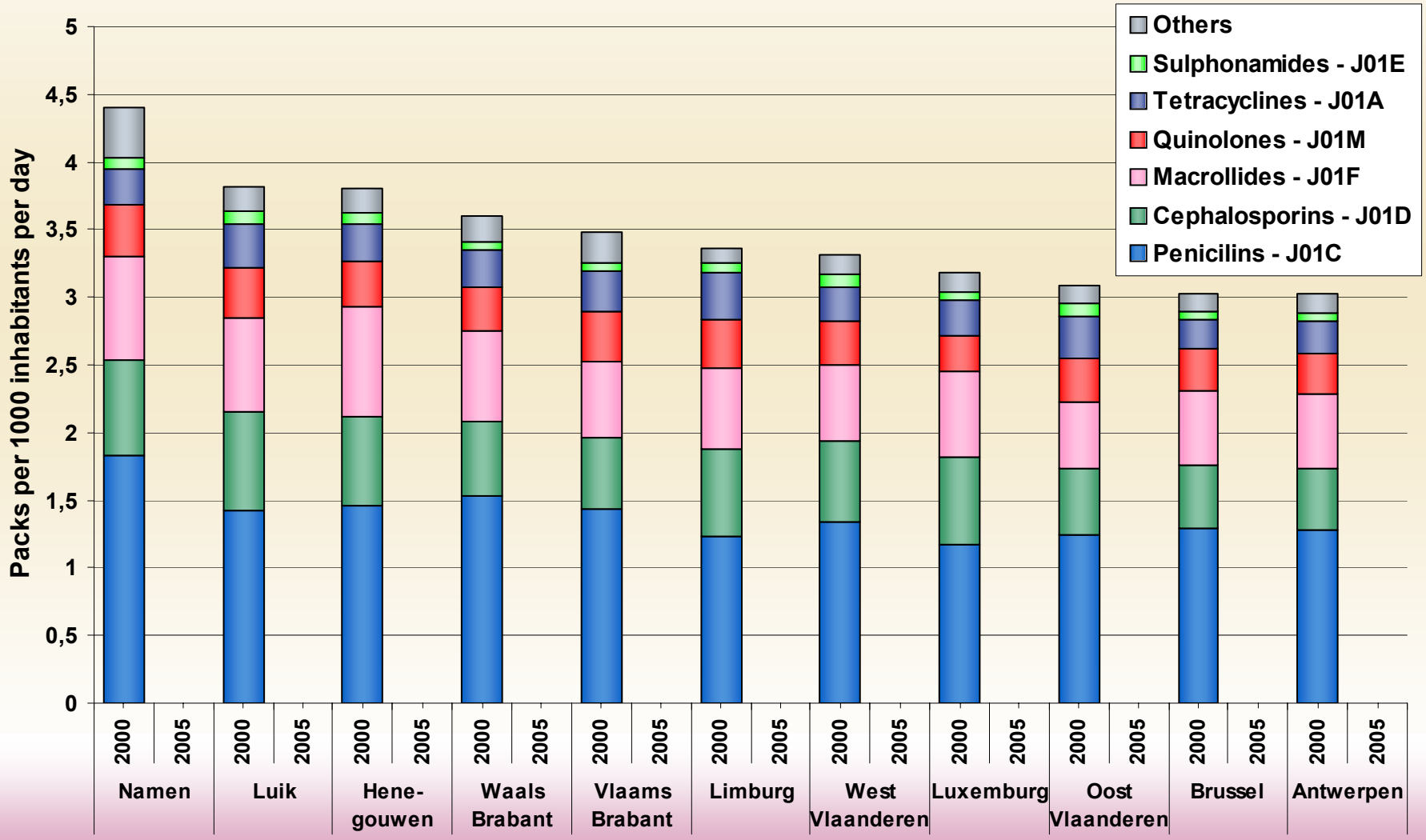
Antibiotic Use in Packages/1000 Inhabitants/day, 1997-2005, Januari - December



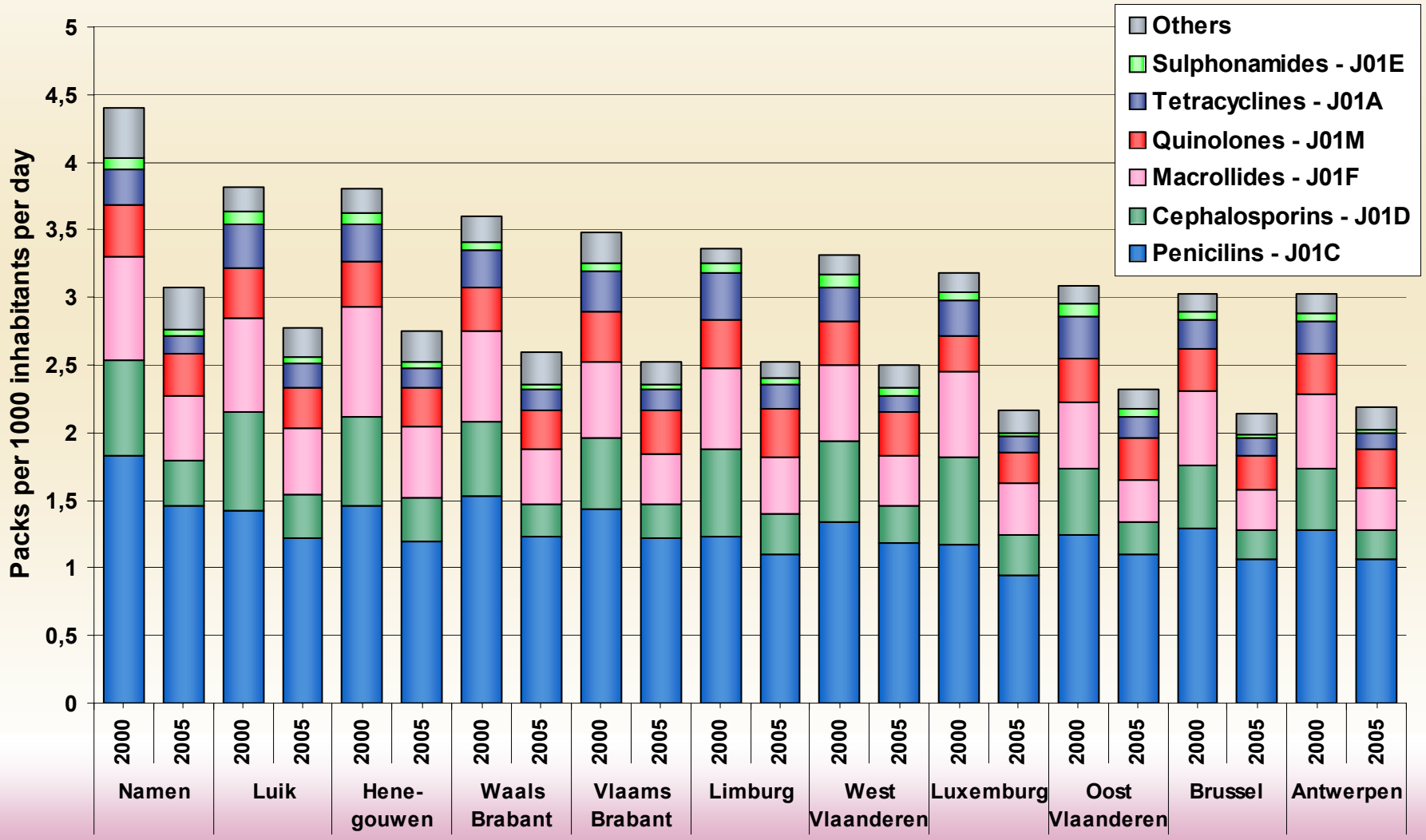
Antibiotic Use in Packages/1000 Inhabitants/Day, 1997 – 2005, June - July



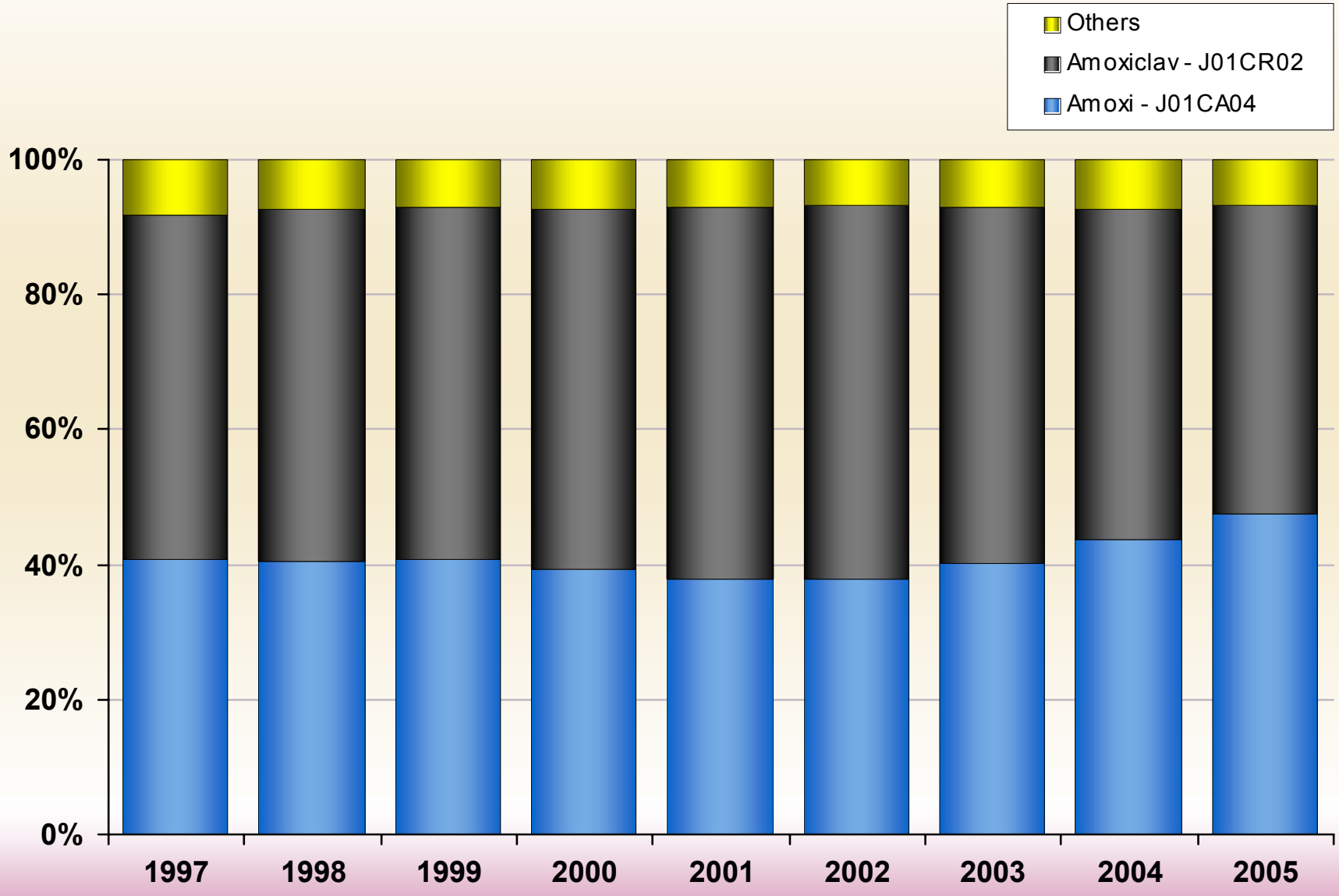
Antibiotic Use in Packages/1000 Inwoners/Day, per Province, 2000 vs 2005



Antibiotic Use in Packages/1000 Inhabitants/Day, per Province, 2000 vs 2005



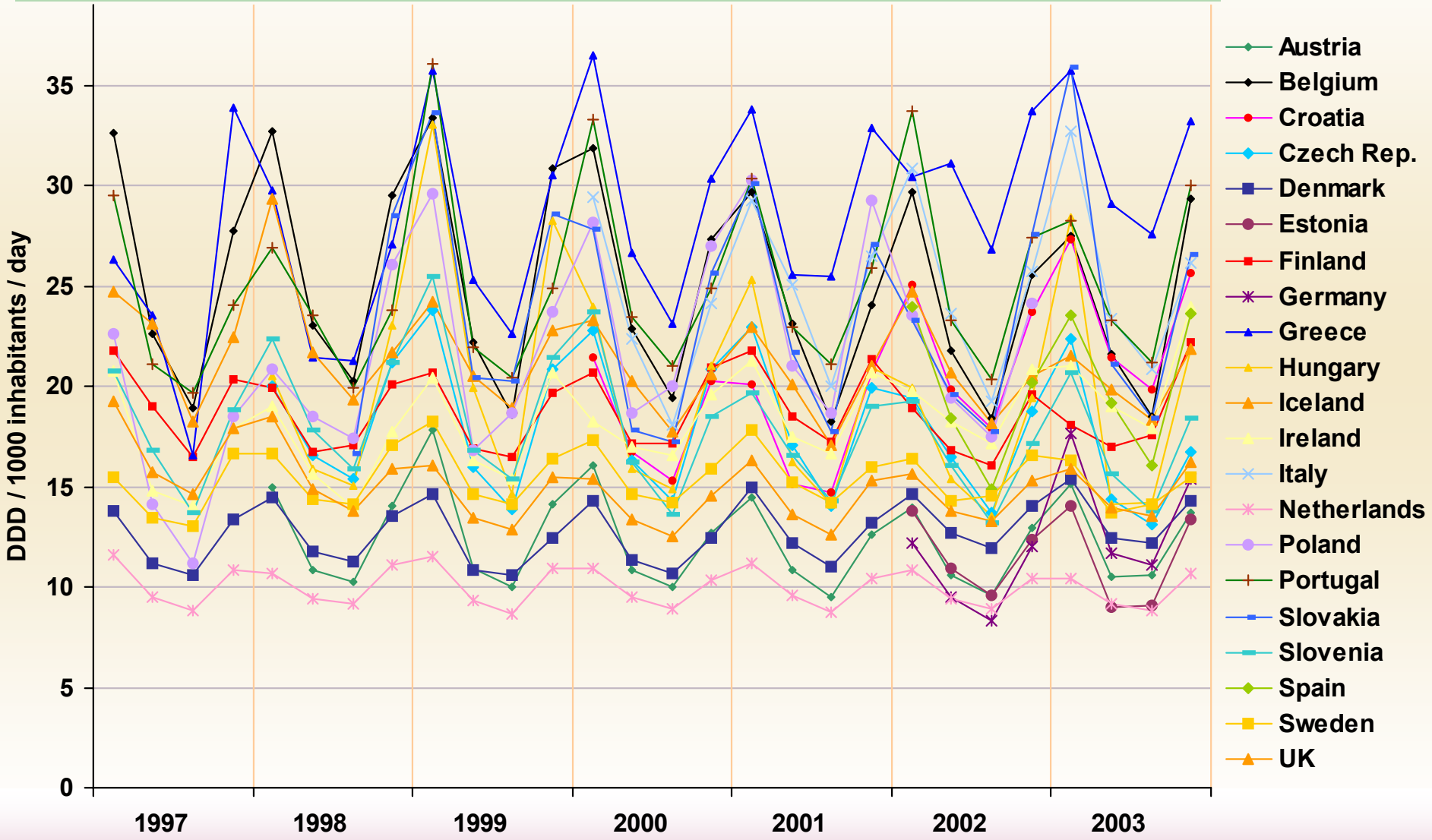
Proportionel Use of the Penicillins, in Packages/1000 Inhabitants/Day, 1997 - 2005



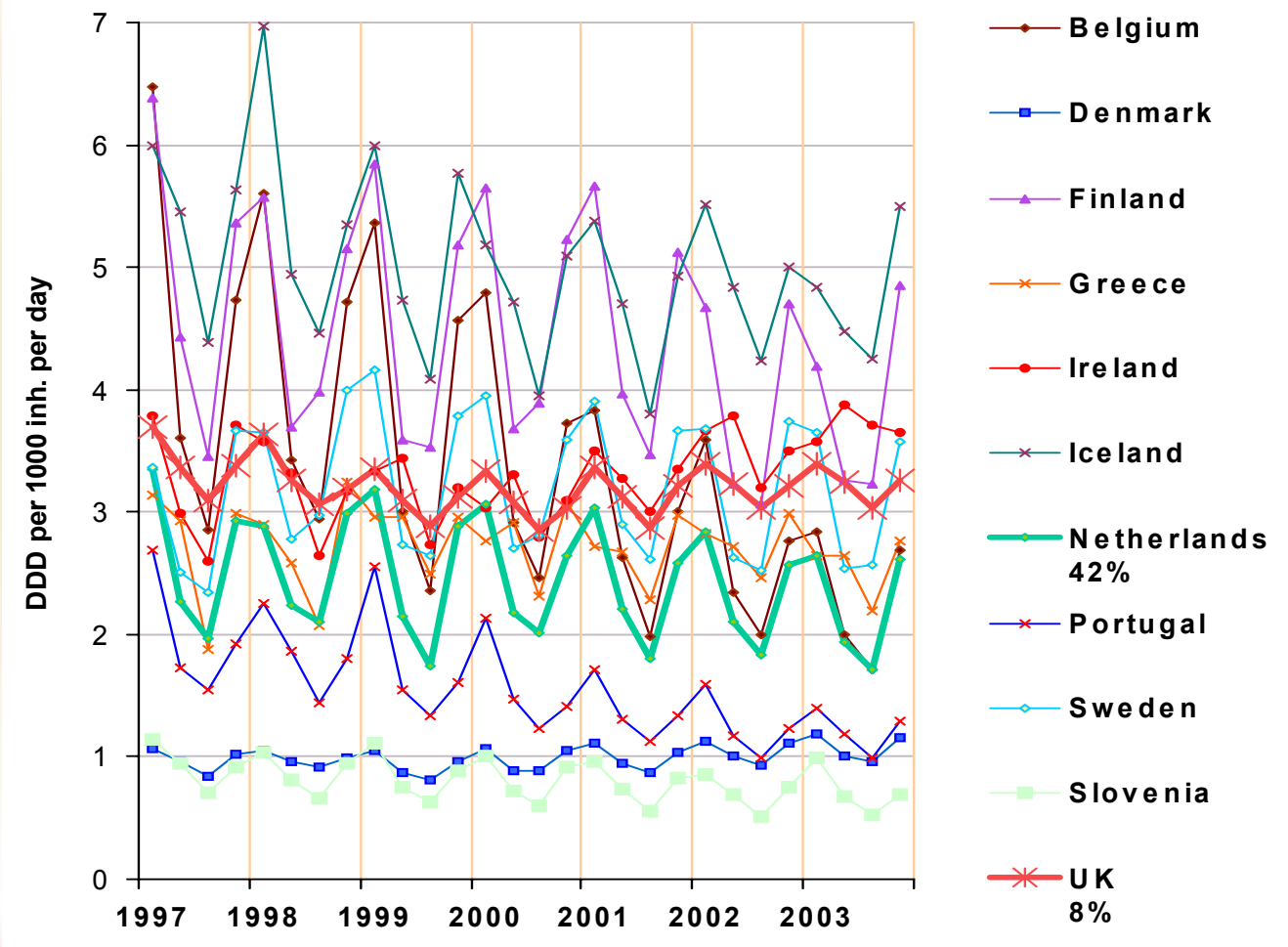
Outpatient Antibiotic Use:

as an indicator of appropriate and inappropriate antibiotic prescribing

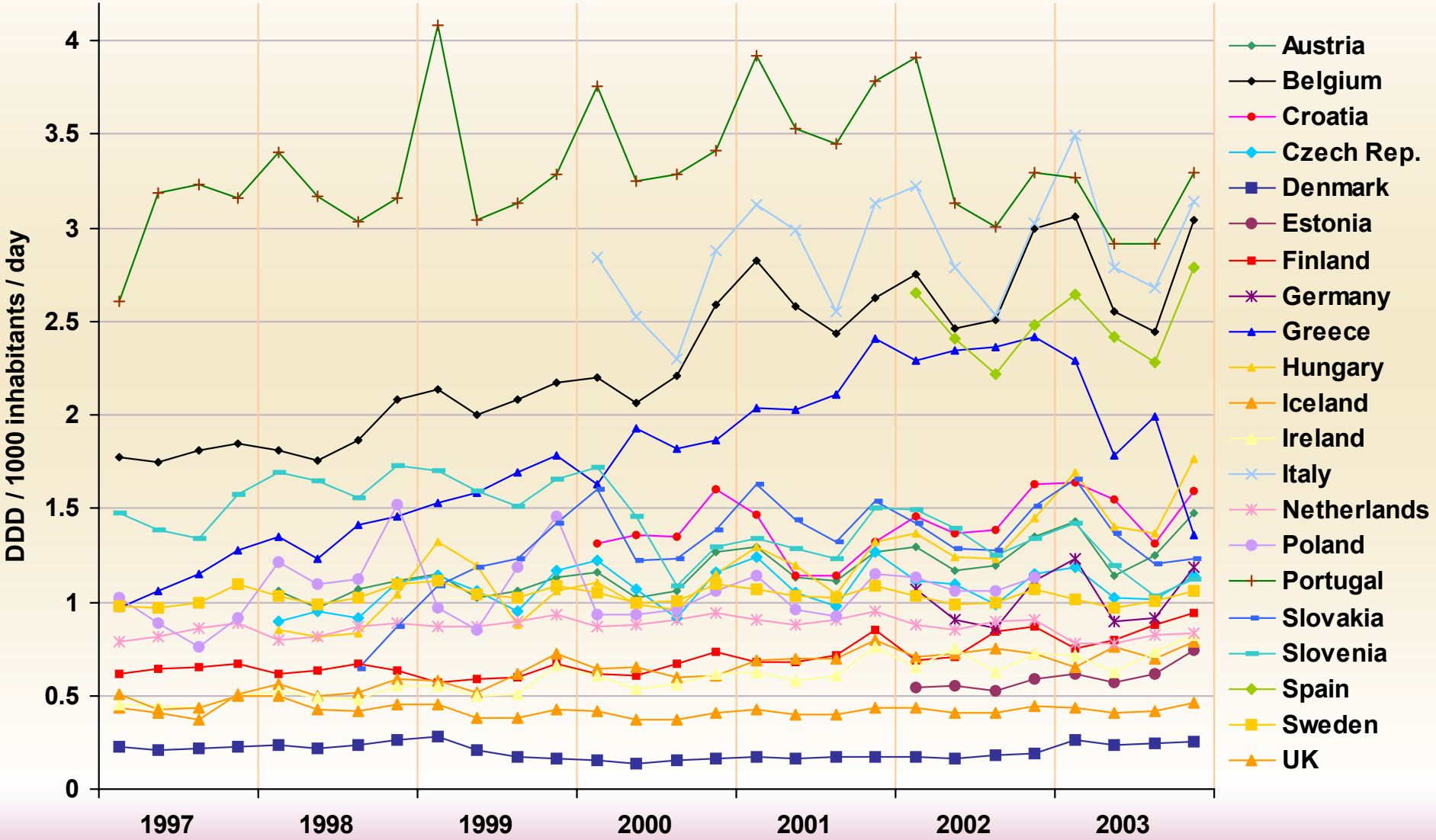
Seasonal Variation of Outpatient Antibiotic Use in Europe



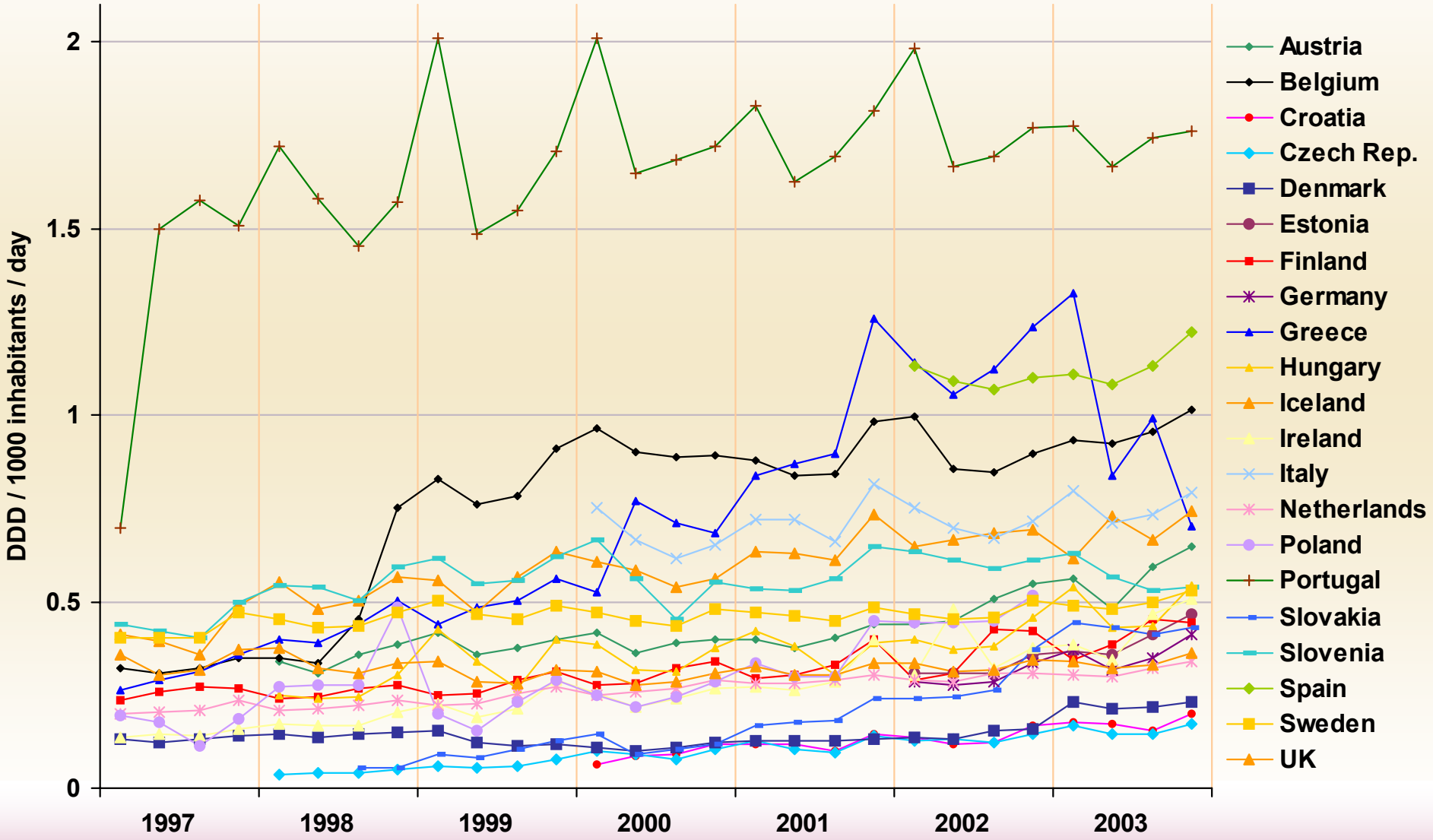
Seasonal Variation of Outpatient Tetracyclines Use



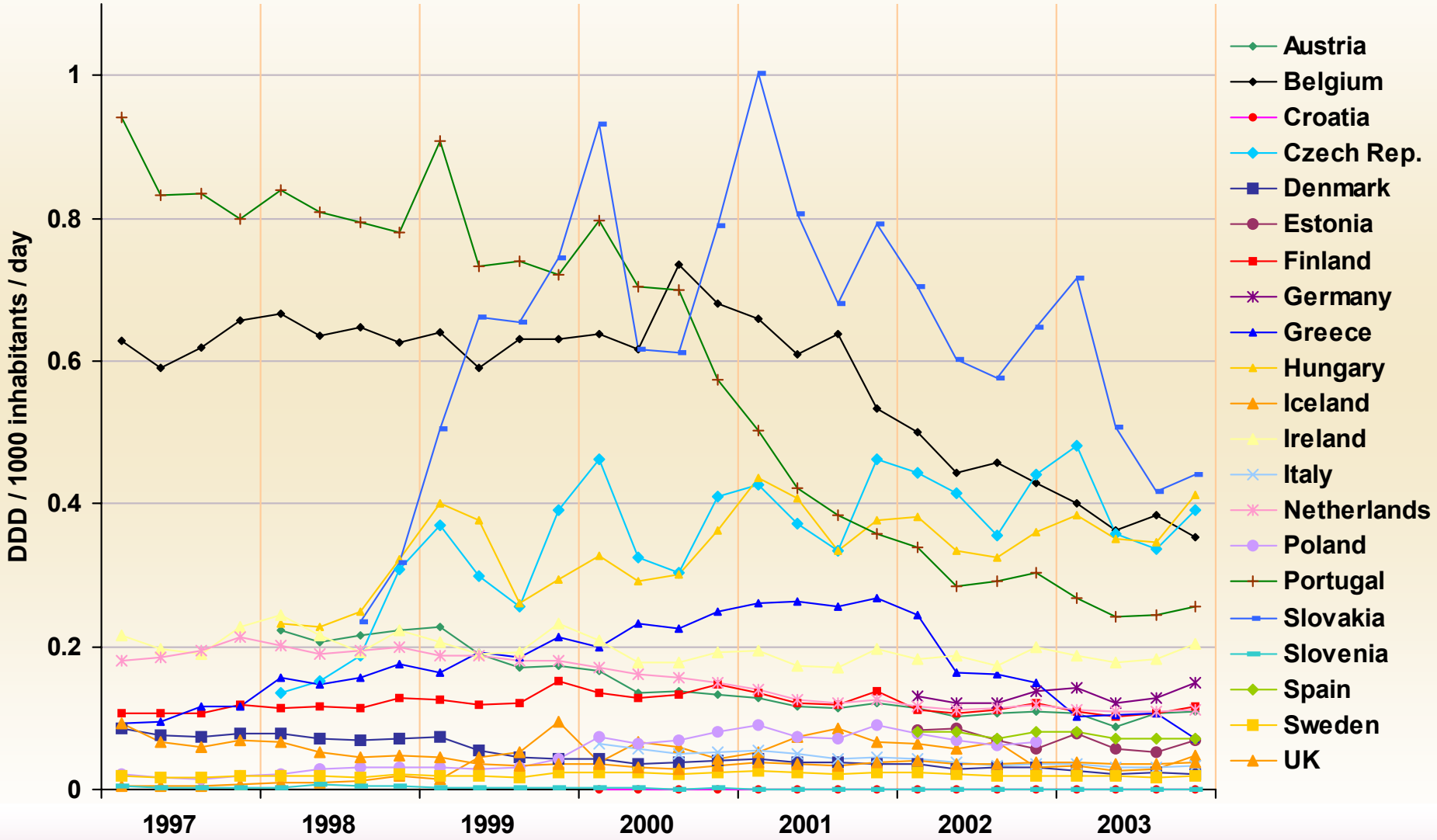
Seasonal Variation of Outpatient Quinolone Use in Europe with Quarterly Data for 1997-2003. (WHO ATC/DDD version 2003)



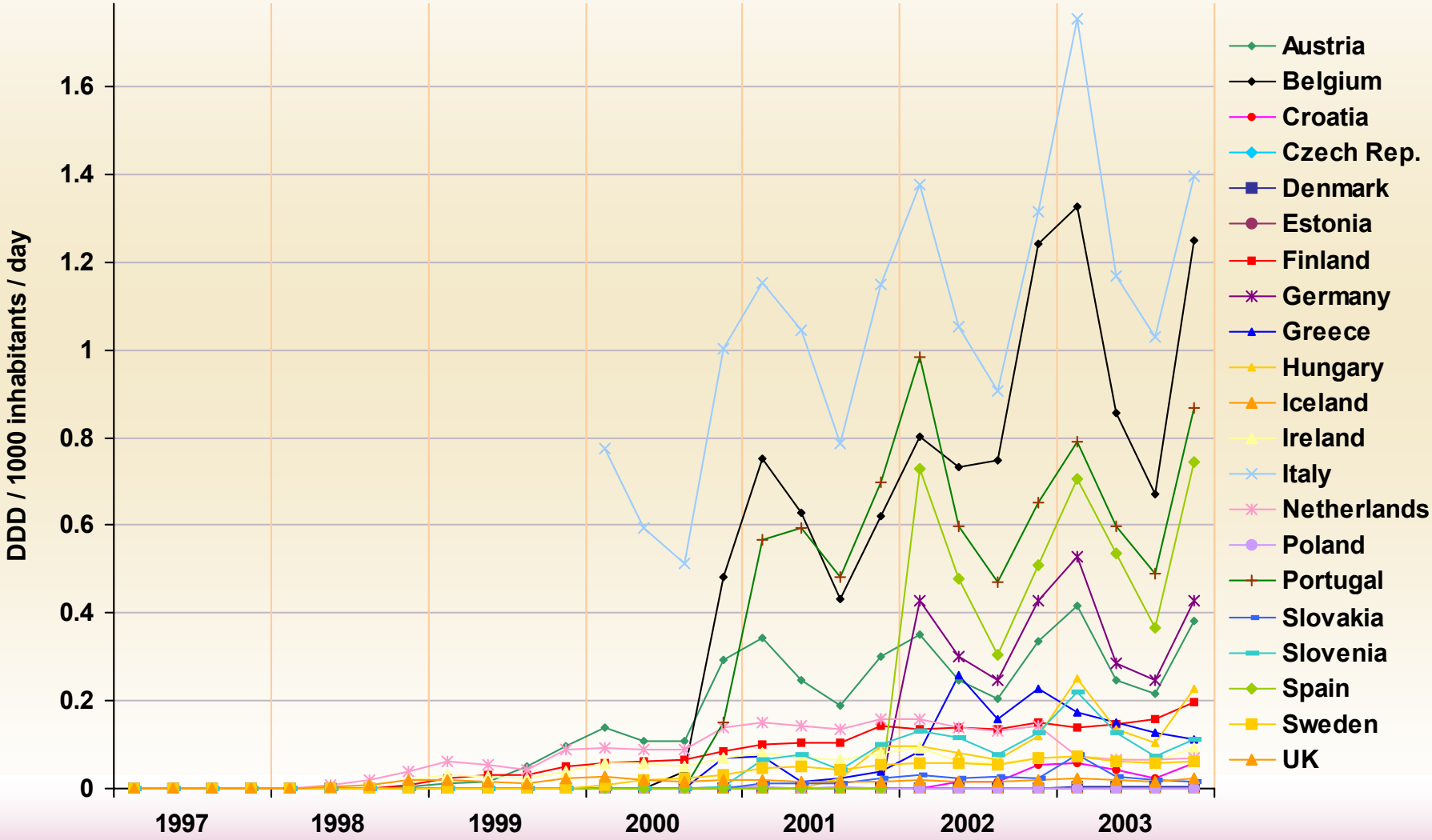
Seasonal Variation of Outpatient Ciprofloxacin Use with Quarterly Data for 1997-2003.



Seasonal Variation of Outpatient Ofloxacin Use with Quarterly Data for 1997-2003.



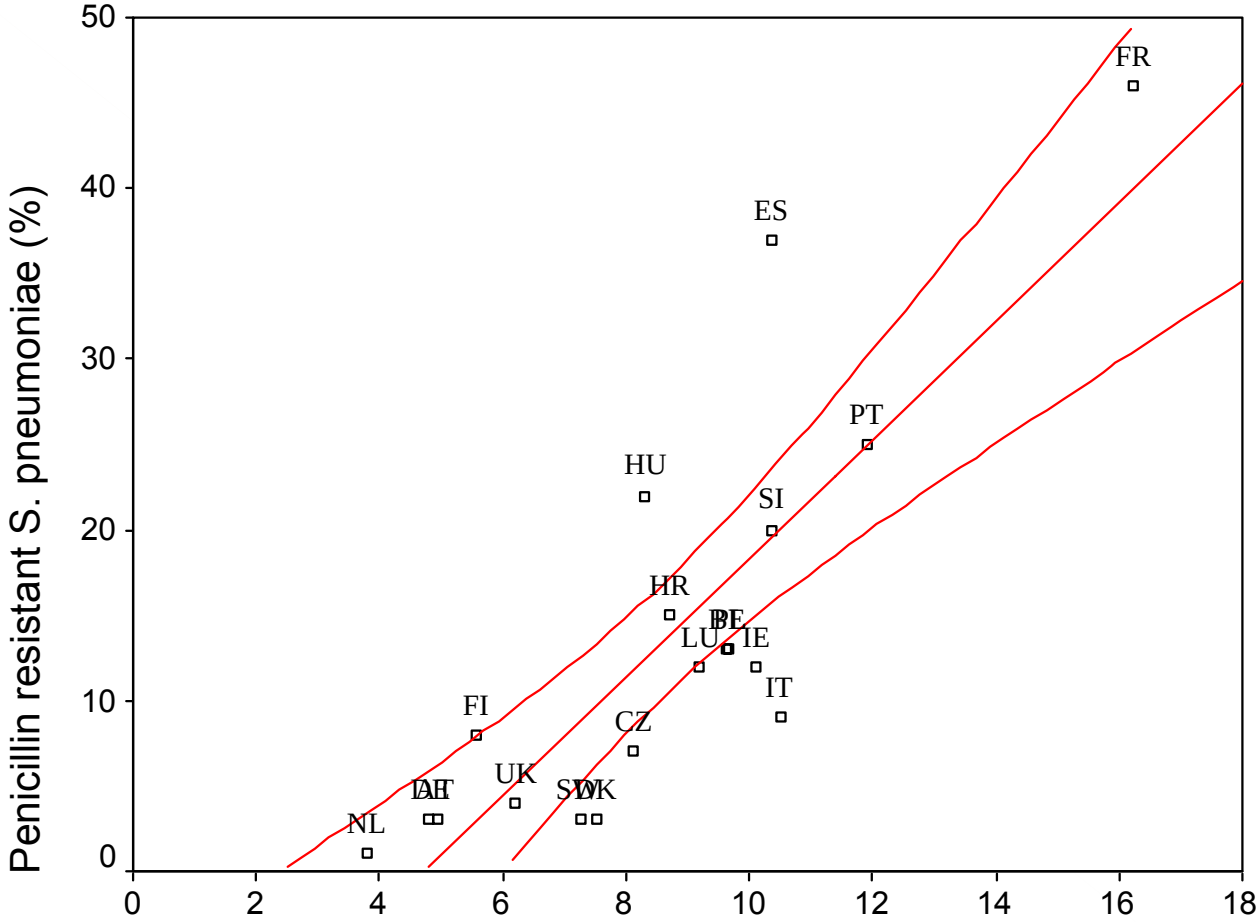
Seasonal Variation of levofloxacin+moxifloxacin Use with Quarterly Data for 1997-2003. (WHO ATC/DDD version 2003)



Outpatient Antibiotic Use:

link with resistance

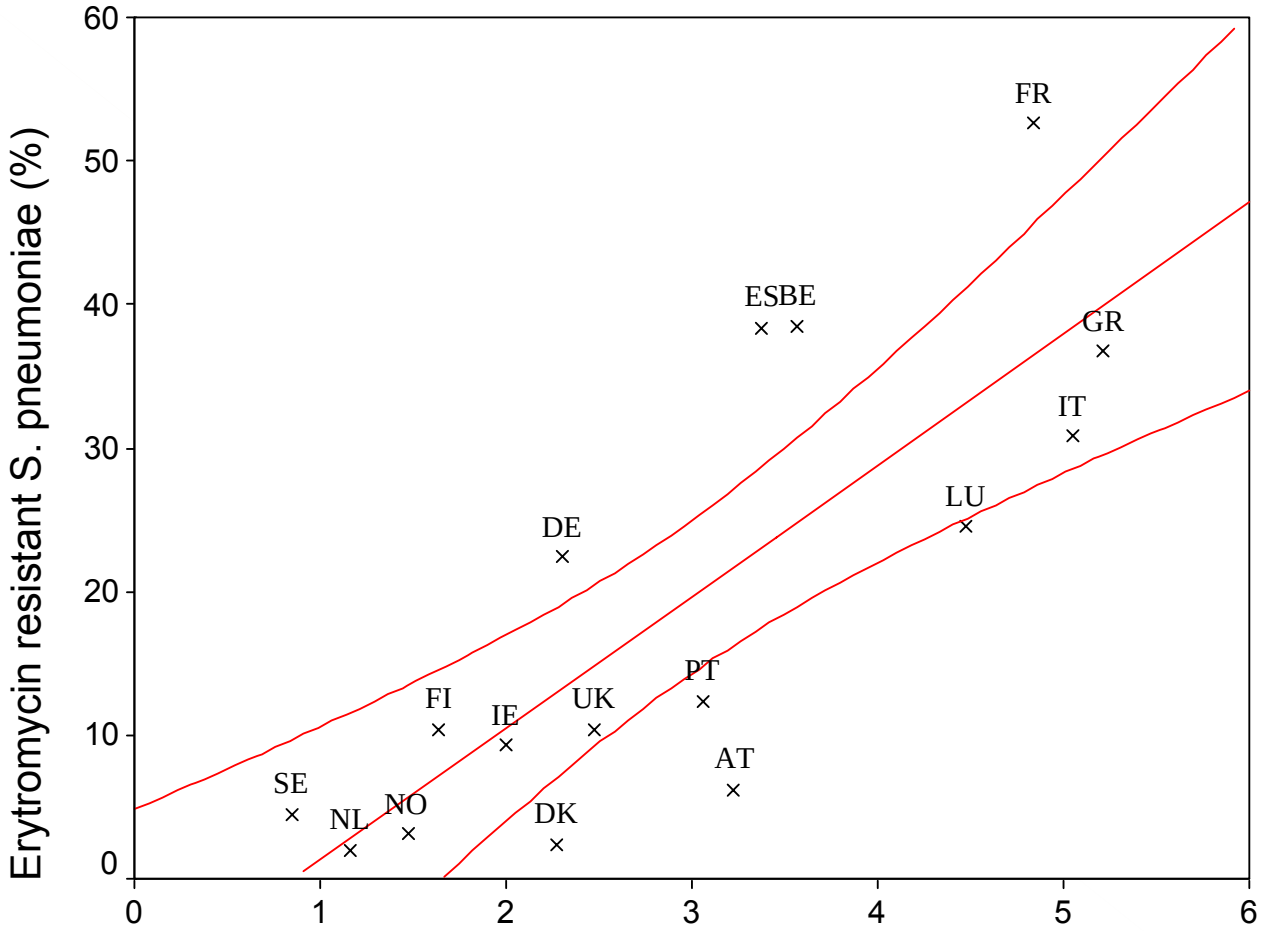
Organism year of isolation *[source of information]*	Antibiotic resistance	Antibiotic use - ATC group (year of data)	No. of countries	Spearman correlation (r) (confidence interval)	P-value
***S. pneumoniae* 2001 [7]**	***Penicillin***	***Penicillins - J01C (2000)***	***19***	***0.84 (0.62-0.94)***	***< 0.001***



Consumption of penicillins (J01C) in DID, AC 2000

Goossens et al, Lancet, February 2005

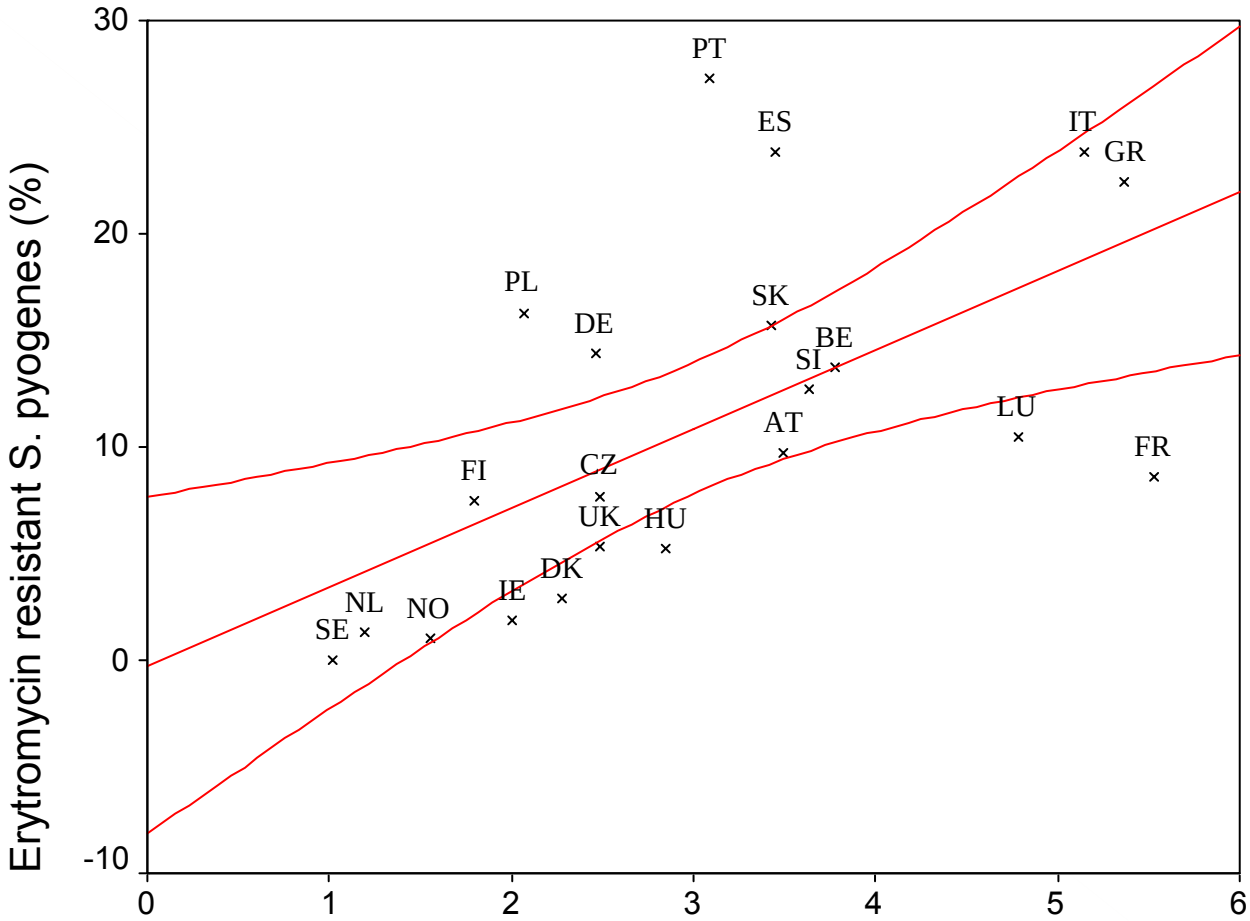
Organism year of isolation *[source of information]*	Antibiotic resistance	Antibiotic use - ATC group (year of data)	No. of countries	Spearman correlation (r) (confidence interval)	P-value
S. pneumoniae **1999/2000** ***[8]***	**Erythromycin**	**Macrolides - J01FA (1998)**	**16**	**0.83 (0.67-0.94)**	**< 0.001**



Consumption of macrolides (J01FA) in DID, AC 1998

Goossens et al, Lancet, February 2005

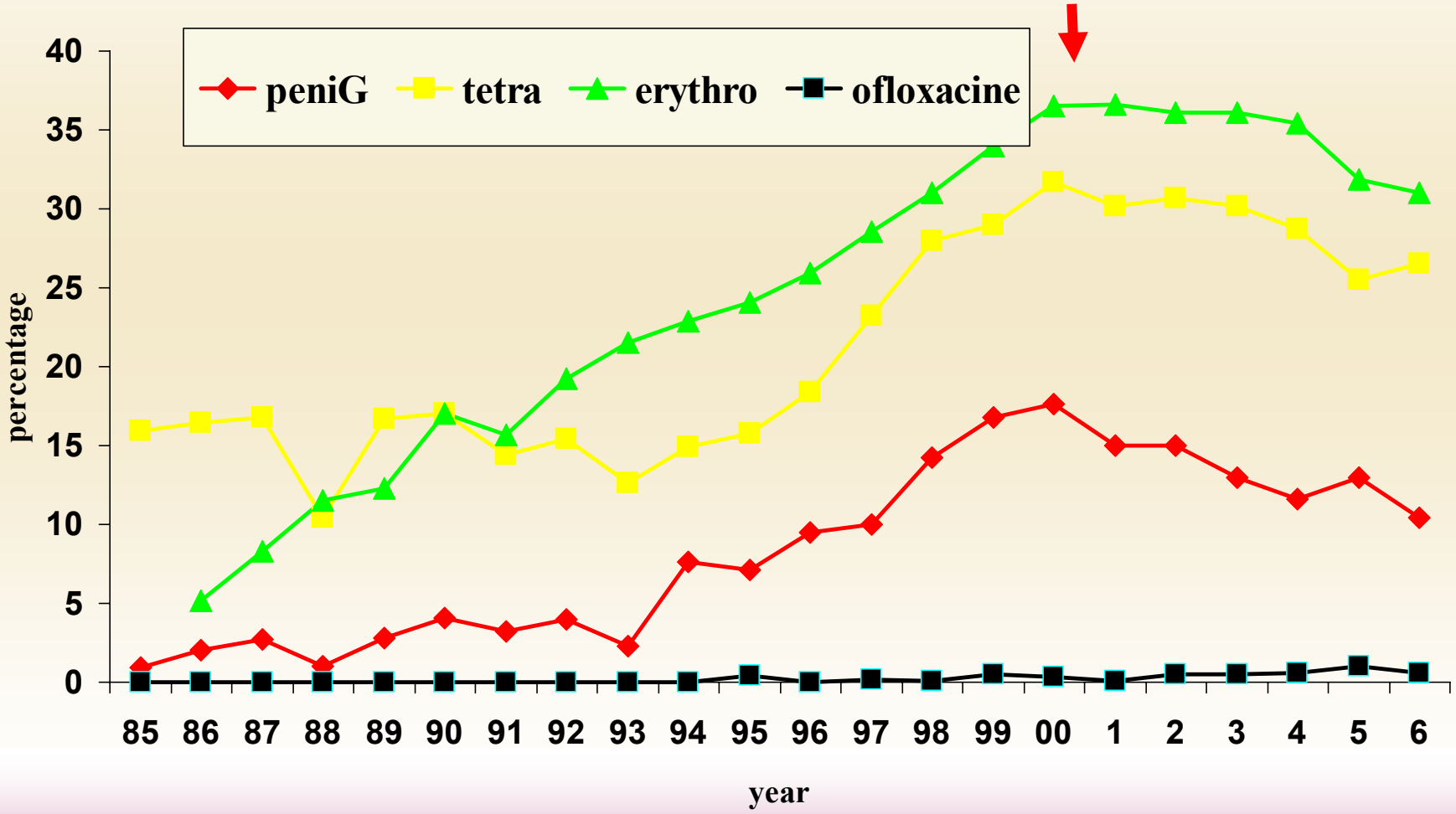
Organism year of isolation *[source of information]*	Antibiotic resistance	Antibiotic use - ATC group (year of data)	No. of countries	Spearman correlation (r) (confidence interval)	P-value
S. pyogenes 1999/2000 [8]	***Erythromycin***	***Macrolides - J01FA and lincosamides - J01FF (1998)***	***21***	***0.65 (0.25-0.86)***	***0.002***



Consumption of MLS (J01F) in DID, AC 1998

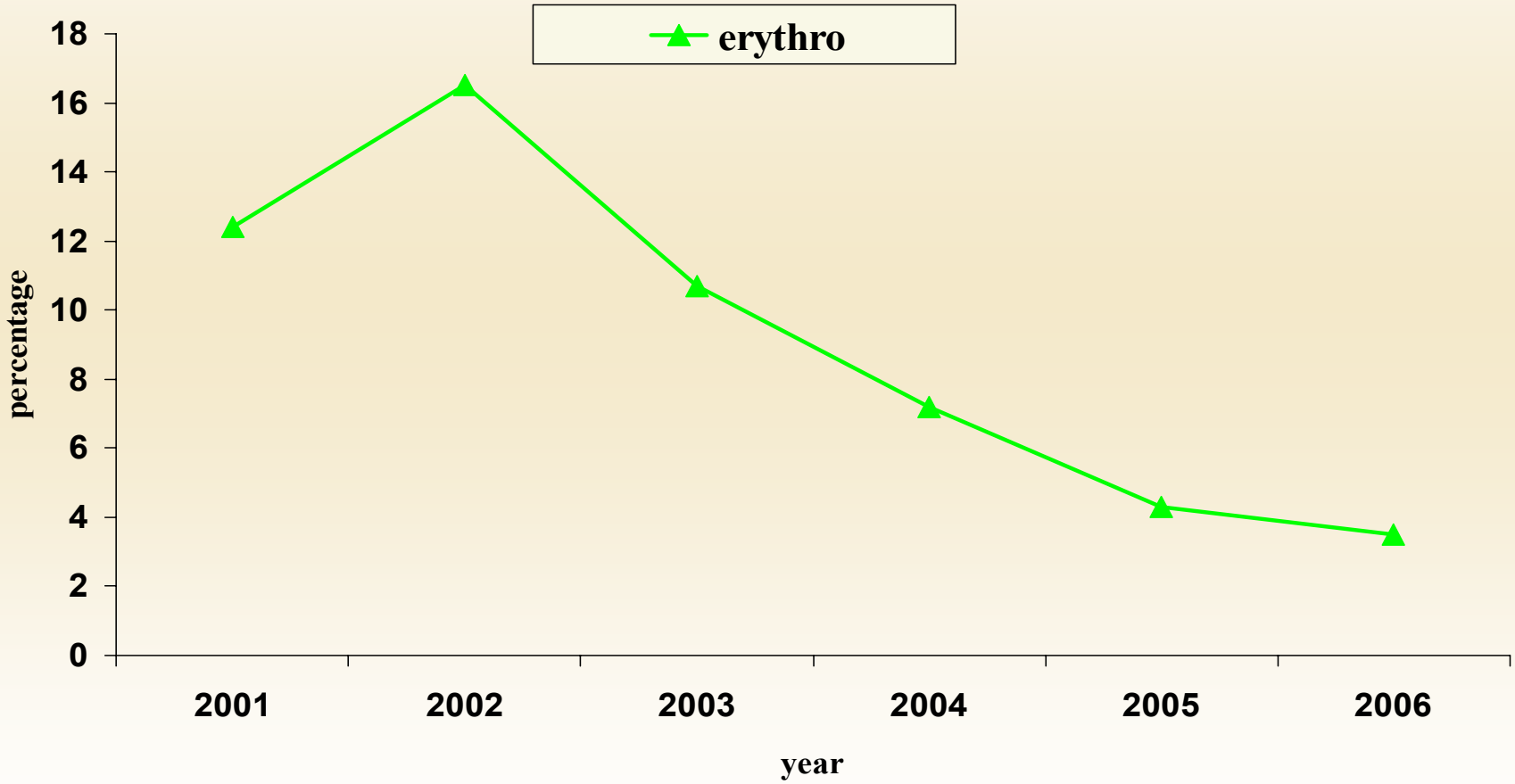
Goossens et al, Lancet, February 2005

Resistence of *S. pneumoniae* in Belgium



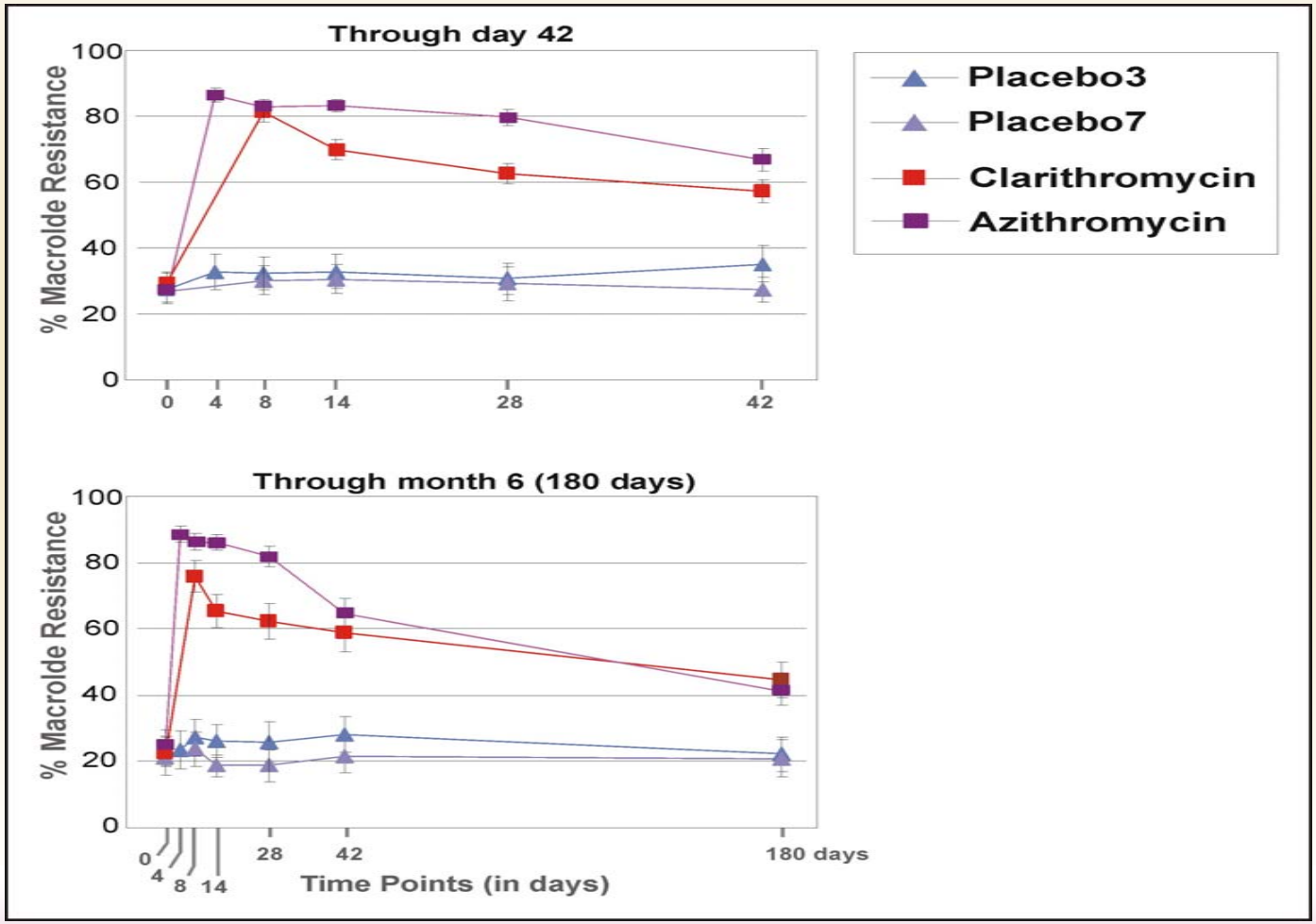
National Reference Centre of *S. pneumoniae* (KULeuven)

Resistence of S. pyogenes in Belgium



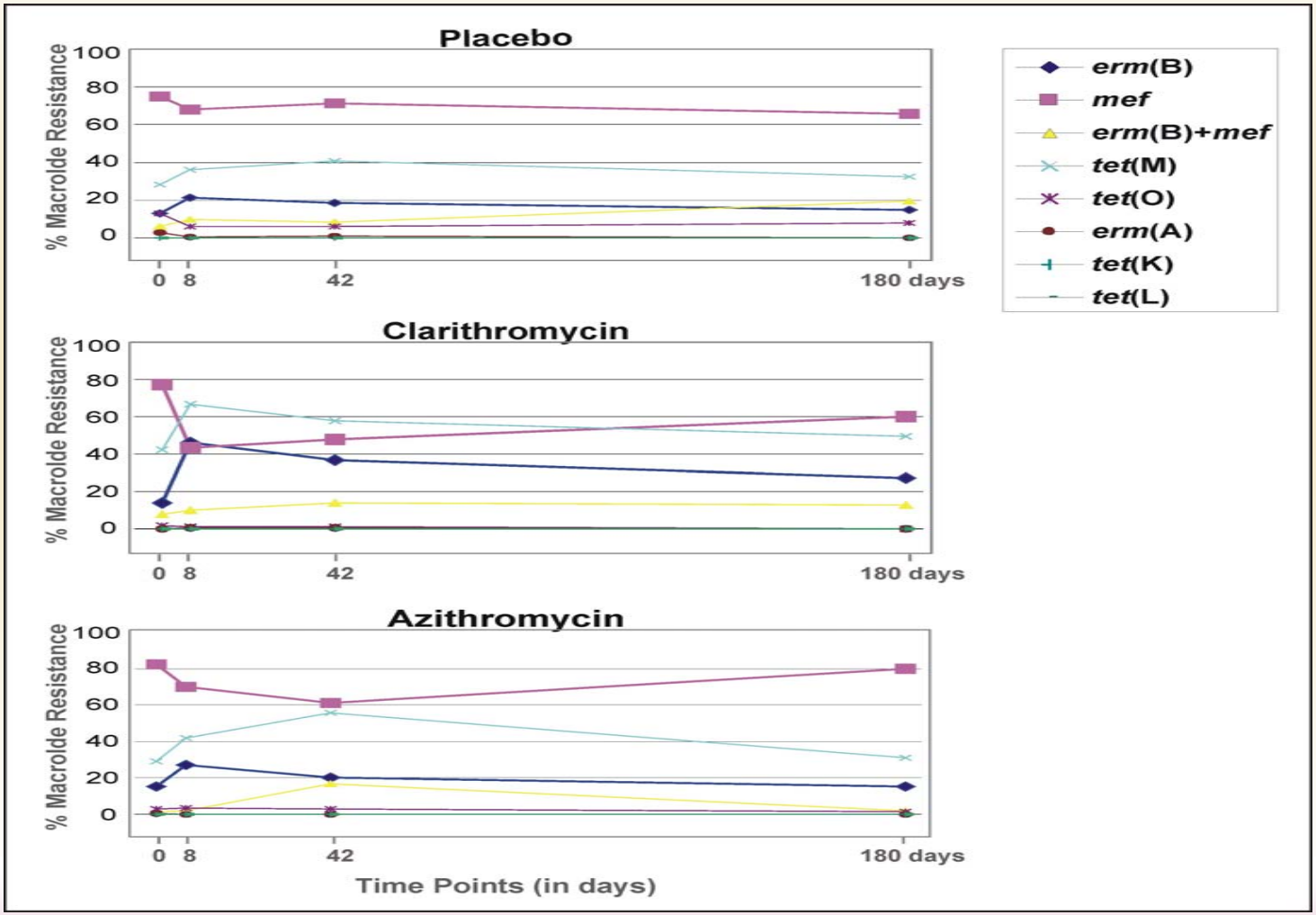
National Reference Cente of *S. pyogenes* (UA)

Semi-quantitative Analysis: Temporal Changes in Proportion of Macrolide-resistant Oral Streptococci



Malhotra et al, Lancet, February, 2007

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



Malhotra et al, Lancet, February, 2007

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

- A framework for prescribing quality indicators
  Eur J Clin Pharmacol 2005;60:831-34

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_%] = 3rd and 4th 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

Indicator 1: Consumption of antibacterials for systemic use (J01) expressed in DDD per 1000 inhabitants per day (DID) [J01_DID]

Definition

Consumption of antibacterials for systemic use (J01) expressed in DDD per 1000 inhabitants per day (DID) gives an estimate of their utilisation in a given area and period, which allows to compare antibiotic use between areas with different number of population.

Public health objective

Antibiotics allow treatment of serious bacterial infections. The largest volume of antibiotics is prescribed in ambulatory care. This use is increasingly recognized as the major selective pressure driving resistance, which in turn makes them ineffective. Therefore antibiotics should be used appropriately, i.e. (no) antibiotics for those who will (not) benefit from the treatment. In addition, unnecessary use of antibiotics requires more resources, motivates patients to reconsult and exposes them to the additional risk of side effects, whereas underprescribing could be associated with higher risk of complications of untreated infections.

Calculation formula:

Numerator: DDD (J01) x 1000

Denominator: Population at risk x Days in data collection period

Benchmark and recommended action

One benchmark value on European level cannot be given, because for different countries the demographical characteristics and epidemiological situation can influence this indicator. We suggest individual countries to position themselves and to define their own benchmark, based on the epidemiology of infectious diseases and national guidelines. A range of acceptable use should be defined rather than one threshold value. If the use is outside the limits of the range, more detailed assessment is recommended in order to define the action required. For any action planned explicit targets should be set.

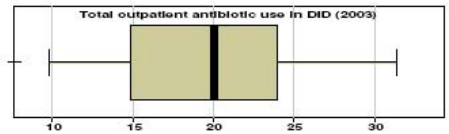
Limitations

DDDs, currently representing the best measure to quantify exposure to antibiotics use on a national level, have some general limitations and ideally should be complemented by alternative measures, if available.

Because of different coverage of different data sources, the population at risk varies between countries.

Some antimicrobial drugs, for example combinations for *Helicobacter pylori* eradication, are classified outside J01.

ESAC boxplot

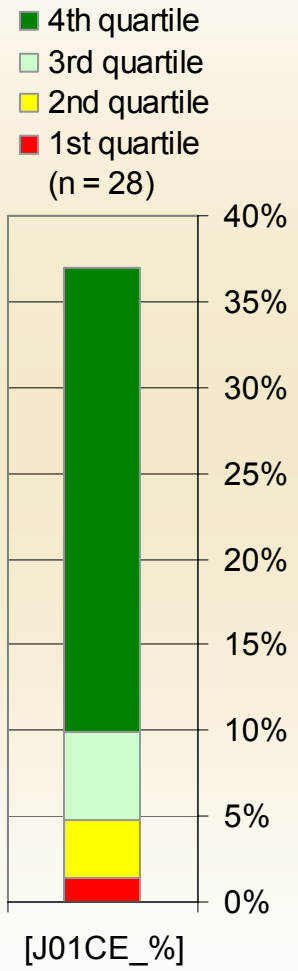


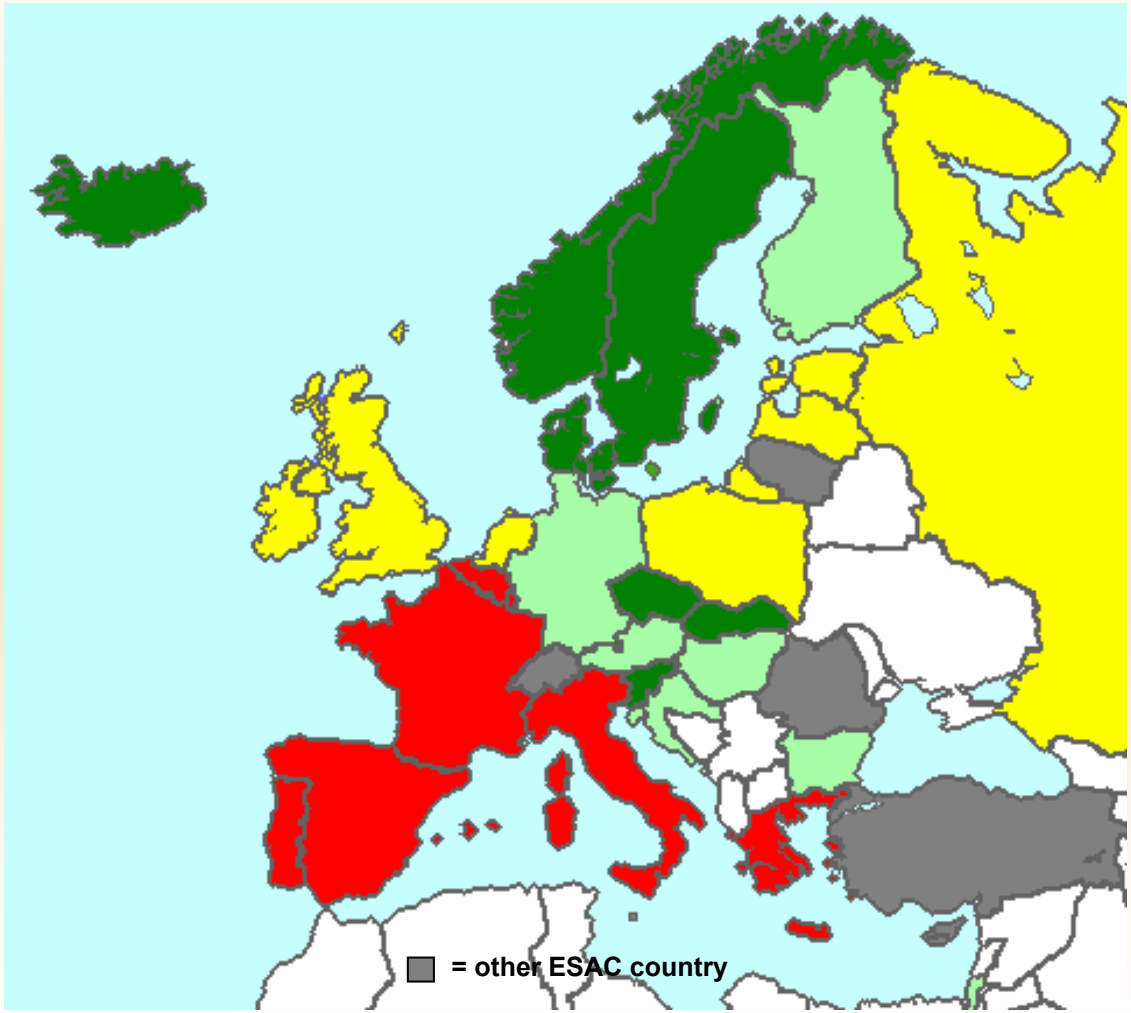
Results

A final set of quality indicators

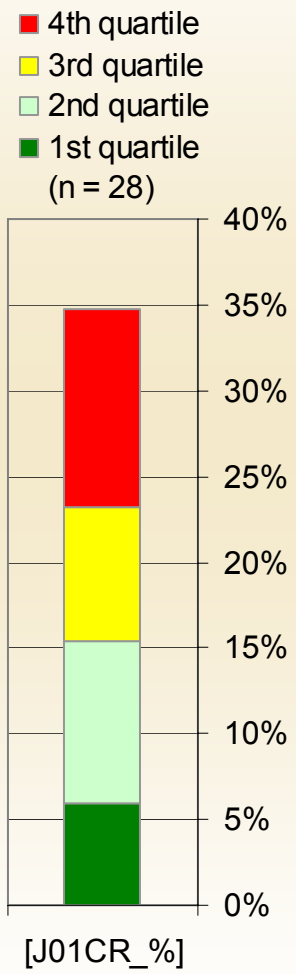
- Experts from 11 countries scored (♂/♀: 16/6)
- Relevant indicators:
  - on all 4 dimensions: n=9.
  - on reducing resistance and public health policy: n=14.
- **[J01MA_%]** overlapped with and scored higher than [J01M_%]
- **[J01MSV]** overlapped with and scored higher than [J01MSVDID]
- Indicator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

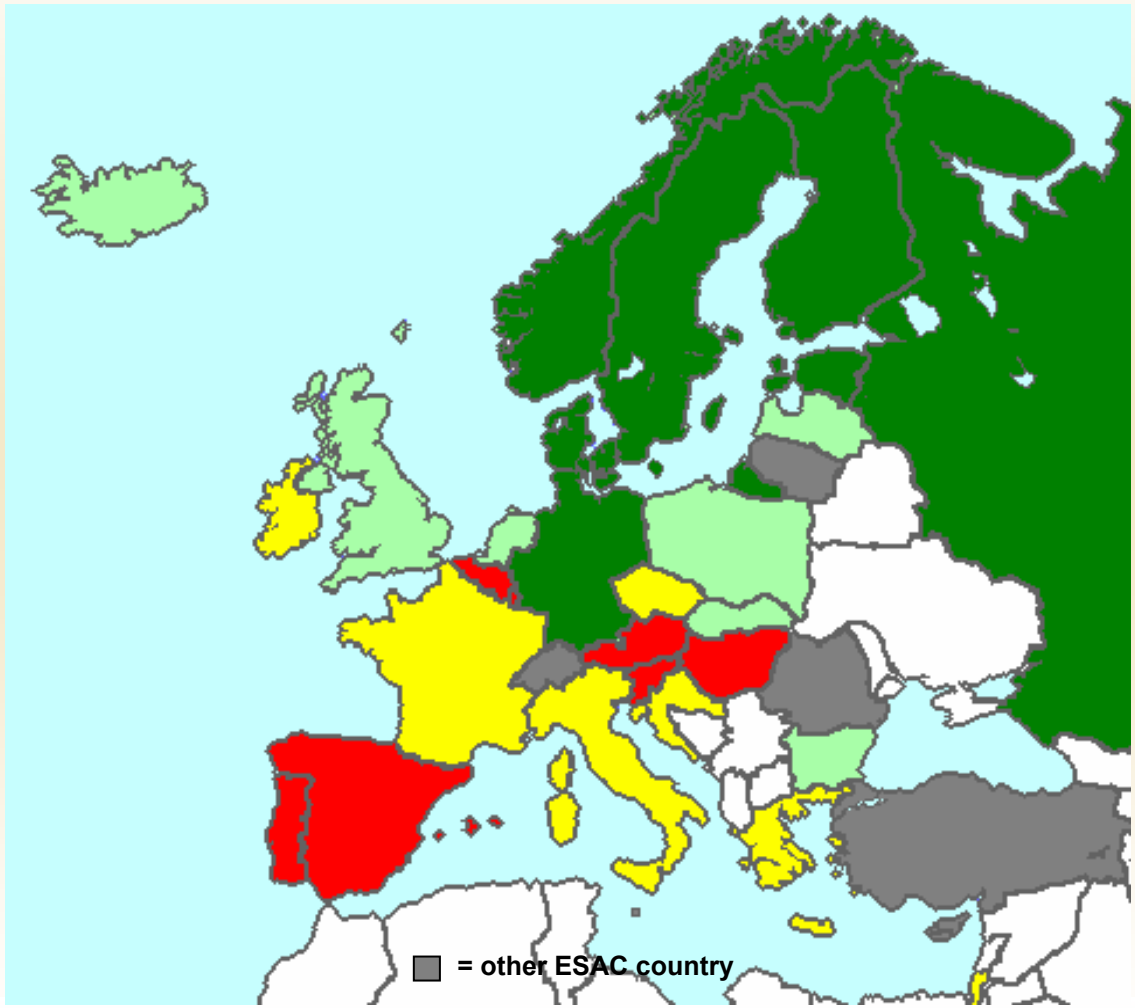
Narrow spectrum penicillins (J01CE) in %



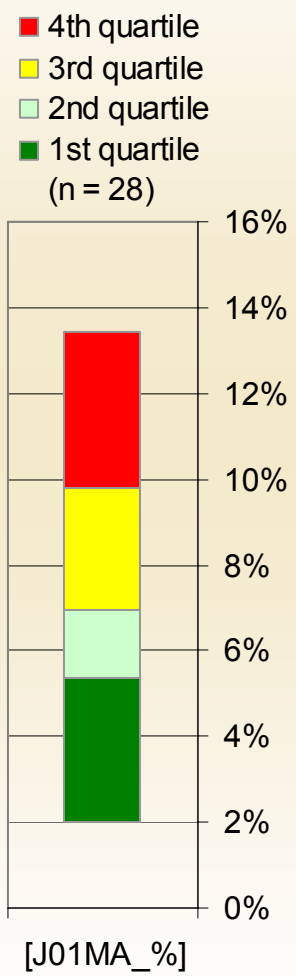


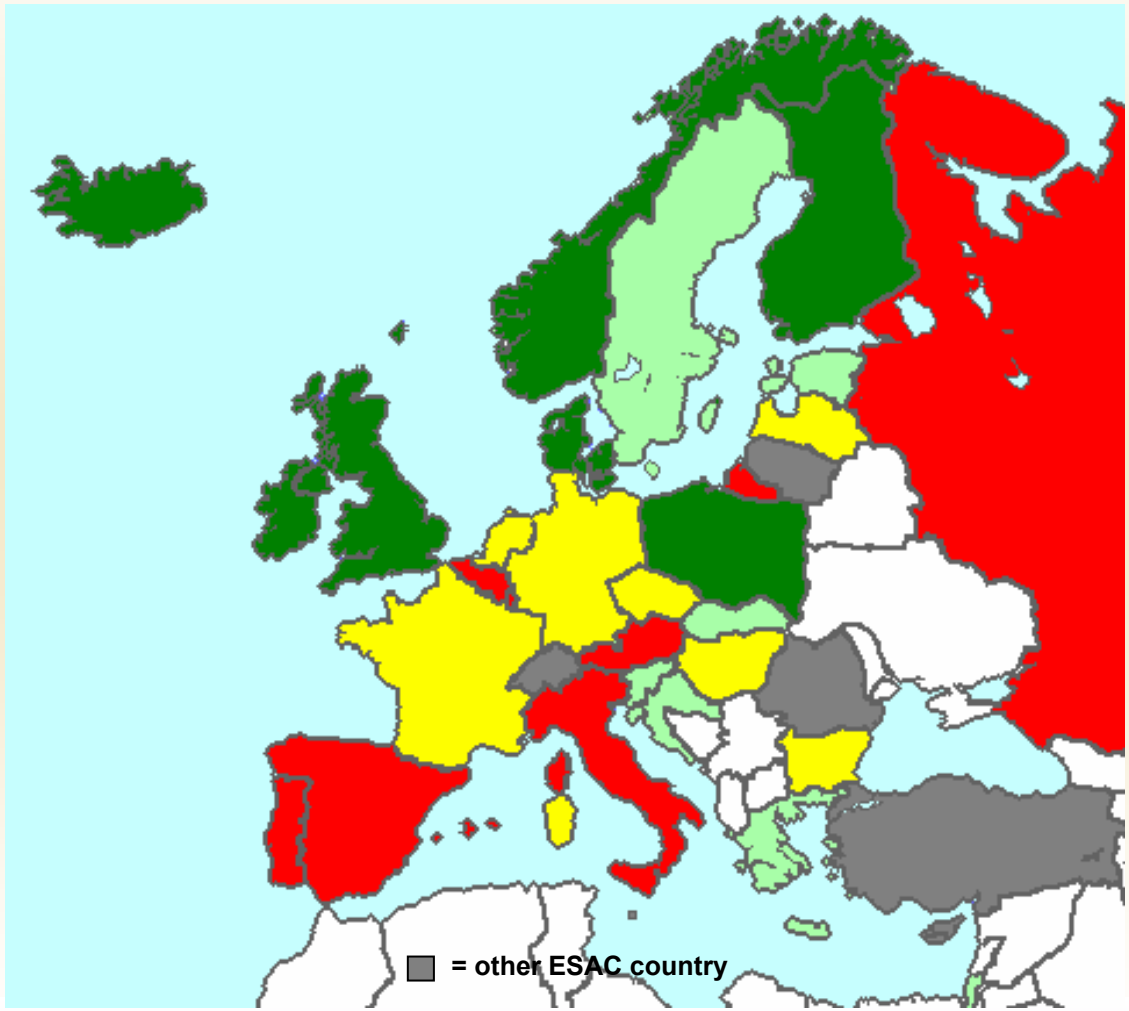
Combinations of penicillins (J01CR) in %



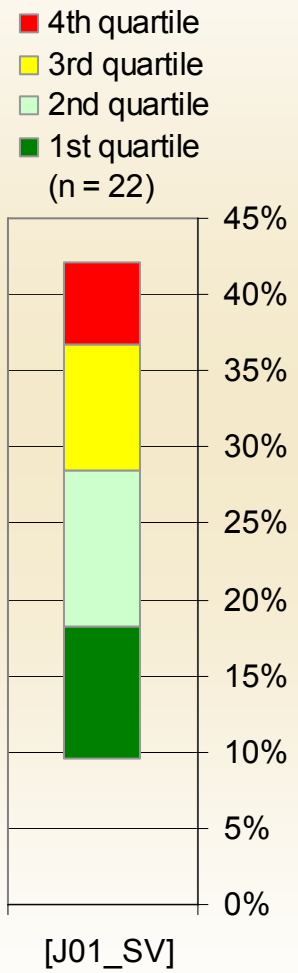


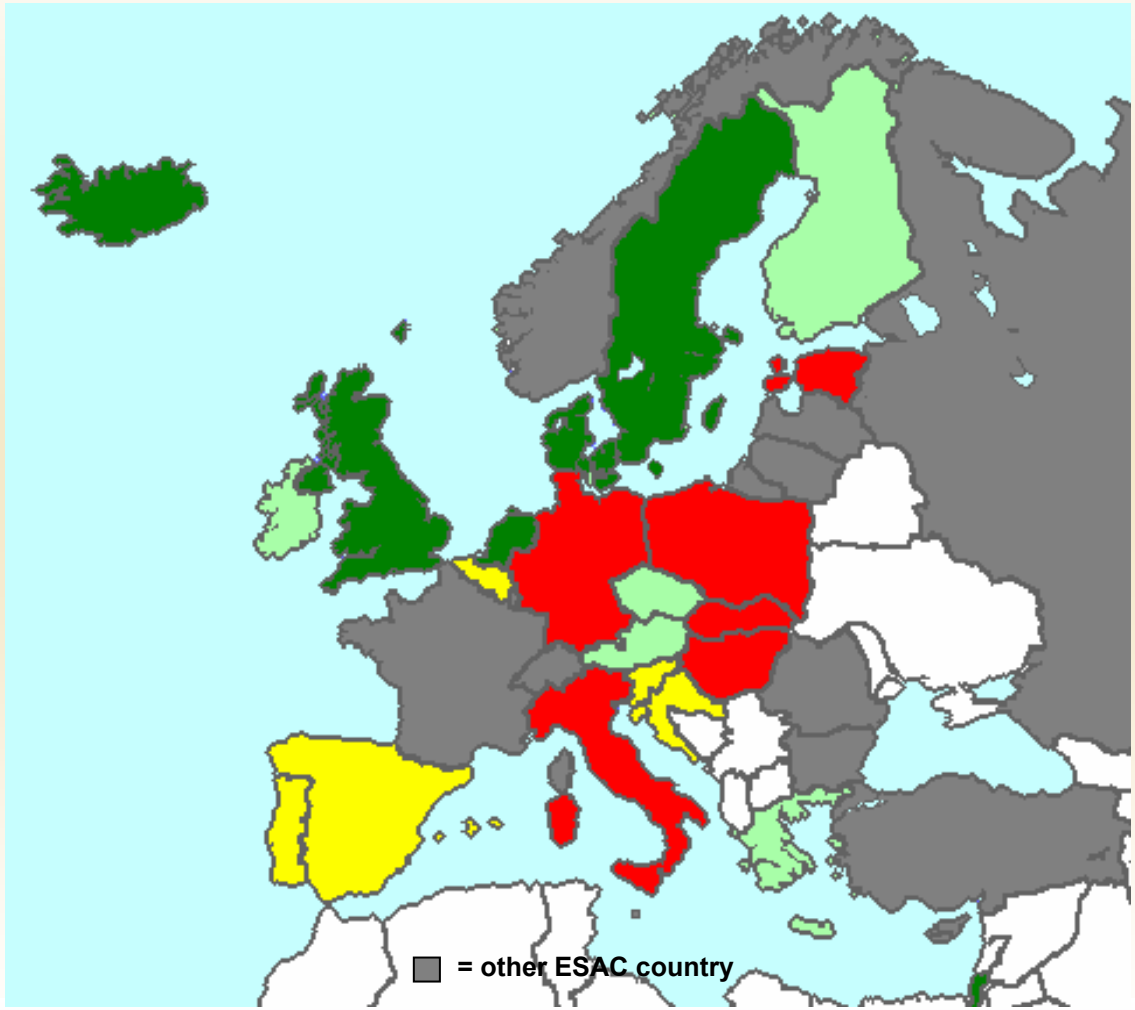
Fluoroquinolones (J01MA) in % of total





Seasonal variation of antibiotic use in %





Conclusion

- 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

	AMBULATORY CARE					
	SEX AND AGE	PRESCRIBER	INDICATION	NURSING HOMES	HOSPITAL CARE	ECONOMICS/ REGIONAL
Leader	Sigvard Mölstad (SE)			Pawel Grzesziowski (PL)	Peter Davey (UK)	Giuliano Masiero (CH)
ESAC MT	Samuel Coenen			Carl Suetens	Herman Goossens	Matus Ferech
Core group	CZ DK EE FI GR NL NO PT SE SK UK			FI NO PL IL LT	AT DE PL DK GR LT NL SI UK LV	AT CH DE DK IT UK
Parti-cipants	BE CZ DK ES FR IE IS LU NL NO RO SE SK UK	AT BE CZ DK ES FR IS LU NL NO PT RO SK UK	DK NL RO SE SK UK	BE FI IL IT LT NO PL PT TR	AT BE BG DE DK ES FI FR GR HU IE IS LU LV LT MT NL NO PL RO SE SI SK UK	AT BE CH DE DK FI FR HR IE IS LU NL MT NO PT RO SE SK UK

ESAC Hospital Care Subproject

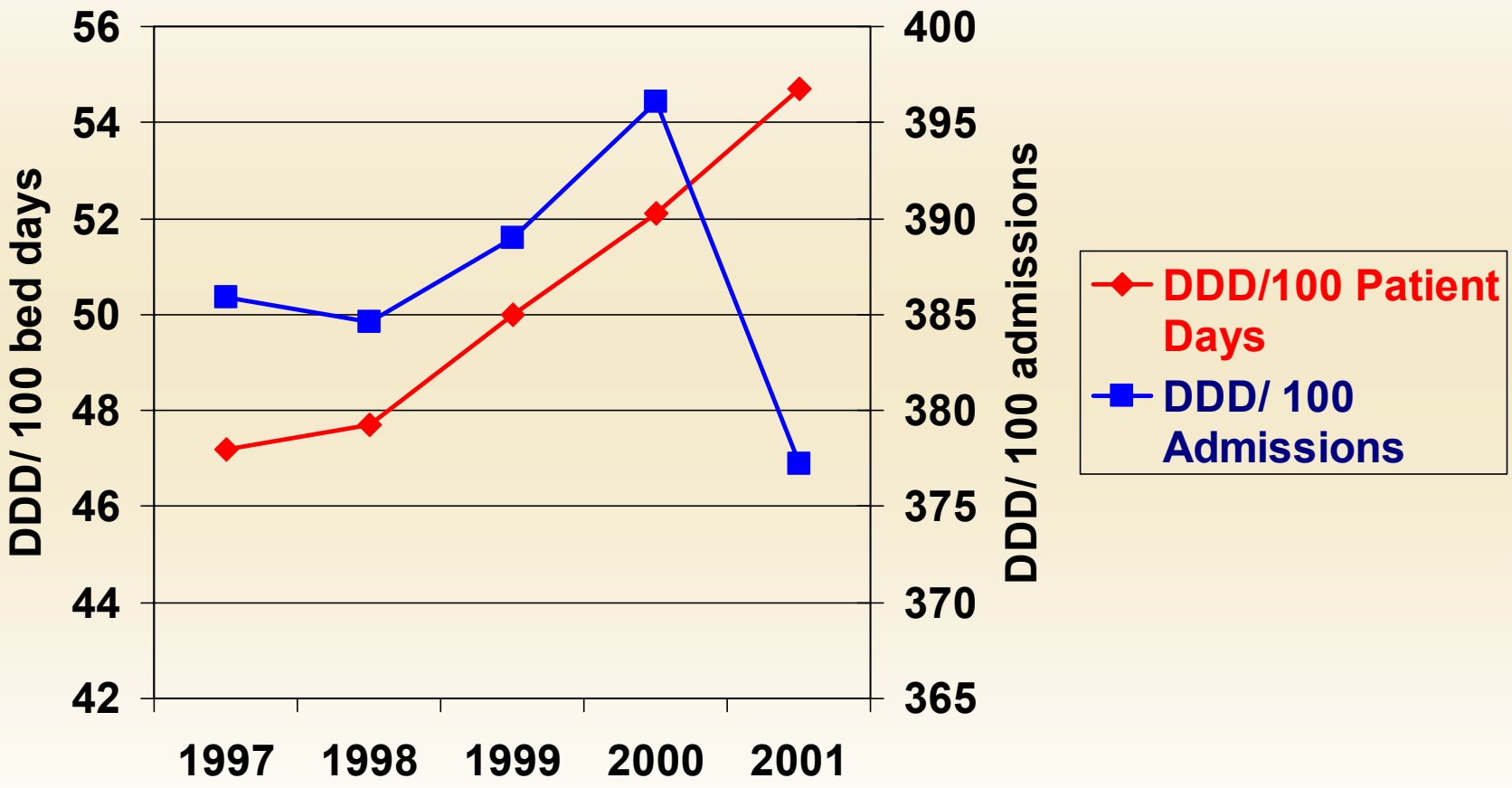
Objectives:

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)

ADMISSIONS or BEDDAYS ??



Filius et al, J Antimicrob Chemother 2005, 55: 805-8

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

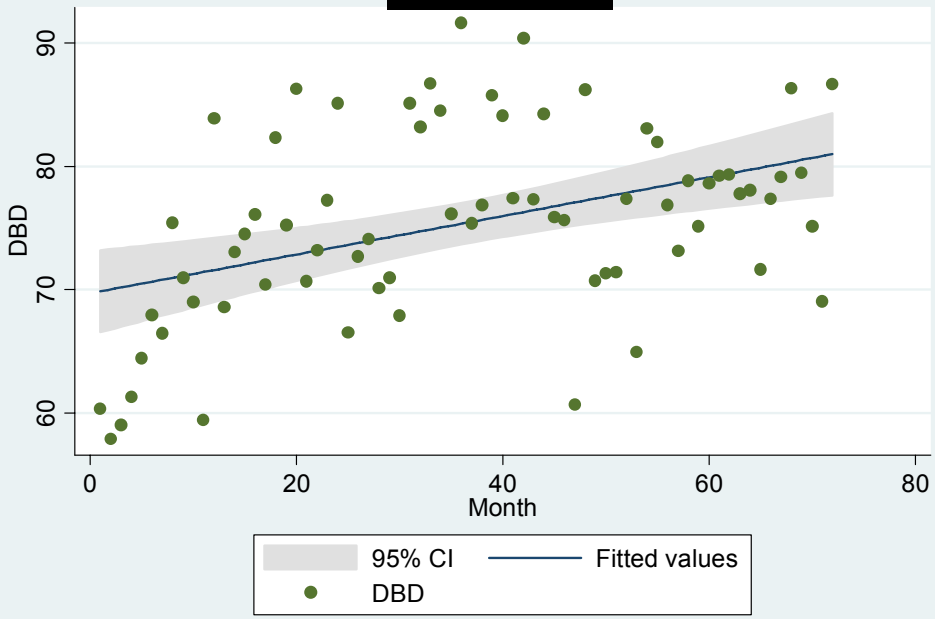
- Monthly data from 1/2000 - 12/2005
- J01 + oral metronidazole and oral vancomycin
- Dispensed from hospital pharmacy to inpatient destinations
- For every dosage form
- Convertible to DDD
- OBDs and admissions

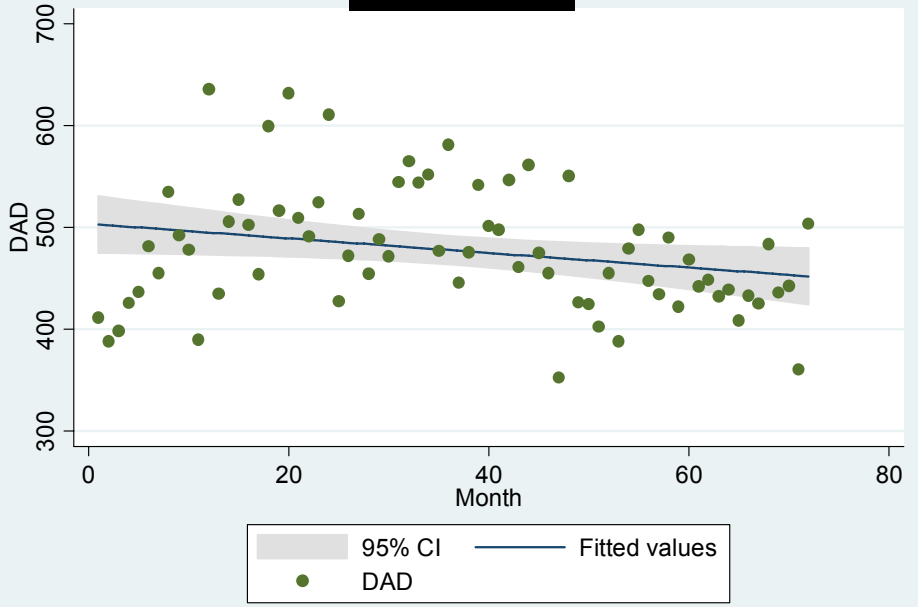
Methods Point Prevalence Study

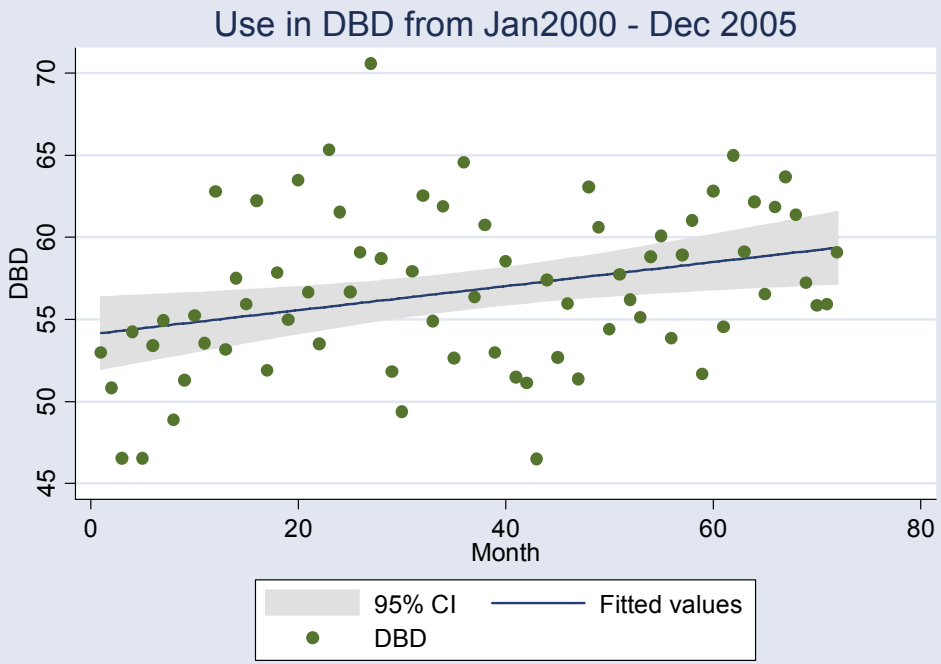
- Data set and software based on STRAMA annual PPS
- English language version written by NEOTIDE
- All patients who were receiving systemic (not topical) antibacterials (not antifungals or antivirals or TB treatment)
  - Treatment – on day of survey
  - Prophylaxis – on day before survey
- Completed 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.

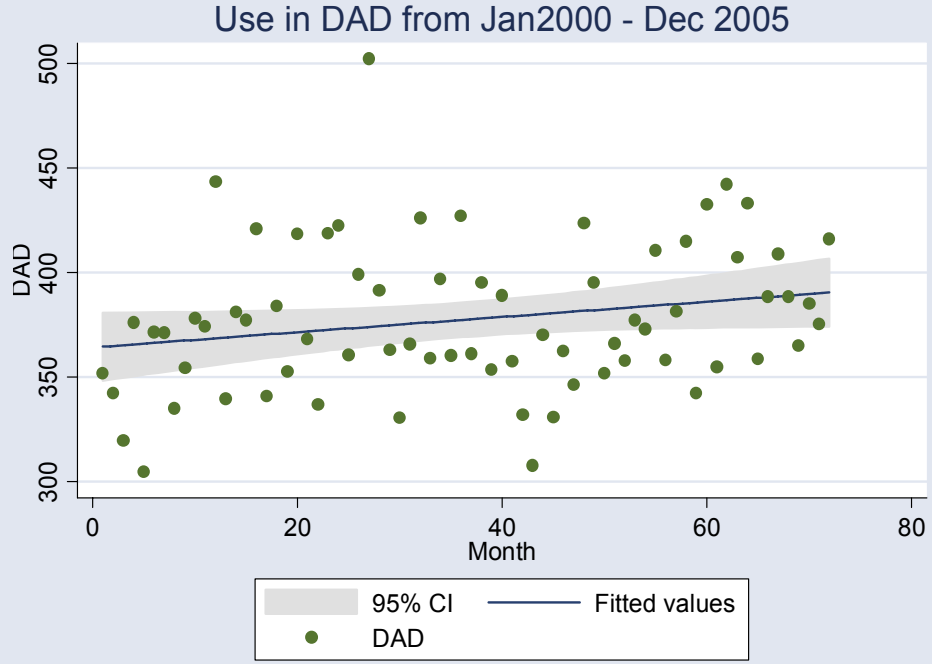
Data Point Prevalence Study

- 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


DBD
90
80
70
60
0
20
40
60
80
Month
95% CI
Fitted values
DBD

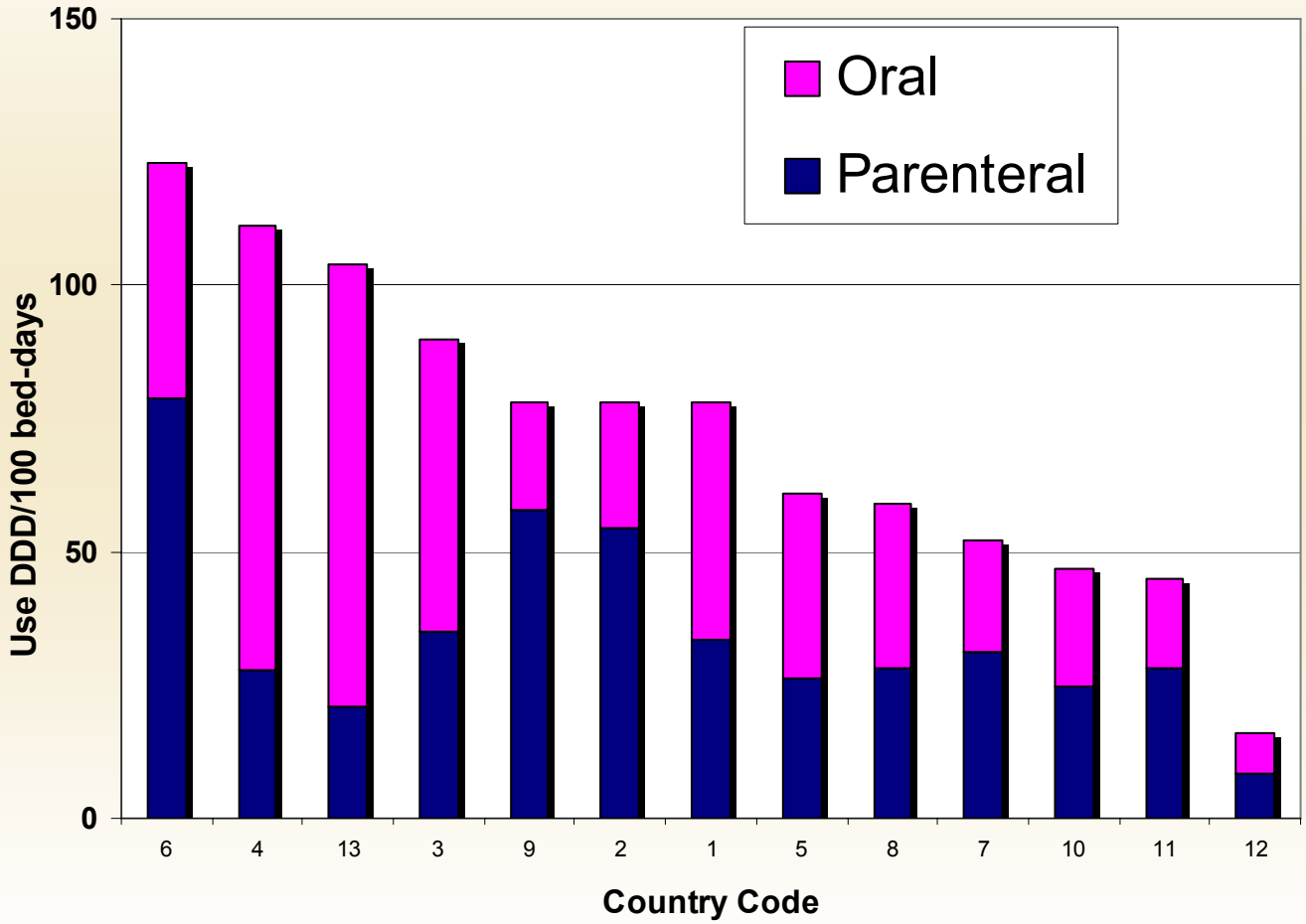

DAD
700
600
500
400
300
0
20
40
60
80
Month
95% CI
Fitted values
DAD


Use in DBD from Jan2000 - Dec 2005
DBD
70
65
60
55
50
45
0
20
40
60
80
Month
95% CI
Fitted values
DBD


Use in DAD from Jan2000 - Dec 2005
DAD
500
450
400
350
300
0
20
40
60
80
Month
95% CI
Fitted values
DAD

Country Code	DDD/100 bed-days	DDD/100 admissions
1	▲▲	▲▲
2	▲▲	▲▲
3	▲▲	▲▲
4	▲	▲
5	▲	▲
6	▲▲	▲
7	▲▲	▲
8	▲▲	▲
9	▲▲	▼▼
10	▲	▼▼
11	▼▼	▼▼
12	▼▼	▼▼
13	▼▼	▼▼

Total Use of Antibacterials in 2005



ESAC Ambulatory Care Subproject

Data extraction protocol

- 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:

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

Year	Age	Gender	Population
2004	0	M	57020
2004	0	F	53874
2004	1	M	56997
2004	1	F	54692
2004	2	M	57061
2004	2	F	54289
2004	3	M	58079
2004	3	F	55877
2004	4	M	59251
2004	4	F	56551
2004	5	M	58452
2004	5	F	56255
2004	6	M	59211
2004	6	F	56459

Variable description:

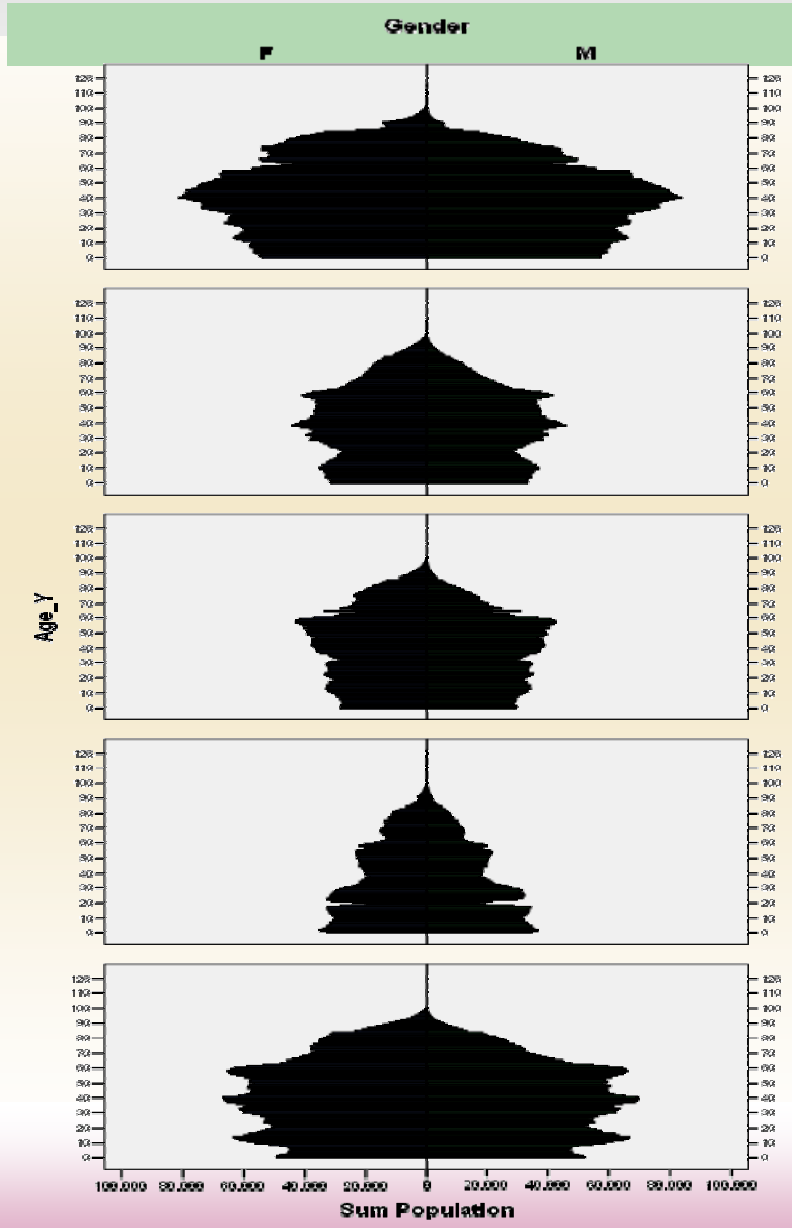
- ATC_7: 7 digit ATC code *(ATC version 2005, or mention version) (see Annex 1);*
- Age: in years;
- Gender: M *(= male)*; F *(= female);*
- Speciality: GP *(= general practitioner)*; PE *(= paediatrician)*; OT *(= others);*
- Packages: number of ATC J01 packages dispensed *(ATC version 2005, or mention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

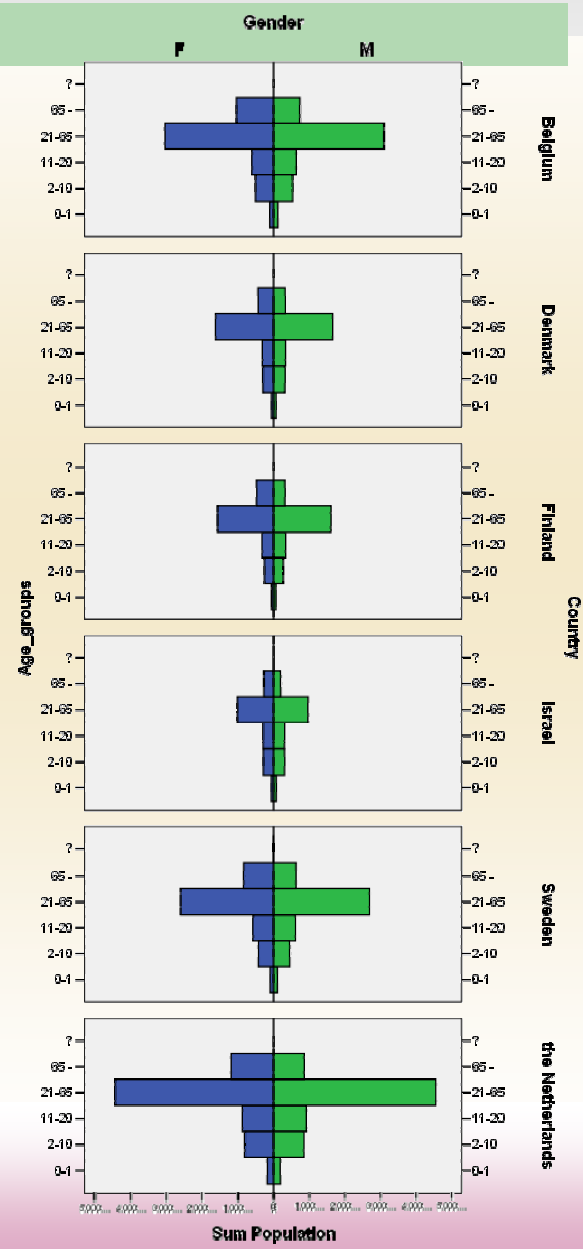
Data provided for A

- **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)

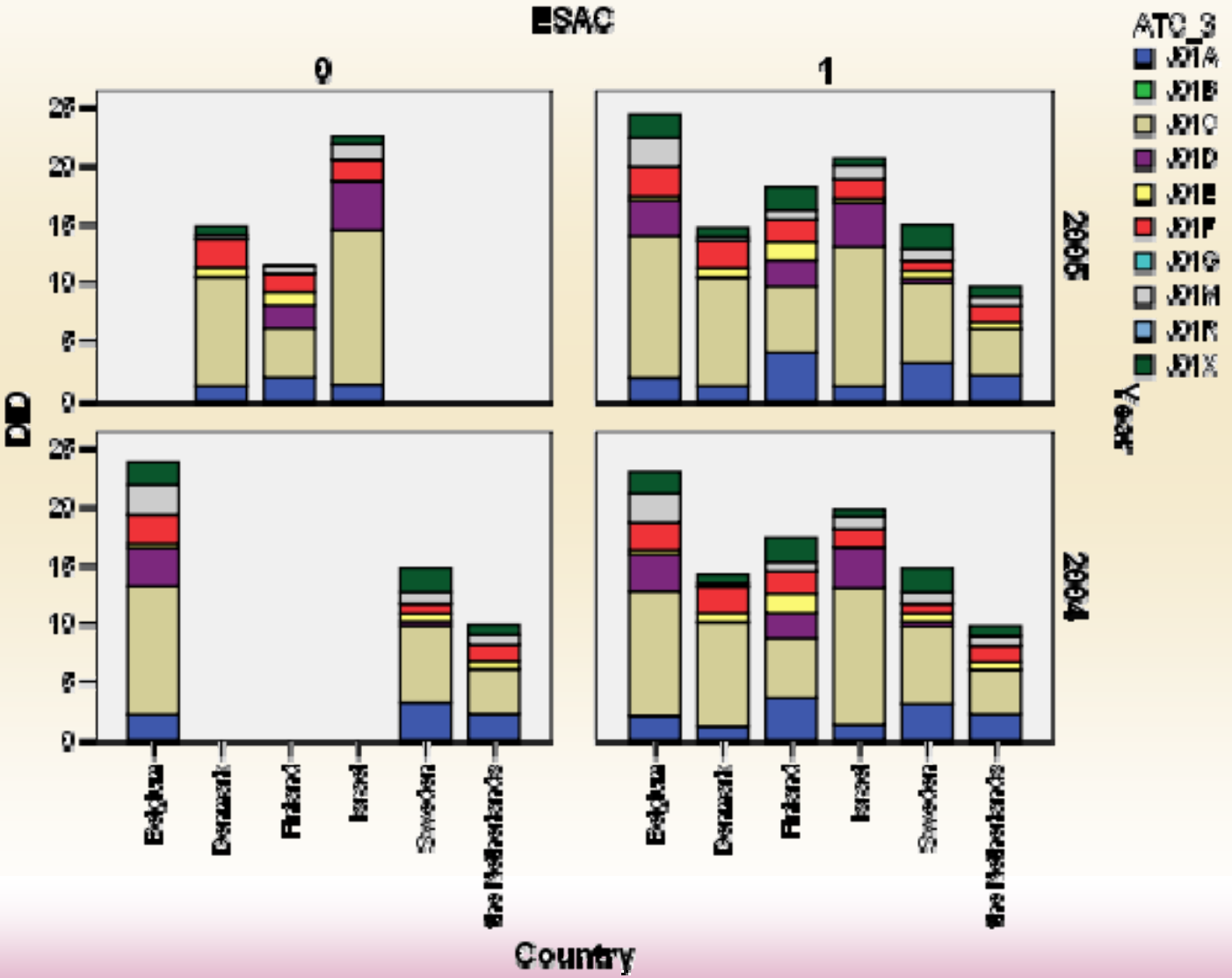
  ➔ GP vs other vs ?

Population piramides

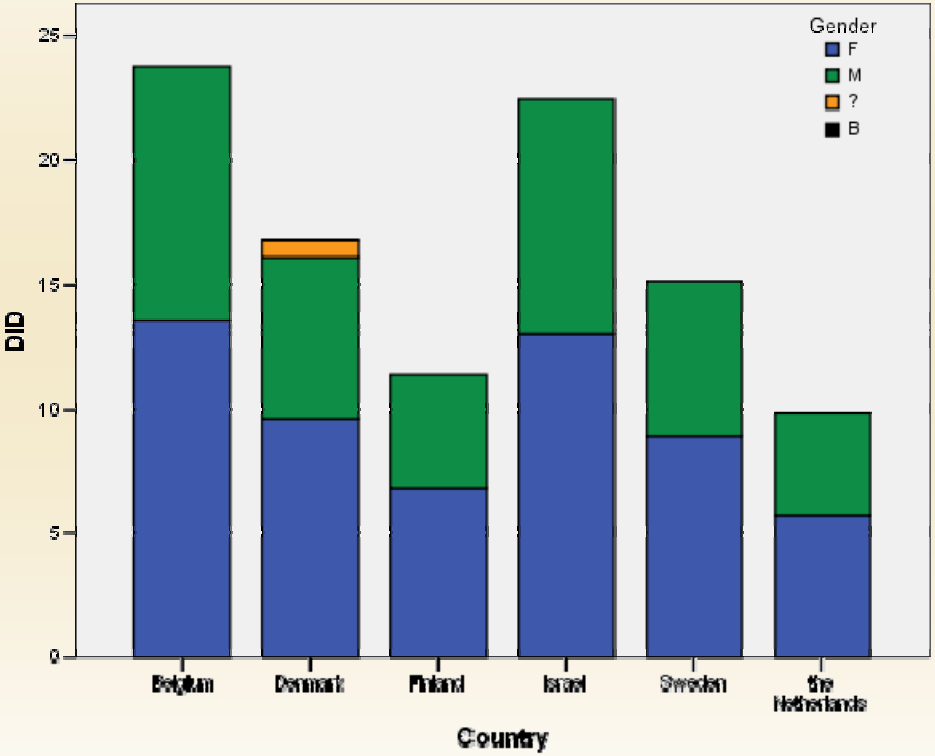


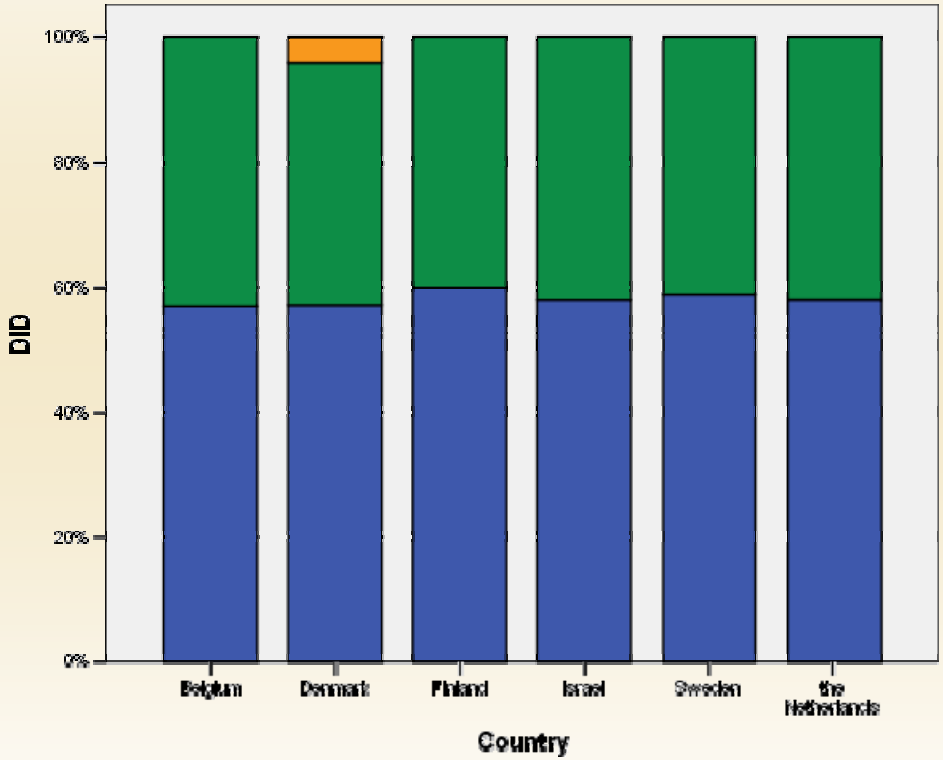


ESAC vs ESAC AC Subproject data

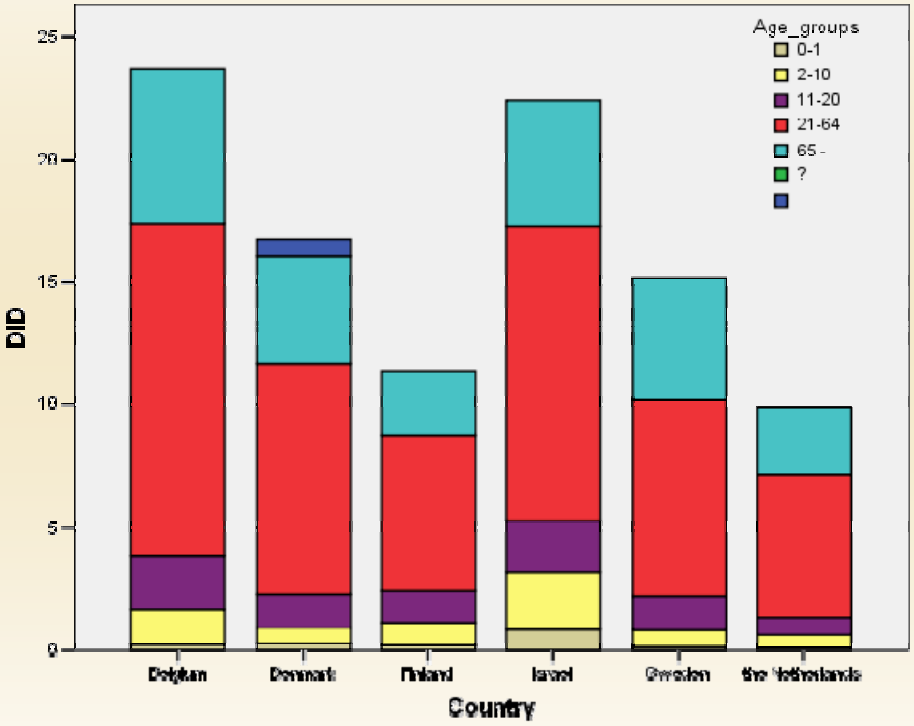


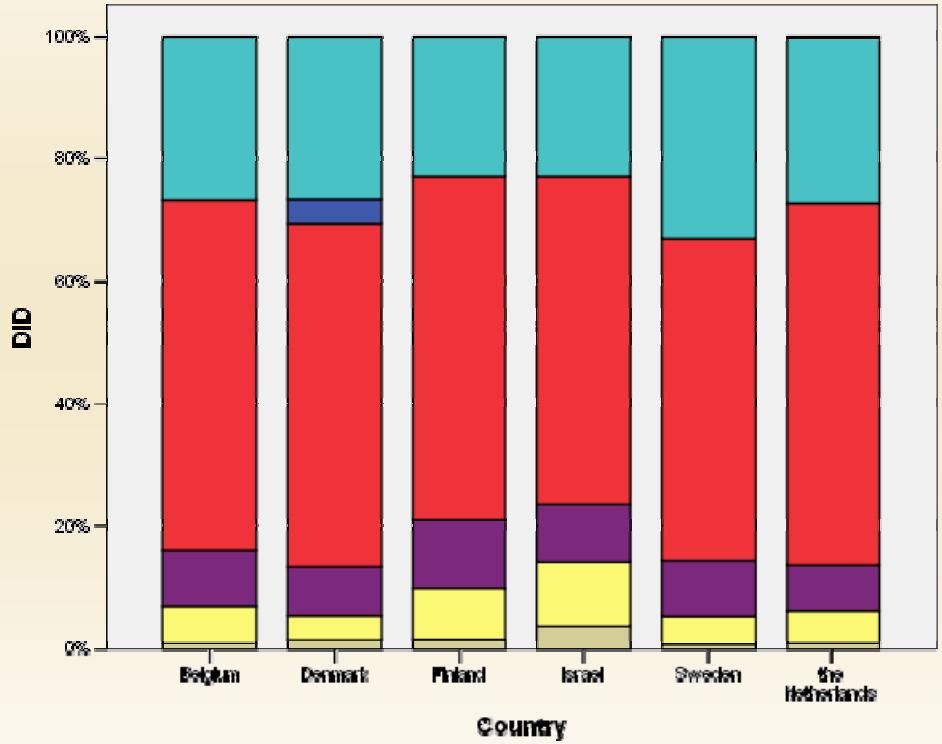
Use by gender



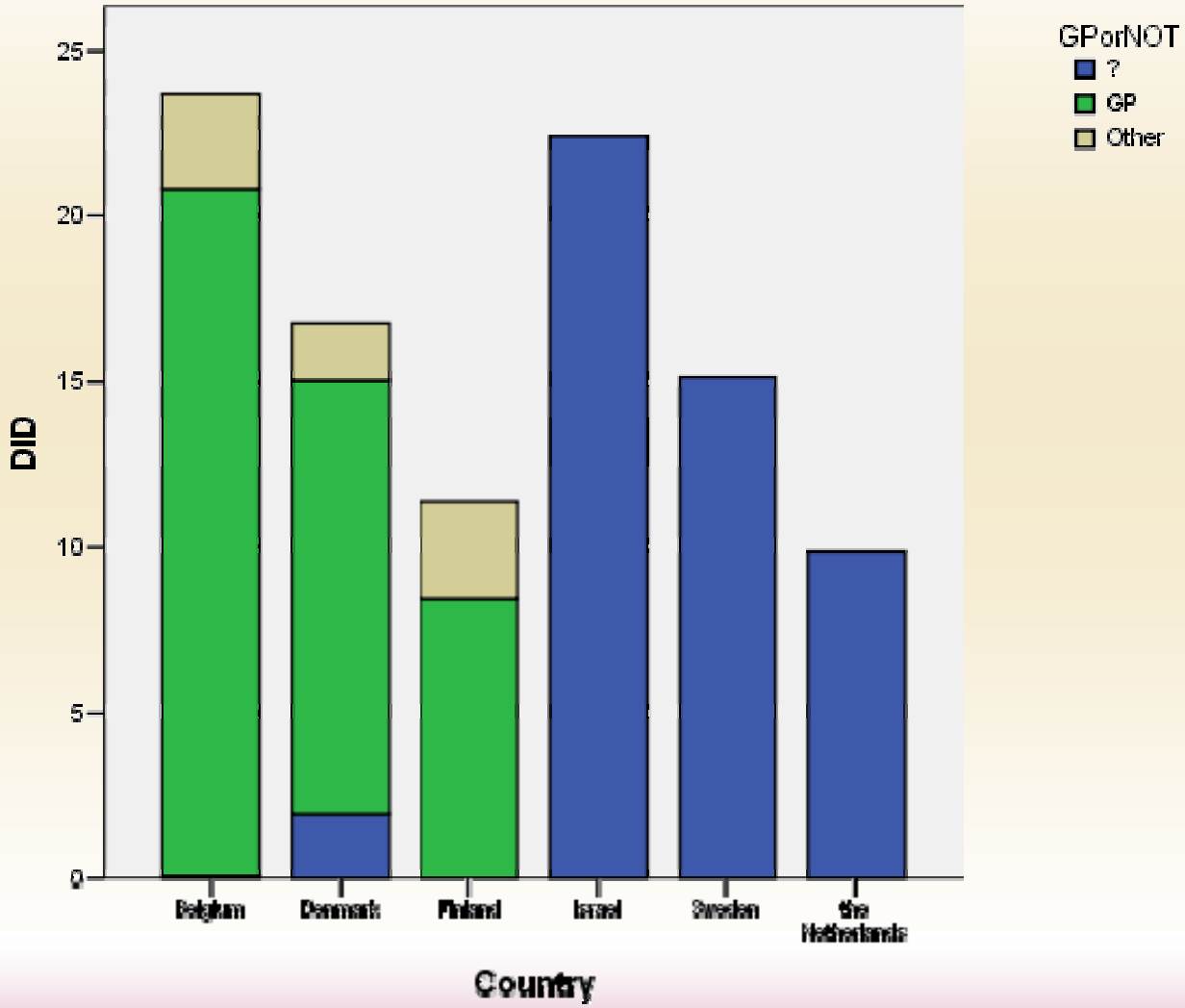


Use by age

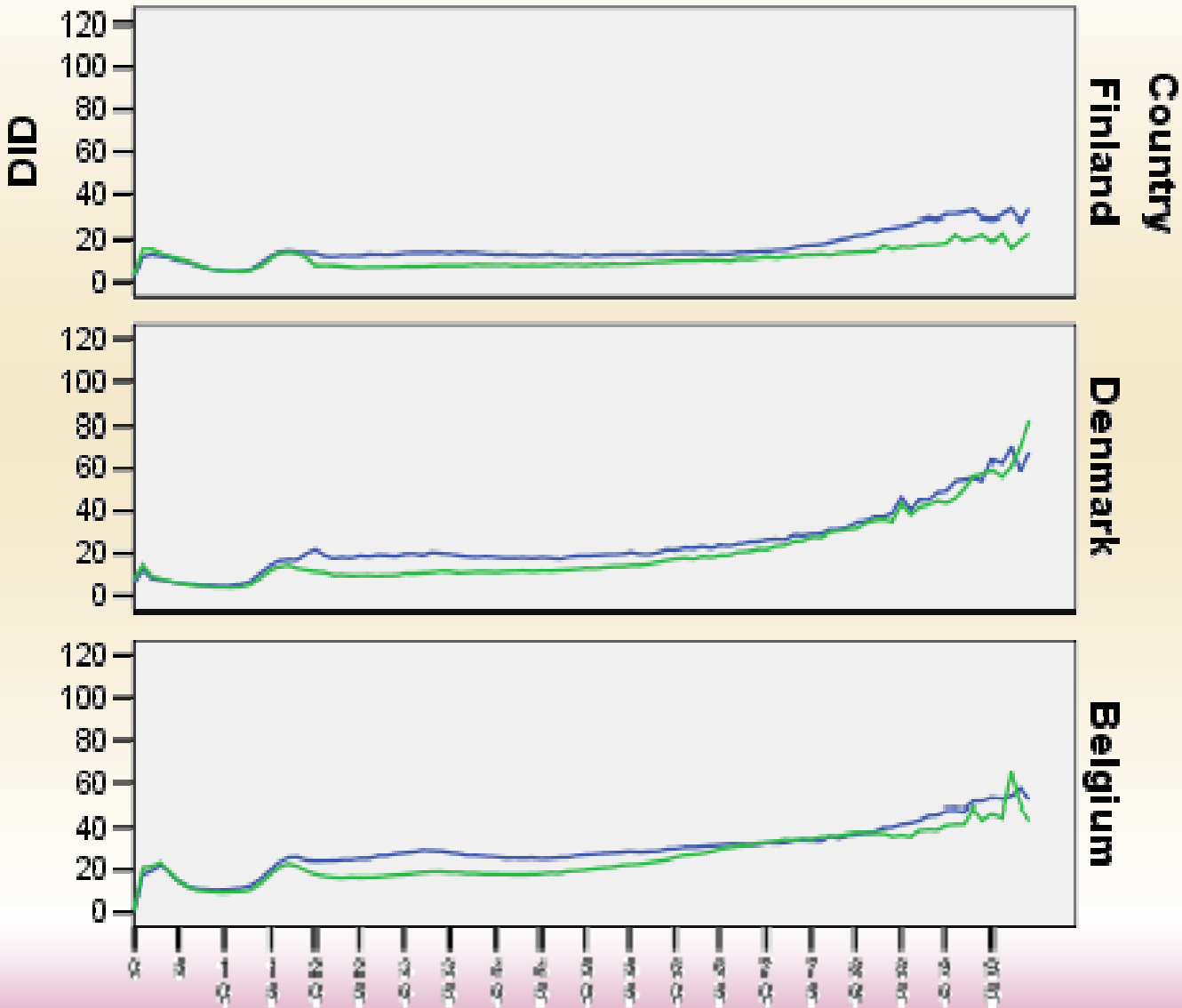

Age_groups
0-1
2-10
11-20
21-64
65 -
?
DID
25
20
15
10
5
0
Belgium
Denmark
Finland
Israel
Sweden
the Netherlands
Country


DID
100%
80%
60%
40%
20%
0%
Belgium
Denmark
Finland
Israel
Sweden
the Netherlands
Country

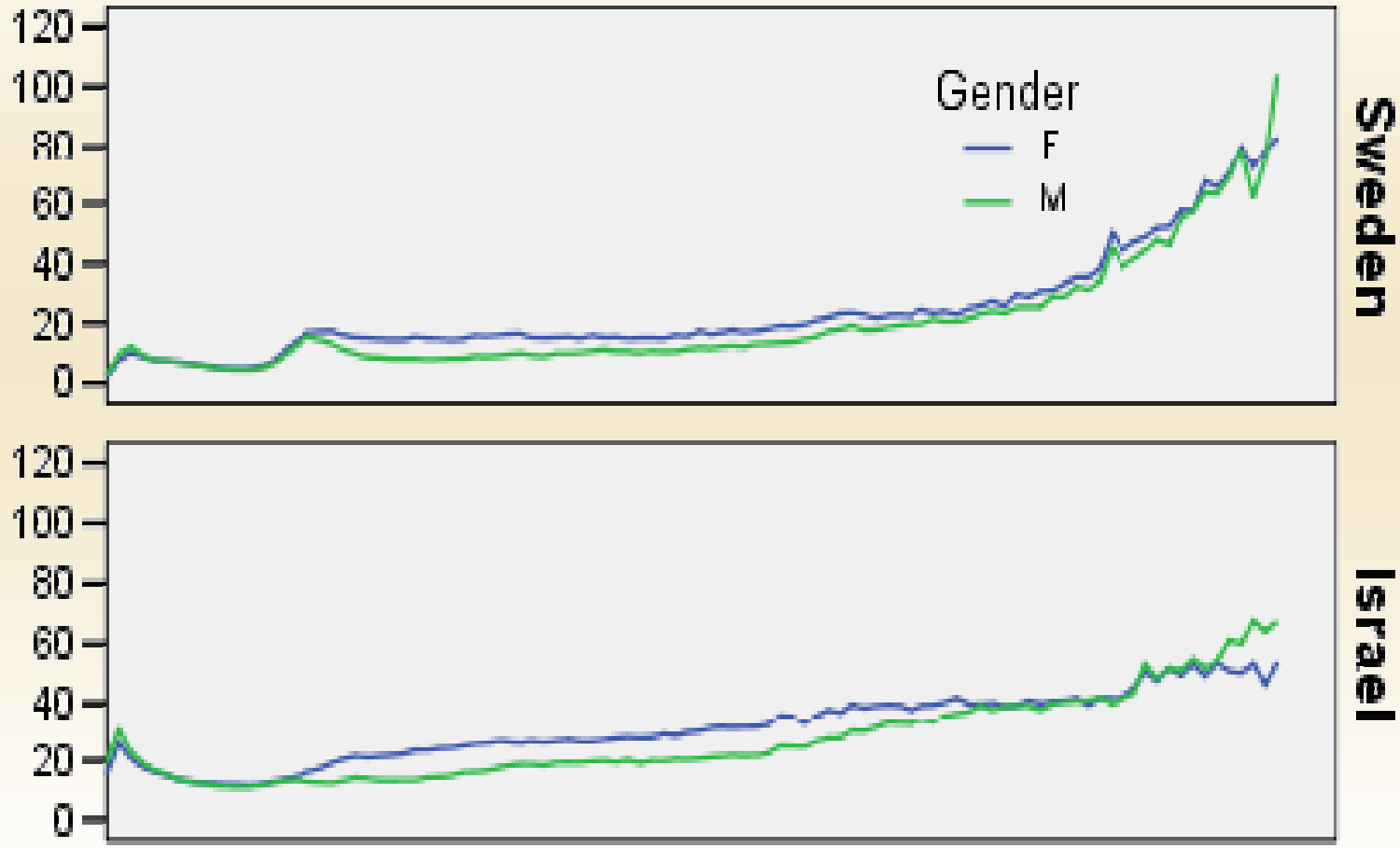
Use by prescriber



Use by age & gender



Use by age & gender



B: Link to age, gender and indication (GP)

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

ATC_7	Age	Gender	ICPC2	Packages	DDD
J01AA02	11	M	A78	1,00	10,00
J01AA02	11	M	S06	1,00	10,00
J01AA02	13	M	R74	1,00	10,00
J01AA02	14	F	S94	1,00	10,00
J01AA02	14	M	A86	1,00	10,00
J01AA02	15	F	H71	1,00	10,00
J01AA02	15	F	R81	1,00	20,00
J01AA02	15	M	A86	1,00	10,00
J01AA02	15	M	R74	1,00	20,00
J01AA02	16	F	S12	1,00	20,00
J01AA02	16	M	A75	1,00	10,00
J01AA02	16	M	R74	1,00	10,00
J01AA02	17	F	R77	1,00	10,00
J01AA02	17	F	R78	1,00	10,00
J01AA02	17	F	S09	1,00	20,00
J01AA02	17	F	S76	1,00	20,00
J01AA02	17	M	R07	1,00	20,00
J01AA02	17	M	R74	1,00	20,00
J01AA02	17	M	R75	1,00	20,00
J01AA02	17	M	S12	1,00	20,00
J01AA02	18	F	R75	2,00	20,00
J01AA02	18	F	R76	1,00	20,00
J01AA02	18	M	H71	1,00	10,00
J01AA02	18	M	R74	1,00	10,00
J01AA02	18	M	R74	1,00	20,00
J01AA02	18	M	R77	1,00	20,00
J01AA02	19	F	R77	1,00	10,00
J01AA02	19	M	A86	1,00	20,00
J01AA02	19	M	S76	1,00	10,00
J01AA02	20	F	R74	1,00	10,00
J01AA02	21	F	R78	1,00	10,00
J01AA02	21	F	U71	1,00	10,00
J01AA02	21	M	A78	1,00	20,00
J01AA02	21	M	R75	2,00	30,00

Age	Gender	Population
0	F	192
0	M	219
1	F	243
1	M	290
2	F	250
2	M	294
3	F	289
3	M	294
4	F	292
4	M	333
5	F	295
5	M	297
6	F	282
6	M	284
7	F	262
7	M	345
8	F	287
8	M	318
9	F	258
9	M	341
10	F	282
10	M	337
11	F	317
11	M	360
12	F	335
12	M	345
13	F	348
13	M	402
14	F	366

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; **R\ID** 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!

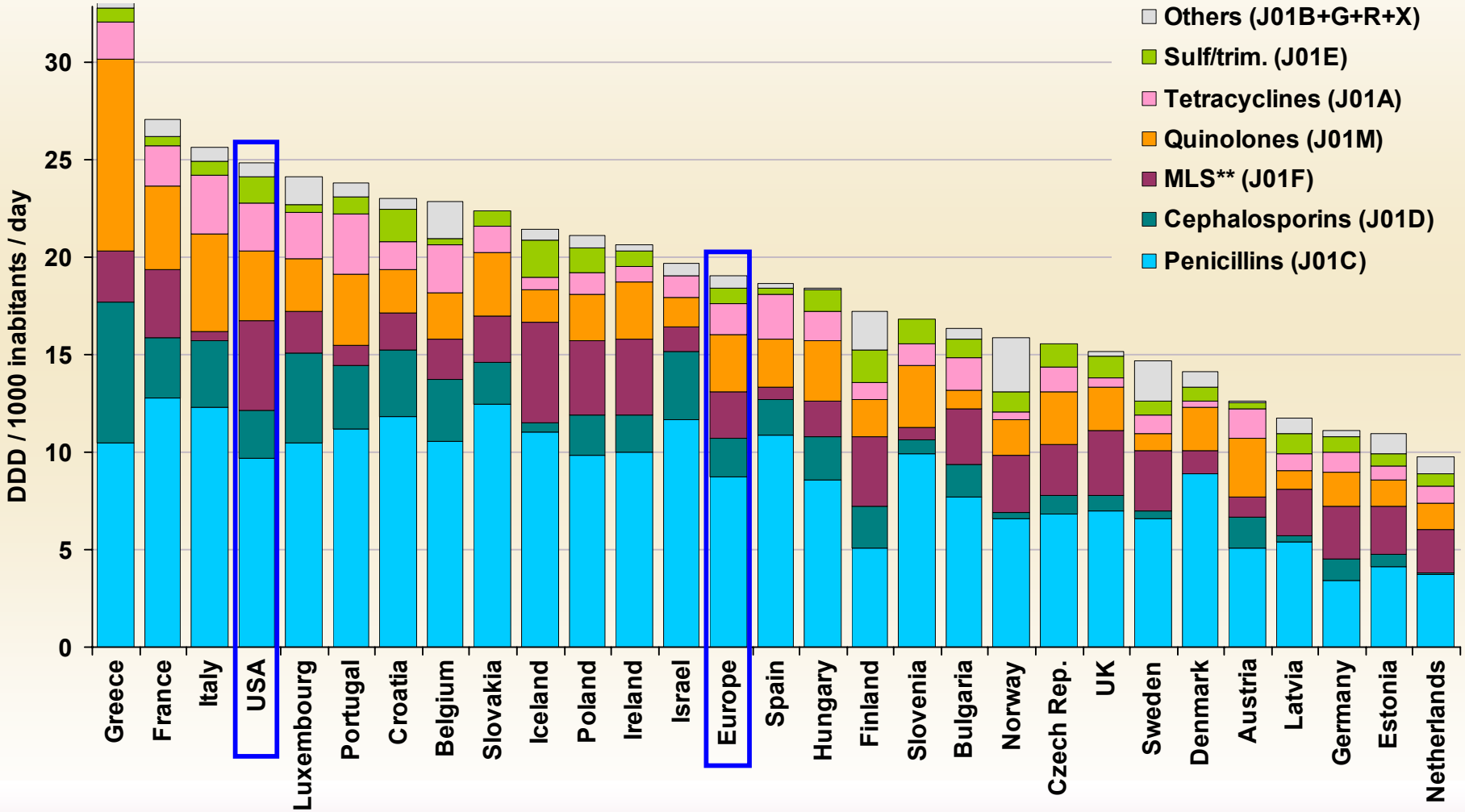
B: Allows to assess differences in use* by indications

* total use and use of different subclasses of antibiotics

More data is needed and is available, but …!

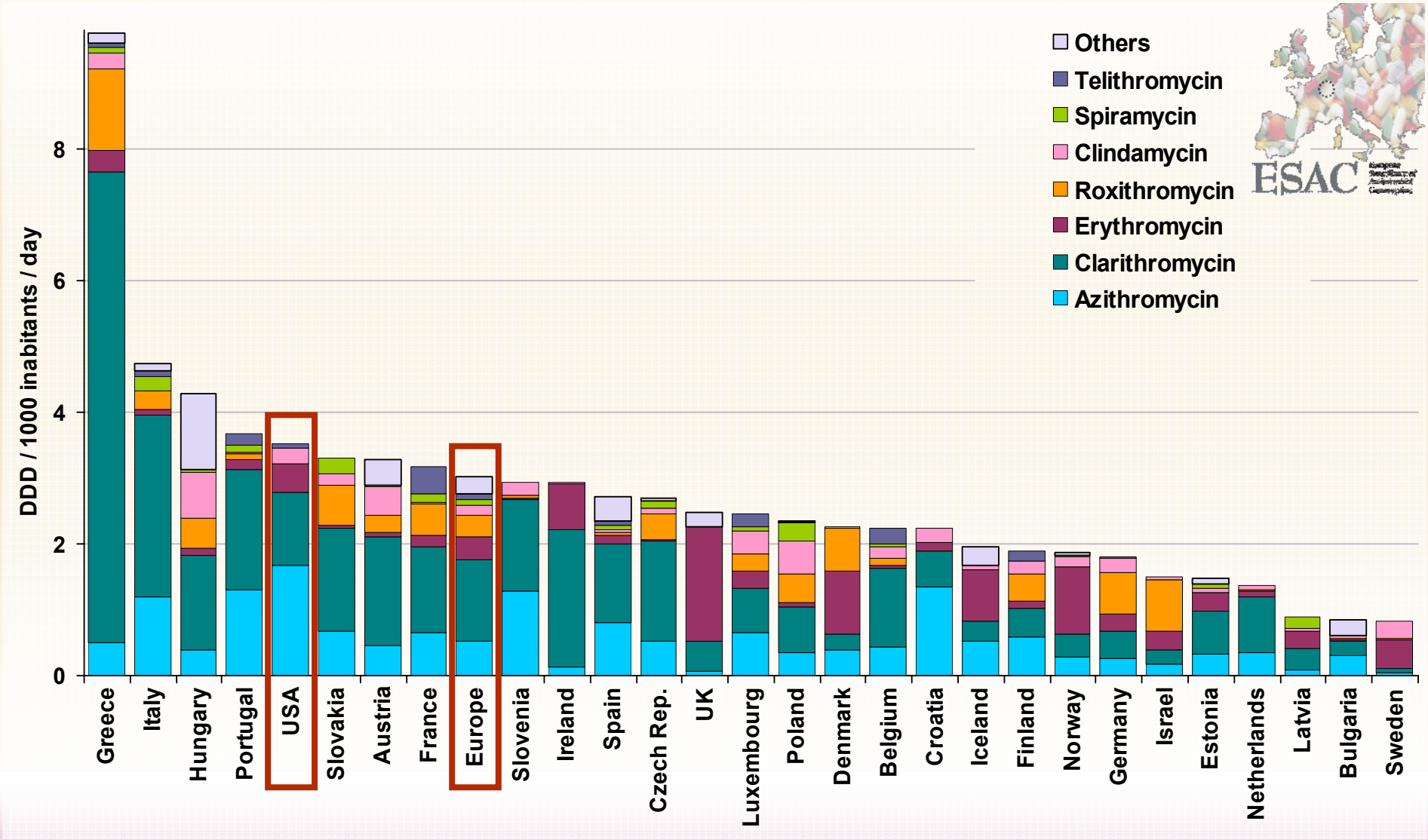
Outpatient Antibiotic Use
Europe versus USA

Total outpatient antibiotic use in 27 European countries and USA in 2004

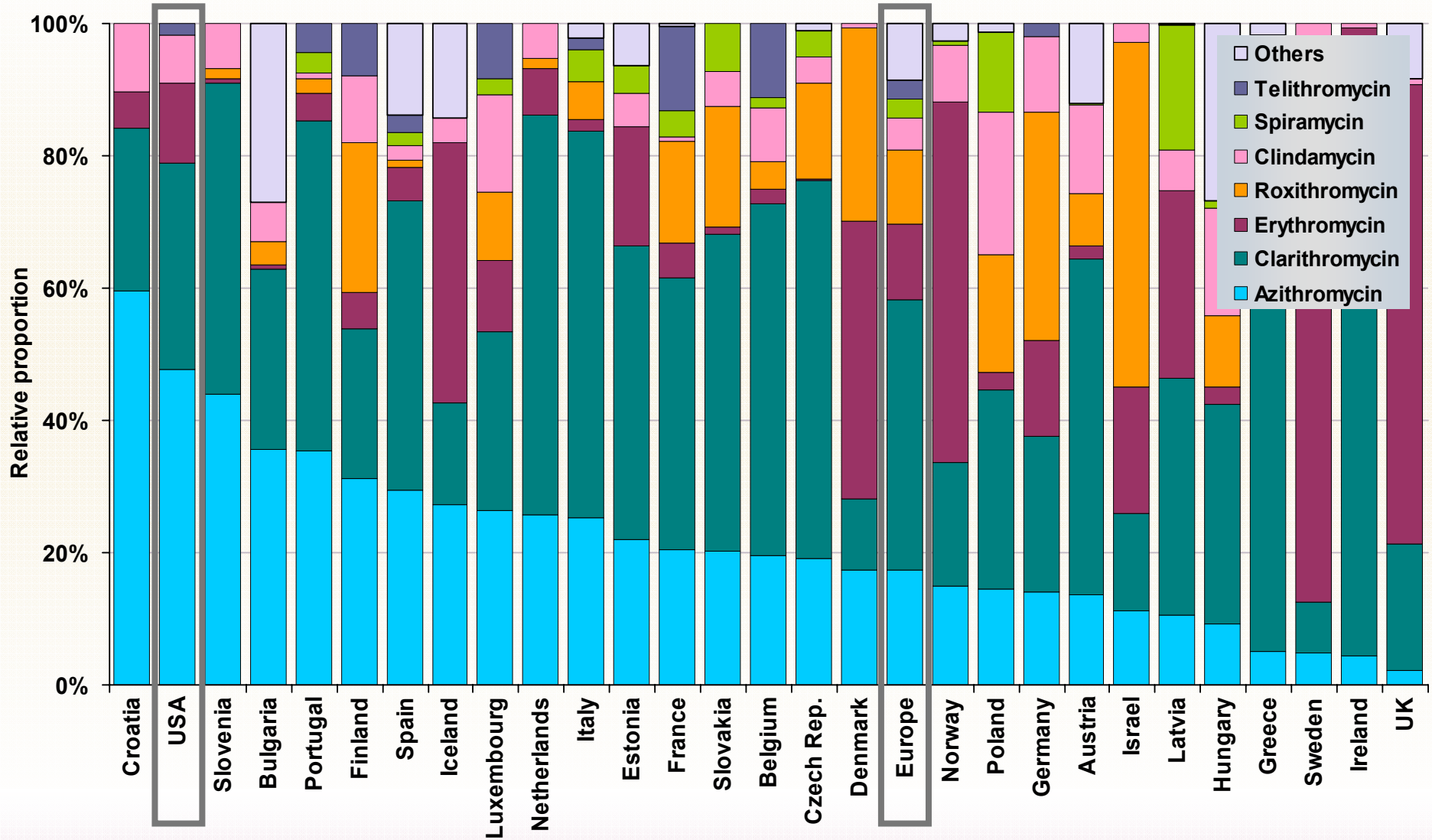


Goossens et al, CID, April 2007

Total Outpatient MLS Use in the United States and 27 European Countries in 2004



Relative Outpatient MLS Use in the United States and 27 European Countries in 2004



Outpatient systemic use of major antibiotic classes in the United States and Europe in 2004

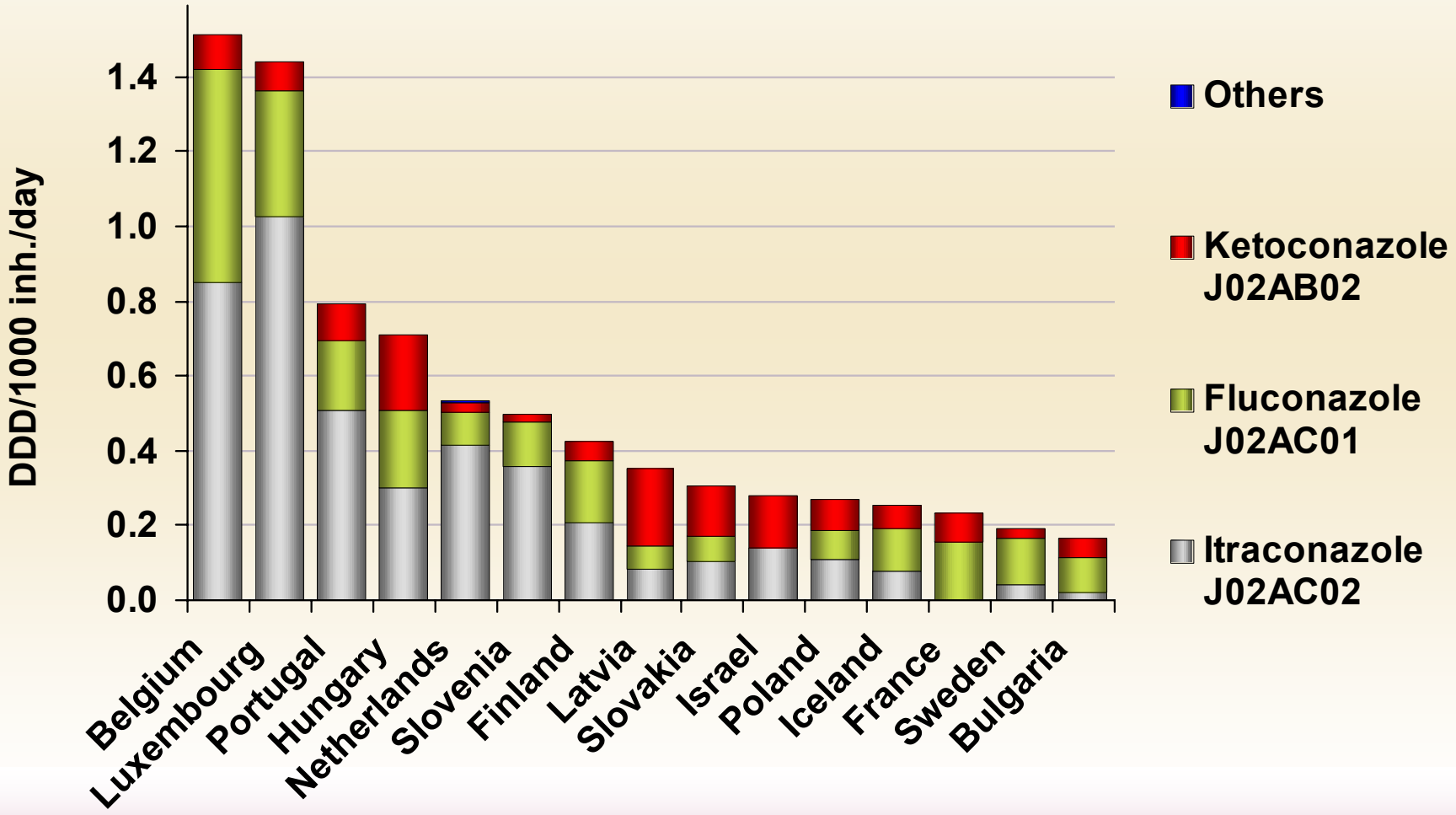
de	Corresponding antibiotics (sub)class	USA DID*	USA (%)	Europe DID*	Europe %
	Tetracyclines	4.63	(18.60)	2.37	(12.42)
	Penicillines [8]	9.70	(38.93)	8.71	(45.73)
J01CE	*Narrow spectrum penicillins*	*0.68*	*(2.71)*	*0.75*	*(3.92)*
J01CA	*Broad spectrum penicillins*	*5.68*	*(22.81)*	*4.49*	*(23.58)*
J01CR	*Combination of penicillins*	*3.29*	*(13.22)*	*3.20*	*(16.82)*
J01CF	*Penicillin resistant penicillins*	*0.05*	*(0.19)*	*0.27*	*(1.40)*
	Cephalosporins, monobactams, carbapenems [9]	2.48	(9.94)	2.03	(10.65)
J01DB	*First generation cephalosporins*	*1.47*	*(5.90)*	*0.31*	*(1.62)*
J01DC	*Second generation cephalosporins*	*0.61*	*(2.46)*	*1.12*	*(5.89)*
J01DD	*Third generation cephalosporins*	*0.39*	*(1.57)*	*0.59*	*(3.11)*
	Sulphonamides and trimethoprim	1.34	(5.37)	0.77	(4.04)
	Macrolides, lincosamides and streptogramins [10]	3.52	(14.14)	2.98	(15.66)
	Short-acting macrolides	*0.43*	*(1.73)*	*0.48*	*(2.54)*
	Intermediate-acting macrolides	*1.16*	*(4.66)*	*1.71*	*(8.96)*
	Long-acting macrolides	*1.68*	*(6.74)*	*0.53*	*(2.77)*
J01FF	*Lincosamides*	*0.25*	*(1.02)*	*0.16*	*(0.85)*
J01FG	*Streptogramins*	*<0.01*	*(0.00)*	*0.10*	*(0.55)*
	Quinolones [11]	2.47	(9.91)	1.58	(8.32)
	First generation quinolones	*0.01*	*(0.03)*	*0.41*	*(2.15)*
	Second generation quinolones	*2.07*	*(8.30)*	*1.01*	*(5.31)*
	Third generation quinolones	*0.39*	*(1.58)*	*0.16*	*(0.86)*
+R+X	Others	0.78	(3.11)	0.61	(3.18)
		24.92	**(100.00)**	**19.04**	**(100.00)**

Outpatient systemic use of antibiotic substances in the United States and Europe in 2004.

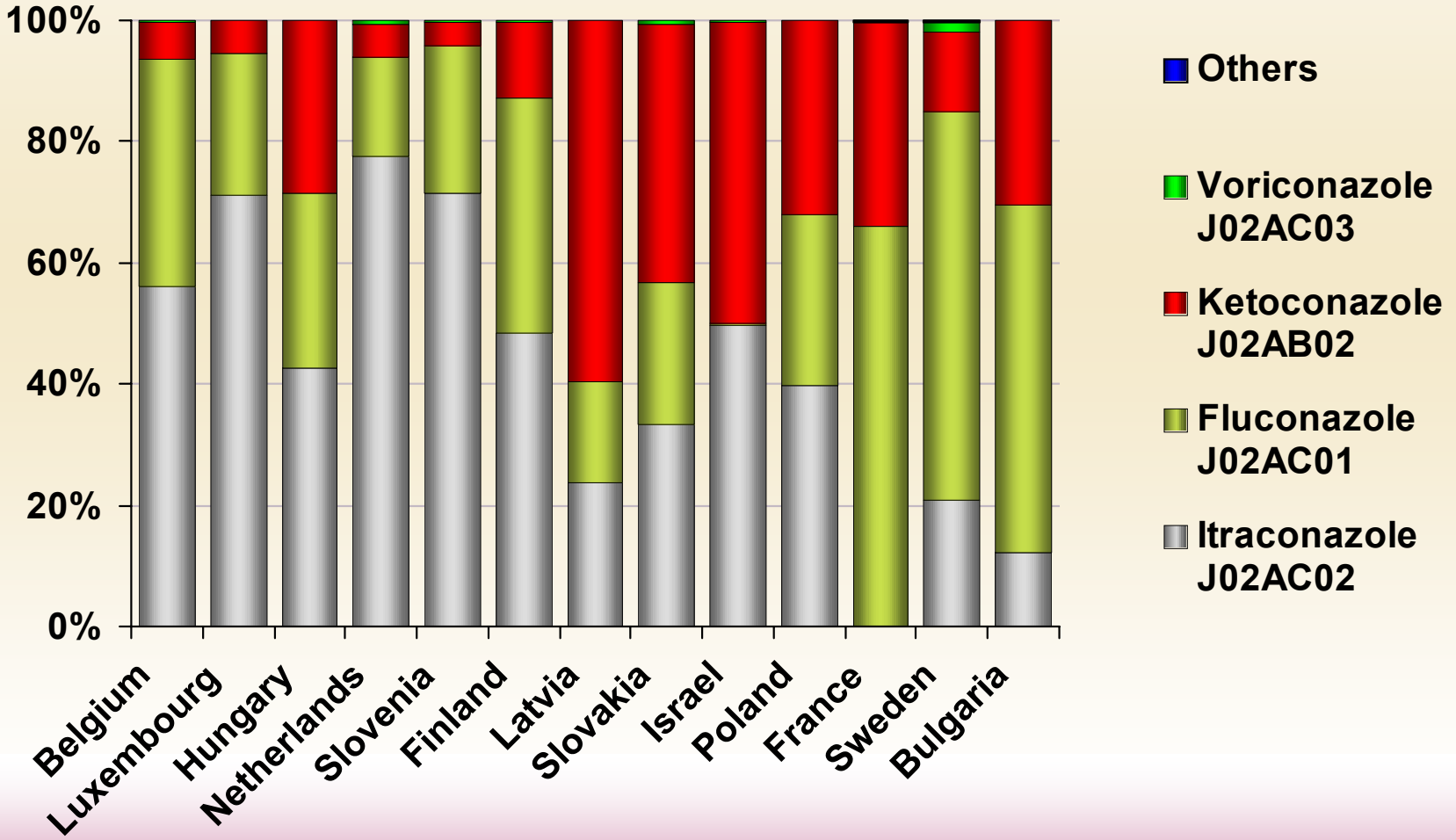
Antibiotic	United States	Europe	Range in Europe	
	DID** (%)	DID** (%)	Highest DID** (country)	Lowest DID** (country)
Amoxicillin	5.59 (22.4)	4.26 (22.3)	12.83 (France)	3.76 (Netherlands)
Co-amoxiclav	3.29 (13.2)	3.16 (16.6)	7.32 (Portugal)	<0.01 (Norway)
Doxycycline	2.98 (12)	1.73 (9.1)	5.17 (Iceland)	0.31 (Italy)
Azithromycin	1.68 (6.7)	0.52 (2.7)	1.34 (Croatia)	0.04 (Sweden)
Cefalexin	1.39 (5.6)	0.17 (0.9)	1.89 (Finland)	No use (Greece)
Co-trimoxazol	1.31 (5.2)	0.56 (2.9)	1.62 (Croatia)	<0.01 (Denmark)
Clarithromycin	1.10 (4.4)	1.23 (6.5)	7.16 (Greece)	0.06 (Sweden)
Minocycline	1.07 (4.3)	0.24 (1.3)	1.36 (Ireland)	No use (>1 country)
Levofloxacin	1.06 (4.3)	0.24 (1.3)	1.05 (Italy)	No use (>1 country)
Ciprofloxacin	0.97 (3.9)	0.59 (3.1)	1.81 (Portugal)	0.17 (Croatia)
Phenoxymethylpenicillin	0.68 (2.7)	0.64 (3.4)	5.23 (Denmark)	No use (>1 country)
Nitrofurantoin	0.63 (2.5)	0.27 (1.4)	0.8 (Netherlands)	No use (>1 country)
Tetracycline	0.57 (2.3)	0.08 (0.4)	1.02 (Finland)	No use (>1 country)
Erythromycin	0.43 (1.7)	0.34 (1.8)	1.72 (UK)	0.01 (Bulgaria)
Cefuroxime	0.35 (1.4)	0.70 (3.7)	3.40 (Luxembourg)	No use (Norway)
Cefdinir	0.34 (1.4)	No use	No use	No use (>1 country)
Clindamycin	0.25 (1.0)	0.14 (0.8)	0.70 (Hungary)	<0.01 (Italy)
Moxifloxacin	0.25 (1.0)	0.16 (0.9)	0.56 (Belgium)	No use (>1 country)
Grand Total	**24.91 (100)**	**19.04 (100)**	33.37 (Greece)	9.75 (Netherlands)

Outpatient Antimycotic Use in Europe

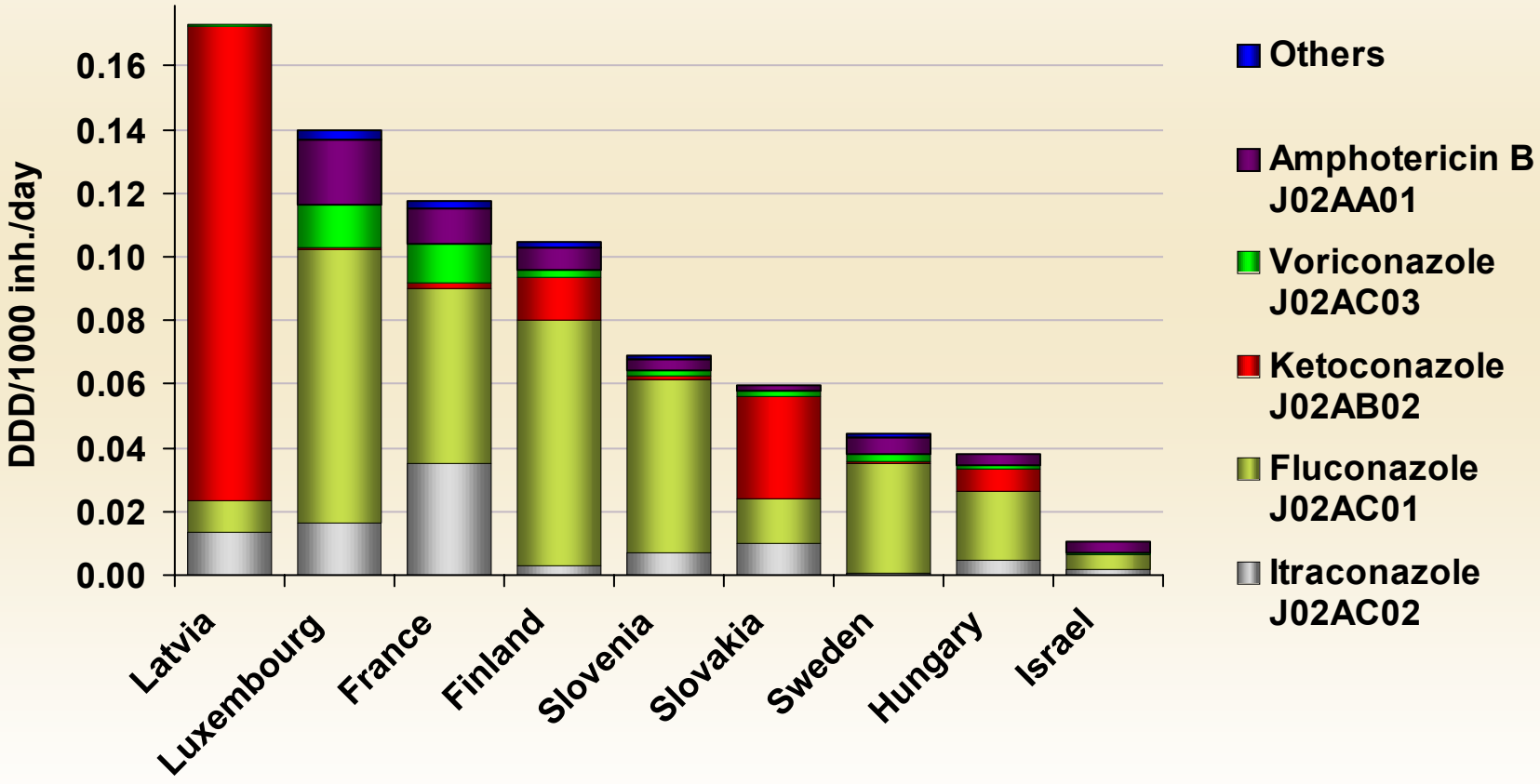
Total outpatient antimycotic use in 15 European countries in 2004



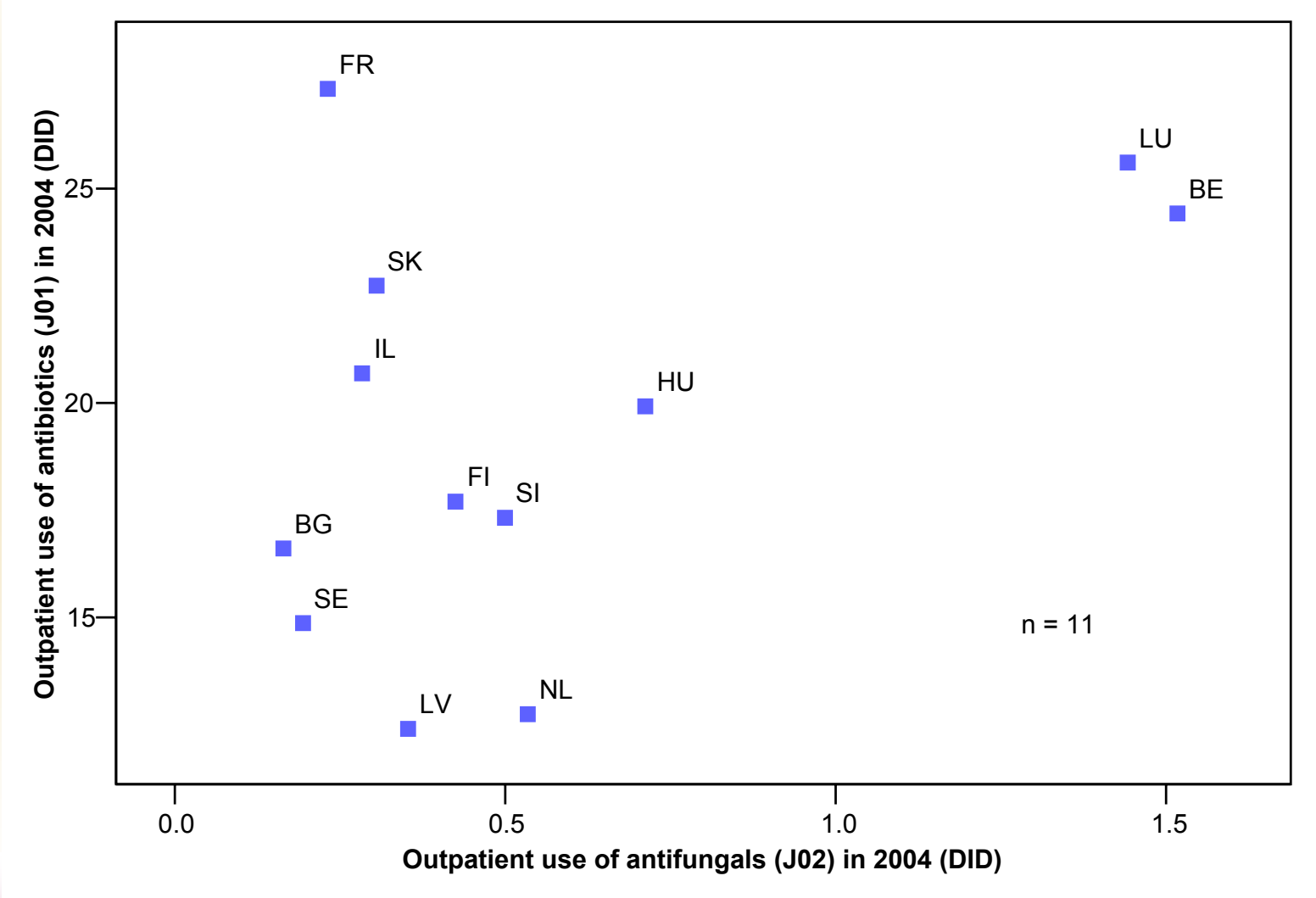
Outpatient use of antimycotics in 15 European countries in 2004



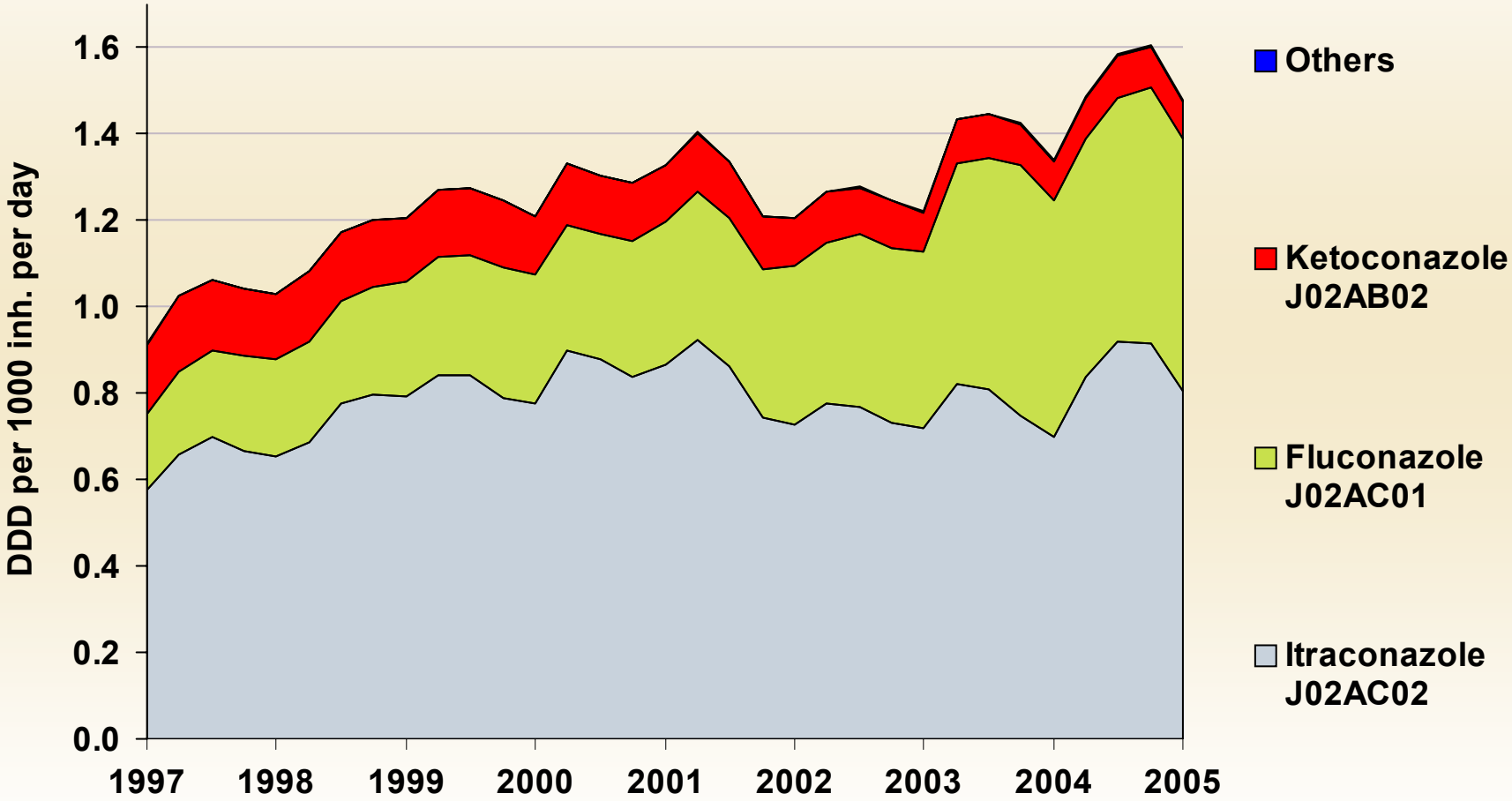
Hospital use of antimycotics in 9 European countries in 2004



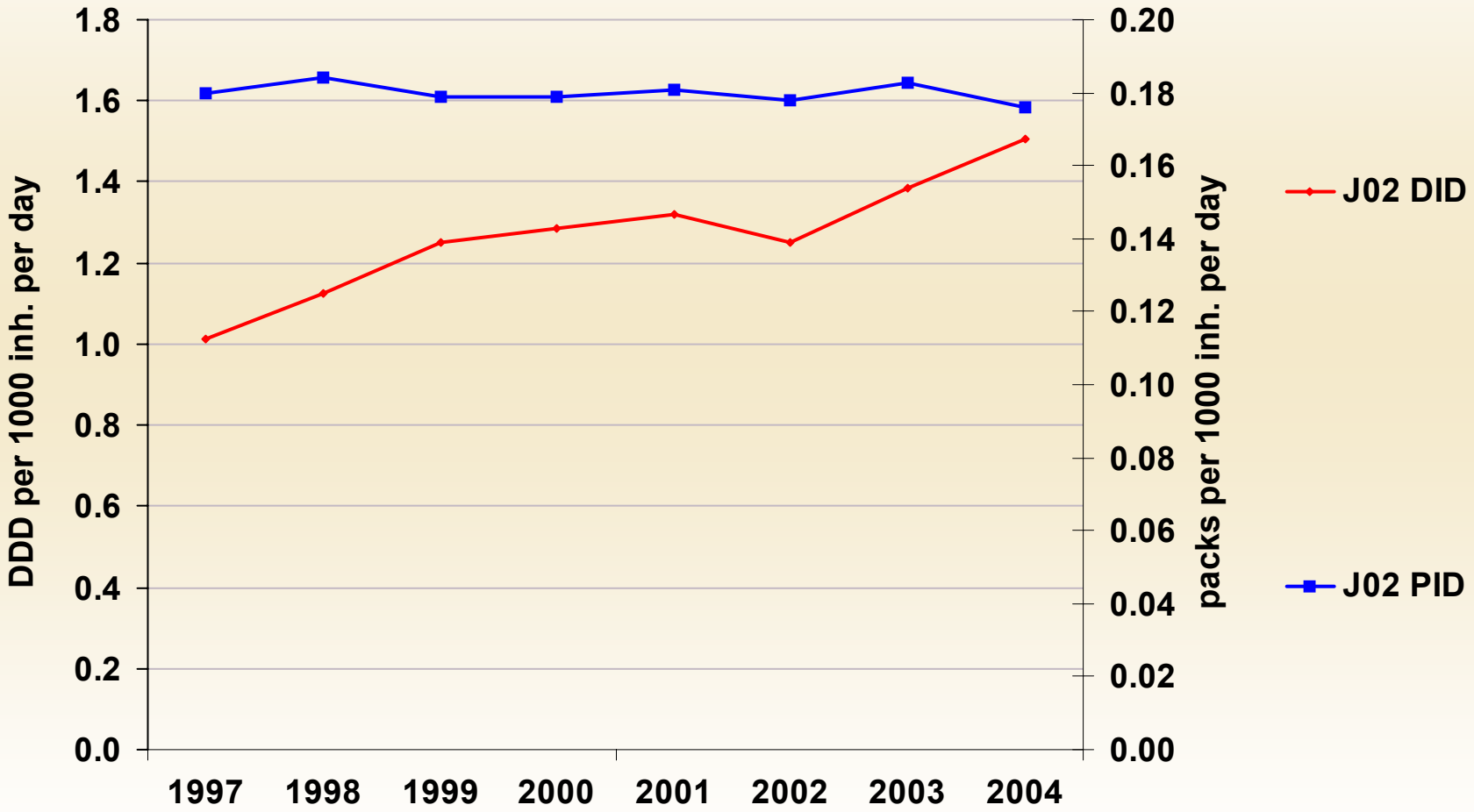
Correlation between outpatient antimycotic use and outpatient antibiotic use in 2004



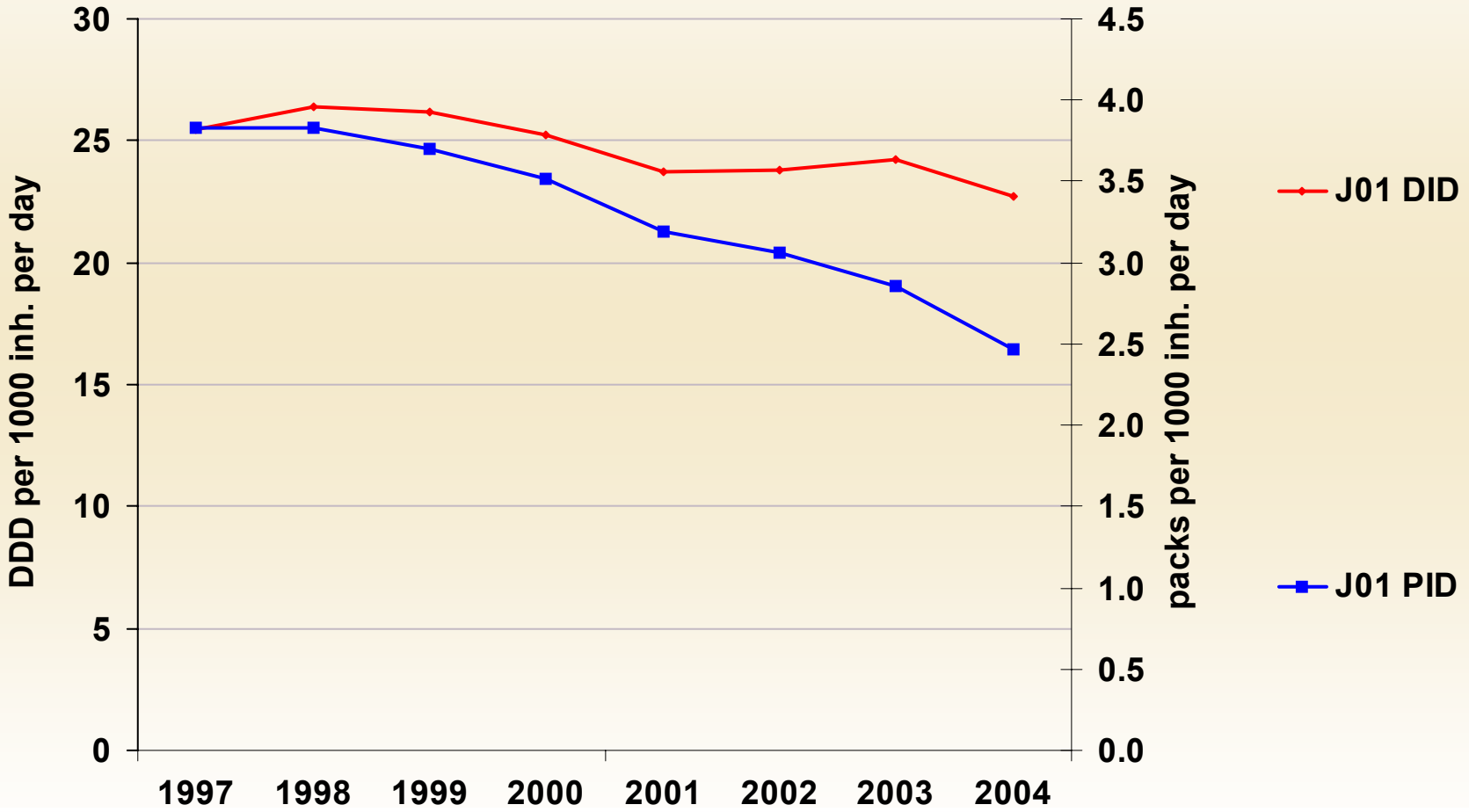
Outpatient antimycotic use in Belgium between 1997 and 2005



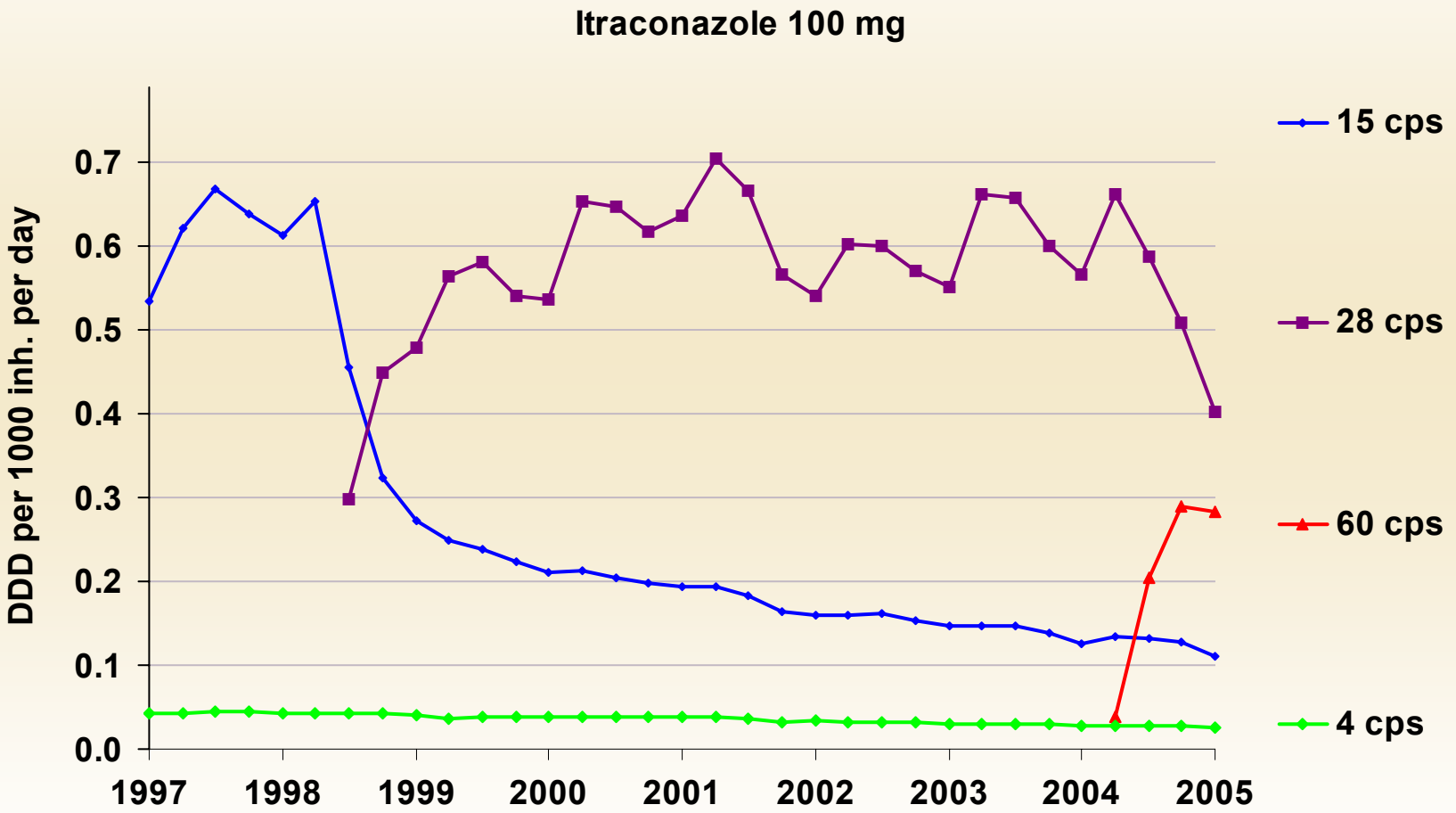
Outpatient antimycotic use in Belgium between 1997 and 2004



Outpatient antibiotic use in Belgium between 1997 and 2004



Outpatient itraconazole use in Belgium between 1997 and 2005



CONCLUSION

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.