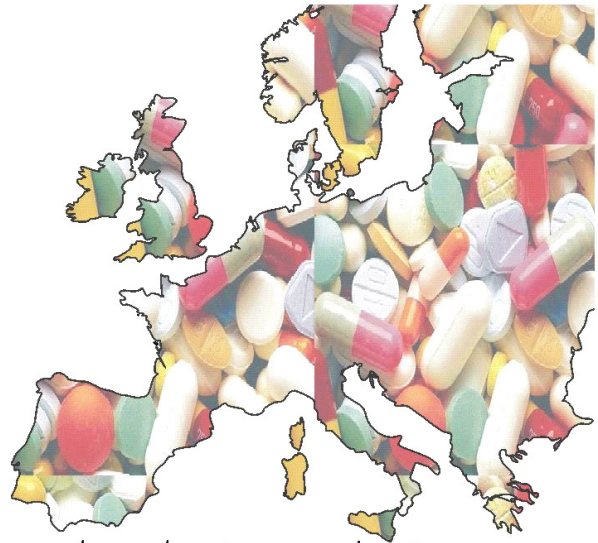
REPORT ON POINT PREVALENCE SURVEY OF ANTIMICROBIAL PRESCRIBING IN EUROPEAN HOSPITALS, 2009

ESAC-3: Hospital Care Subproject Group



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LIST OF ABBREVIATIONS

ATC	Anatomical Therapeutic Chemical
CAI	Community Acquired Infection
DDD	Defined Daily Dose
DU	Drug Utilisation
ECDC	European Centre for Disease Prevention and Control
EEA	European Economic Area
EFTA	European Free Trade Association
ESAC	European Surveillance of Antimicrobial Consumption
HAI	Hospital Acquired Infection
HALT	Healthcare Associated Infections and Antibiotic use in Long-Term Care Facilities
HC	Hospital Care
ICU	Intensive Care Units
LS	Longitudinal Survey
PDA	Personal Digital Assistant
PPS	Point Prevalence Survey
STRAMA	Swedish strategic programme against antibiotic resistance.
WHO	World Health Organisation

SUMMARY

The ESAC Point Prevalence Survey (PPS) is the only European multicenter survey of antimicrobial prescriptions in hospitals. This survey has previously been successfully implemented in 20 hospitals during the 2006 PPS and in 50 hospitals in 2008. The aim of PPS-2009 was to perform a PPS in a larger sample of European hospitals compared to the previous 2 PPS.

Data was collected during a maximum of two weeks from May-July and in November 2009. A total of 193 hospitals from 25 European countries were enrolled of which 177 were able to deliver compatible data for analysis. The protocol was quasi identical to the protocol of PPS 2008, with the addition of 'Compliance with Guidelines' and removal of 'Relevant samples taken for culture'. A web-based application was used for data entry and upload. Antimicrobial prescriptions were recorded using the ATC classification. Demographic data on treated patients, indications, diagnoses, culture pre-therapy and reasons for treatment recorded in notes were collected.

A large number of hospitals from the United Kingdom (namely England [45] and Scotland [32]), Belgium [21] and Ireland [21] participated. In order to eliminate possible bias by these countries a sample of hospitals, not exceeding 5/country was randomly selected. Thus from a total of 177 hospitals from 25 countries a sample of 75 hospitals was used in this analysis.

Among the 37,352 admitted patients, 10,677 (28.4%) received antimicrobials for a total of 14,742 therapies. The majority of treated patients (71%) received monotherapy. This was different in intensive-care, which had the highest proportion of treated patients (58%) with 96 therapies/100 patients. The combination penicillins including β-lactamase inhibitors were the most popular across all specialties and indications. However, in intensive-care, hospital-specific agents (e.g., carbapenems, glycopeptides and aminoglycosides) ranked high in use. These drugs are mainly used via the parenteral route which was 93% for intensive-care. Community-acquired-infections (CAI) accounted for 52% of all indications. A third (32%) of CAI was due to respiratory-tract-infections, which was the most common site also in hospital-acquired infections (26%). Pneumonia (18%), skin and soft-tissue infections (11%) and intra-abdominal infections (7%) were the most common diagnoses. Prolonged duration (>1 day) of surgical prophylaxis was practised in more than half (57%) of the cases. At ATC level 4, 37 drug-classes were used as monotherapy whilst combination therapy included 618 different types of prescriptions including combinations.

The PPS 2009 results are concordant with the 2006 and 2008 PPS data. The survey confirmed that duration of surgical prophylaxis is a key quality indicator in the surgical departments. The ESAC web-based tool can be rolled out in the near future to other continents with interest expressed from North America, Africa and Oceania.

INTRODUCTION

1. Background

In 2007, the European Centre for Disease Prevention and Control (ECDC) granted a third phase of the European Surveillance of Antimicrobial Consumption project (ESAC-3) for a period of 3 years (2007-2010). The overall aim of the project is to consolidate the continuous collection of comprehensive antimicrobial consumption data, in ambulatory and hospital care, from the 27 Member States, 3 EEA/EFTA (Iceland, Norway and Switzerland), 3 candidate countries (Croatia, Former Yugoslavian Republic of Macedonia, and Turkey)[1], Russia, and Israel.

Additionally, the project aims to deepen the knowledge of antimicrobial consumption by focusing on specific consumption groups and/or patterns in collaboration with those countries where the appropriate data are available. In-depth hospital care data collection focuses on collection of consistent data from hospitals in each country in order to develop a standard method that can be used throughout the European Union.

Within ESAC-1, it was recognised that there was no cohesive hospital information on antimicrobial use across the European countries. The explanations included the lack of standardised methods for producing valid data either for hospital antimicrobial use or for denominator data related to clinical activity, such as occupied bed days or admissions. A subproject of ESAC-2 on Hospital Care focused on consistent data collection from individual hospitals in order to develop a standard method that could be rolled out to other hospitals in Europe. Two surveys were carried out, one Point Prevalence Survey (ESAC-2 PPS) and one Longitudinal Survey (ESAC-2 LS). It was concluded that antimicrobial use was influenced by number of admissions and by the length of stay; therefore adjustment for clinical activity should include both admissions and occupied bed days. The ESAC-2 LS showed wide differences in antimicrobial use trends, patterns, and hospital characteristics between European hospitals. ESAC provided a simple tool that provided important detail about management of individual patients that can be used to produce quality indicators. This simple tool was implemented successfully in the hospitals and identified important targets for quality improvement (e.g. peri-operative prophylaxis; antibiotics used to treat infections in accordance with the hospital guidelines; documentation of antibiotic therapy).

ESAC-3 uses the methodology developed within the ESAC-2 Hospital Care subproject. It includes one Longitudinal Survey (LS 2009) and two Point Prevalence Surveys (PPS 2008 & PPS 2009). A simplified version of the protocol of the 2006 PPS was used. A web application was specifically developed for data entry and automatic feedback.

2. Aims

- To establish a European network for point prevalence surveys.
- To organise a European wide point prevalence survey.
- To investigate hospital characteristics which could, at least partially, explain variation in antibiotic use.
- To have as many hospitals as possible committed to our point prevalence survey so that the pledge is translated into improved antibiotic prescribing.
- To identify targets for quality improvement.
- To develop quality indicators of antimicrobial consumption in the hospital care sector.

European benchmarking between European countries is NOT an aim.

METHODS

1. Survey design and data source

The 2009 PPS was performed in 193 hospitals from 25 European countries. The PPS-2008 protocol of was minimally modified removing 'sample for culture and sensitivity testing' and adding 'Compliance to Guidelines'. The Web-PPS, specifically developed for data entry and automated feedback and reporting for the participating hospitals for PPS-2008 was once again used.

2. Data collection

Data on antibiotic use was collected by reviewing all inpatients during a maximum of two calendar weeks between May November 2009 in all wards of the hospitals. Patients were reviewed by dedicated teams including infectious diseases specialists, microbiologists, pharmacists and/or infection control nurses.

All inpatients that were present in the hospital at least 24 hours before the survey and present at 8 am on the day of survey in the ward were included in the study. The number of admitted patients at 8 am in each ward was entered in the PPS Database as the denominator value. All other patients e.g. day patients and outpatients were defined as ambulatory care patients. Hence, day care patients such as renal dialysis and cancer wards were excluded from the survey. Surgical wards were surveyed on Tuesday, Wednesday, or Thursday in order to capture information on prophylaxis during the previous 24 hours. Medical wards were surveyed on Monday, Tuesday, Wednesday, or Thursday. Depending on the number of beds, hospitals decided to complete the survey on either one or more days. However, all beds in each administrative unit (e.g. Internal Medicine, General Surgery, Intensive Care*., etc.*) had to be completed in a single day.

Patients who were receiving antimicrobials at 8 am on the day of the survey were followed in detail. For these patients, information was collected on age, gender, antimicrobial agent according the ATC classification (dose per administration, number of doses per day, and route of administration), anatomical site of infection or target for prophylaxis according to the list of diagnosis groups, indication for therapy (community acquired infection, hospital acquired infection or prophylaxis), relevant culture before therapy and indication for given therapy in medical records. For surgical patients, administration of prophylactic antimicrobials was checked for the previous 24 hours. The details were recorded as surgical prophylaxis. The reason was to code the duration of prophylaxis as either one dose, one day or more than 1 day.

Each ward was assigned to a speciality that was linked to a general activity (medicine, surgery, intensive-care and other). Intensive-care-units (ICU) also included high dependency units, burns units and neonatal units. The survey form is provided in Appendix 1 and the list of included antimicrobials at the ATC level 4 in Appendix 2.

Antimicrobial use was reported as the number of treated patients and the number of therapies. Therapy was defined as the prescription of one substance in one route of administration. These indicators were calculated for the entire hospital and by type of units: medicine, surgery, intensive care and other. For the analyses, the average or median were used as central indicator where appropriate.

3. ESAC Web-PPS Tool

For the ESAC-2 PPS, data submission was done using the STRAMA application, adapted by ESAC team for the specific needs of ESAC. In ESAC-3, a web-based tool was developed in-house, the Web-PPS. The tool is a web application developed in Java where data are backed up in a 'Postgresql' database for which open source software has been used. Basically, the programme mapped the paper forms to web forms. In addition, a personal digital assistant (PDA) form was also developed in order to use these devices for data entry.

RESULTS

1. General overview of the survey

ESAC collected compatible data for analysis on antimicrobial therapies from 177 hospitals from 25 countries. However for these analyses, a maximum of 5 hospitals per country were randomly selected (Table 1). A simulation method was used to select 30 samples of 75 hospitals with not more than five hospitals per country. The selection of 5 hospitals within a country was robust to random variation. Therefore, from this point forward reference is made exclusively to the 75 randomly selected hospitals using SAS software (Proc surveyselect) was applied when the hospital number per country was above five. The selected hospitals were distributed as follows: 28 were tertiary, 32 were secondary, 10 were primary, 3 infectious diseases and 1 was paediatric institution. Teaching hospitals represented 35 of the 74 hospitals. A list of the participating hospitals can be found in Appendix 4, which also contains a number of hospitals which either did not validate their data or reported to have no patients on treatment.

Table 1 List of Participating/Selected Hospitals per country

Countries	Participating hospitals			Included Hospitals		
	n	Treated patients	Total patients	n	Treated patients	Total patients
AUSTRIA	7	747	2732	5	572	2136
BELGIUM	21	2054	7538	5	481	1737
BULGARIA	1	112	564	1	112	564
SWITZERLAND	2	557	2136	2	557	2136
CYPRUS	2	278	591	2	278	591
CZECH REPUBLIC	4	696	2685	4	696	2685
DENMARK	2	198	535	2	198	535
ESTONIA	3	298	1461	3	298	1461
ENGLAND	45	7200	24870	5	875	3438
SPAIN	2	516	1322	2	516	1322
FRANCE	3	407	1639	3	407	1639
CROATIA	3	484	1729	3	484	1729
HUNGARY	1	733	2771	1	733	2771
IRELAND	21	1954	5679	5	685	1886
ISRAEL	1	103	496	1	103	496
ITALY	2	395	1004	2	395	1004
LATVIA	2	305	993	2	305	993
MALTA	1	270	744	1	270	744
N. IRELAND	4	632	2074	4	632	2074
NORWAY	2	144	582	2	144	582
PORTUGAL	2	379	656	2	379	656
RUSSIA	3	172	1484	3	172	1484
SCOTLAND	32	2447	8794	5	129	383
SLOVENIA	5	515	1668	5	515	1668
WALES	6	754	2746	5	741	2638
Grand Total	177	22350	77493	75	10677	37352

2. Patient overview

Among the 37,352 admitted patients, 10,677 received antimicrobials for a total of 14,742 prescriptions. Figure 1 shows the distribution of the number of included patients (median: 348; range: 17-2,771) and the distribution of the number of treated patients/100 patients (median: 29.5; range: 2.5-69.6). The median age of the treated patients was 64 years (range: 0-103). The hospital proportion of female patients was 45.7% (range: 21.9-85.7).

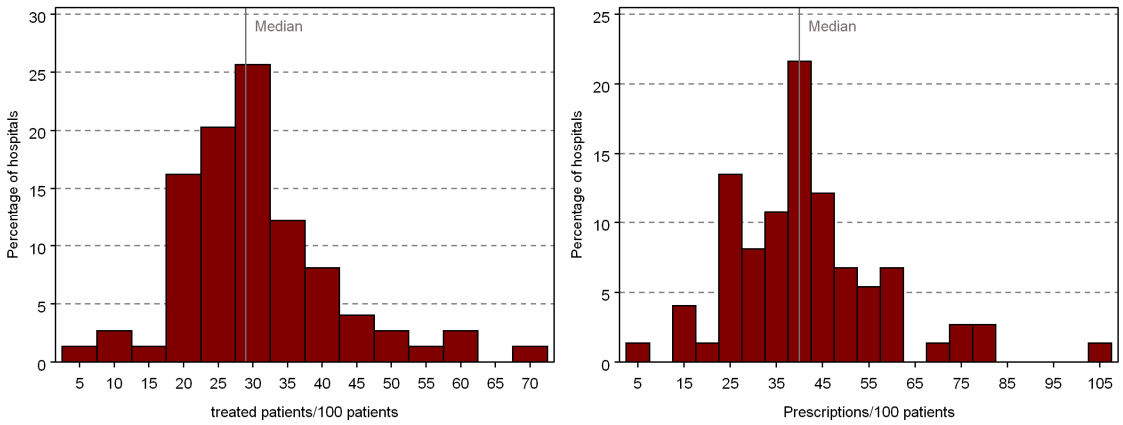


Figure 1 Distribution of the number of treated patients /100 patients (left), distribution of the number of prescriptions/100 patients (right)

The average of treated patients/100 patients in hospitals was higher in ICU units (ICUs) as summarised in Table 2 and Figure 2.

Table 2 Proportion of treated patients/100 patients and therapies/100 patients split by specialties

Specialties	N	Average treated patients/ 100 patients	Average therapies/ 100 patients	Average prescriptions/ patient
Medicine	**75**	29.83	40.1	1.32
Surgery	**70**	32.61	42.66	1.30
Intensive-care (ICU)	**68**	58.34	96.04	1.63
Other	**25**	14.18	19.73	0.96
Total	**75**	**31.07**	**42.26**	**1.35**

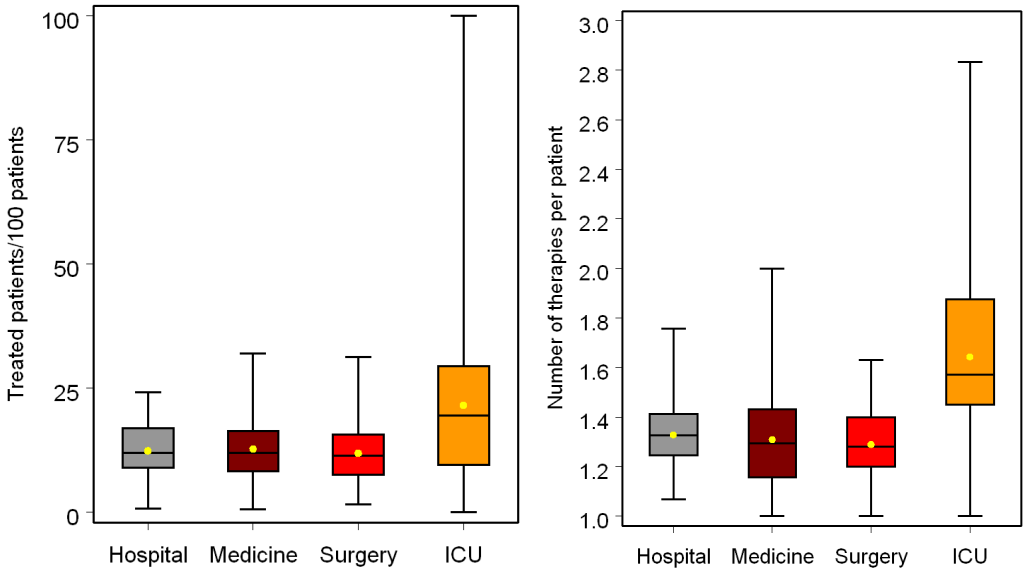


Figure 2 Proportion of treated patients (left) Therapies/patient - by specialty (right)

The overall mean number of therapies was 1.3 per patient. It was highest in ICU (1.63). The proportions of monotherapy, 2-3 therapies and >3 therapies are shown in Figure 3 which indicates that non-J01 antimicrobials are less frequently used as monotherapy.

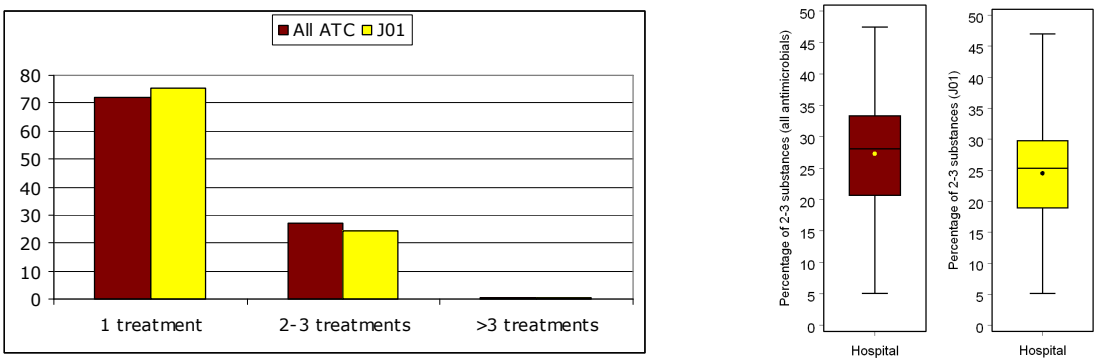


Figure 3 Proportion of the number of therapies given to treated patients (left), distribution of the percentage of treated patients with 2 to 3 therapies among hospitals (right)

3. Drug utilisation

3.1. ATC 2 level

The proportion of antibacterials for systemic use (J01) was 92.9% (range: 75.0-100), antifungals (J02, D01AB) 4.1% (range: 0-22.2), rifampicin (J04) 0.7% (range: 0.0-3.8) and 'Others' (A07, P01) 4.4% (range: 0.0-14.6), respectively (Fig. 4).

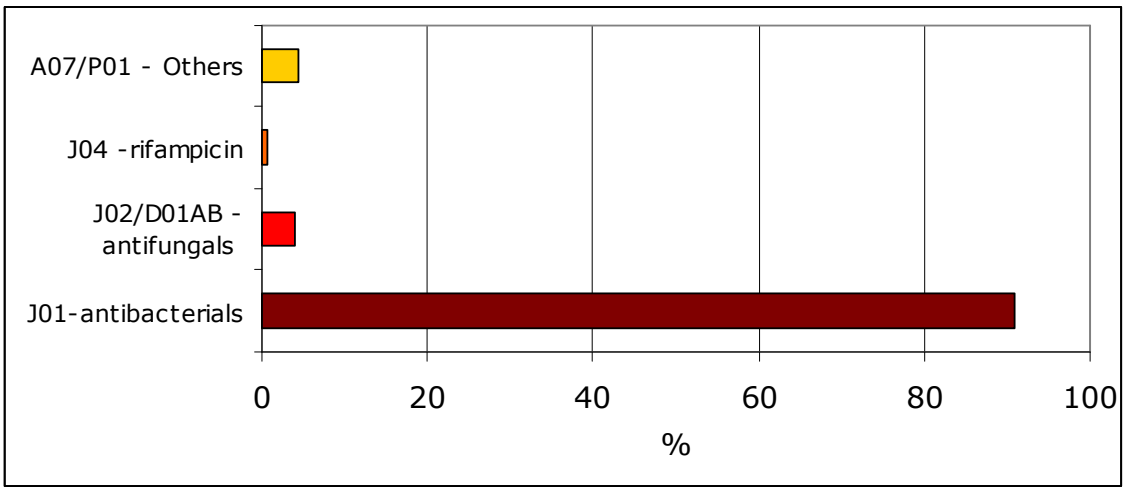


Figure 4 Proportion of antimicrobial agents at ATC2 level

Out of the 75 hospitals, four reported use only of antibacterials (J01) whilst 39 reported no use of rifampicin. Only 2 hospitals reported use of D01 and a total of 17 reported no use of antifungals, whilst 15 reported no use of 'Others' which include oral/rectal metronidazole. A total of 39 hospitals reported no use of at least one of these three drug classes.

There was a significant difference between the proportions of treated patients/100 patients between all department categories. The overall proportion of treated patients was 29.1%. The difference between departments ranged from 54.4% in ICU, to 30.7% in surgical, 26.7% in medical and 7.9% 'other' departments, respectively.

3.2. ATC 3 level

The proportion of penicillins (J01C) was significantly different between Medicine (32%), Surgery (29%) and ICU (23%), respectively (p <0.01). For the other β-lactams (J01D) there was no significant difference between Surgery and ICUs, both of which were significantly different to medicine (p <0.01) (Fig. 5). J01C was more prominent in medicine than in ICUs whilst the opposite applied for other β-lactams (J01D).

At ATC 3 level the major difference is between the treatment of patients within an intensive care setting as opposed to all other settings both in the quantity and quality of drugs used (Fig. 6). The penicillins (J01C) were used almost twice as much in ICUs. However, the major differences between ICU's and the rest of the hospital, is observed in other beta-lactams, aminoglycosides and glycopeptides.

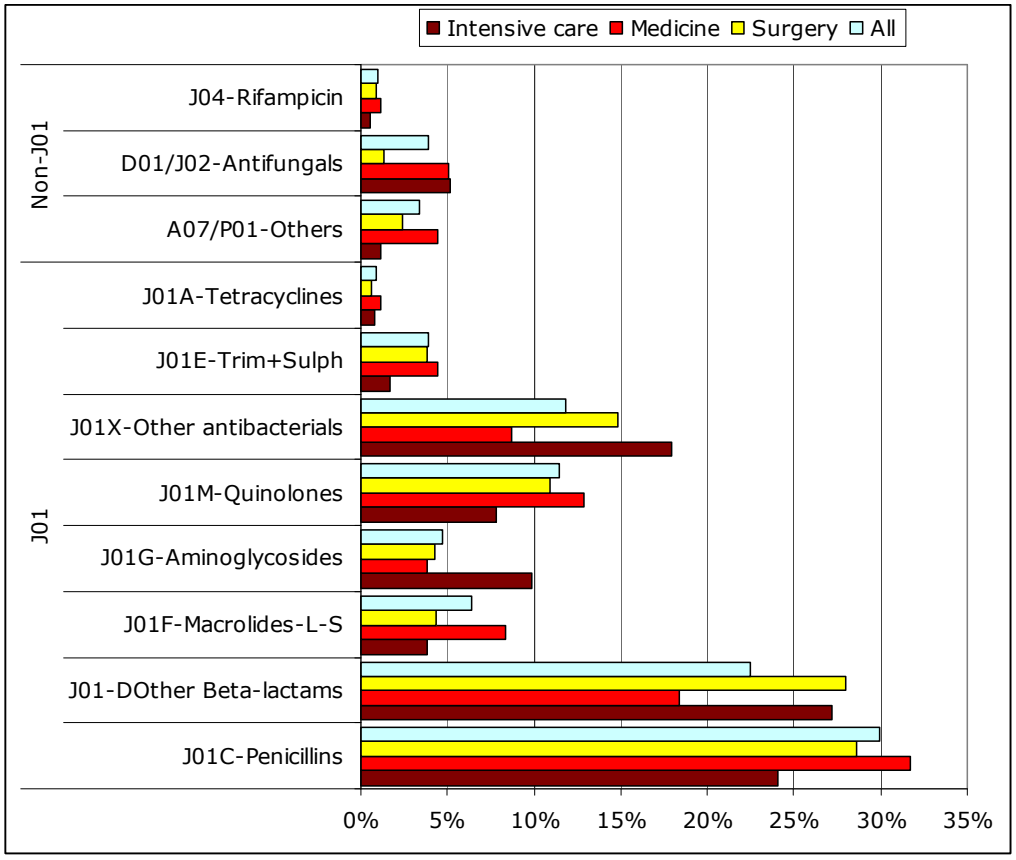


Figure 5 Proportion of use at ATC3 level by specialty

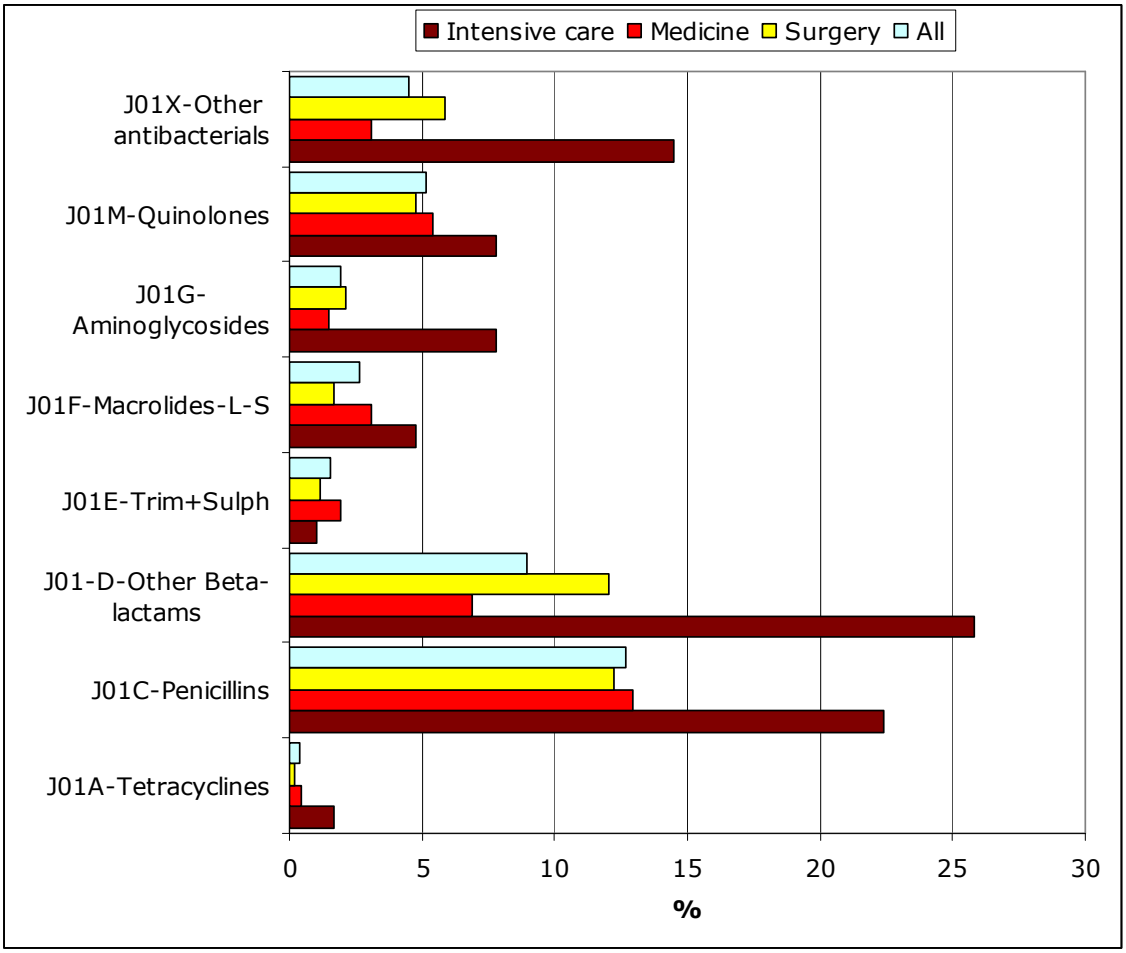


Figure 6 Proportion of treated patients/100 patients at ATC3 level by specialty

Figure 7 shows the combinations of penicillins with β-lactam inhibitors (J01CR), fluoroquinolones (J01MA) and third generation cephalosporins (J01DD) were the most commonly prescribed, on average 8.5% (range: 0-20.8), 4.9% (range: 0-13.2) and 3.4% (range 0.0-21.7), respectively within the hospitals. In ICU, the prevalence of treated patients was higher for most classes. The major class at ATC4 level, in ICUs, was also penicillins with β-lactam inhibitors (J01CR) followed by carbapenems (J01DH), third generation cephalosporins (J01DD), and the other aminoglycosides (J01GB). The proportion of treated patients/100 patients for all therapies is provided in Appendix 3.

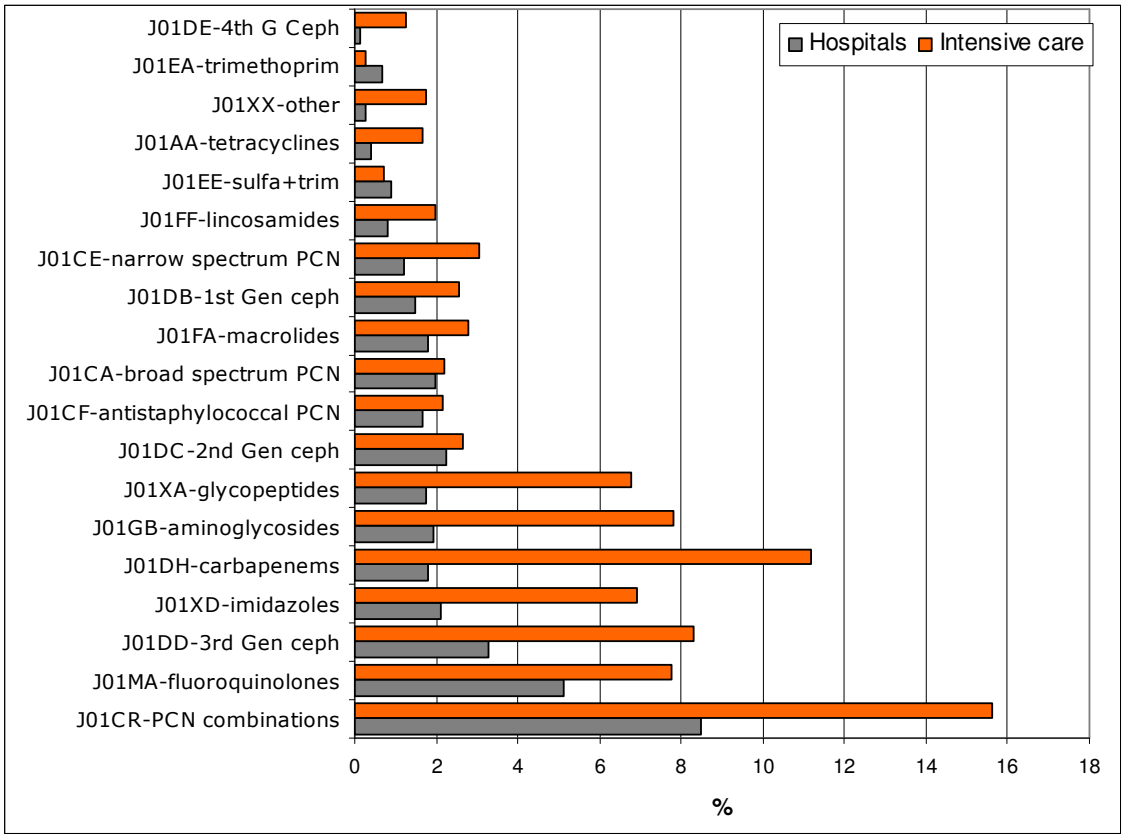


Figure 7 Proportion of treated patients/100 patients aggregated at ATC4 level

3.3. Route of administration

The proportions of parenteral use within: hospitals; medicine; surgery; and ICU were – 66% (range: 21-94), 57% (range: 9-89), 69% (range: 32-100), and 96% (range: 74-100), respectively. However, the parenteral proportion varied widely between hospitals as shown in Figure 8.

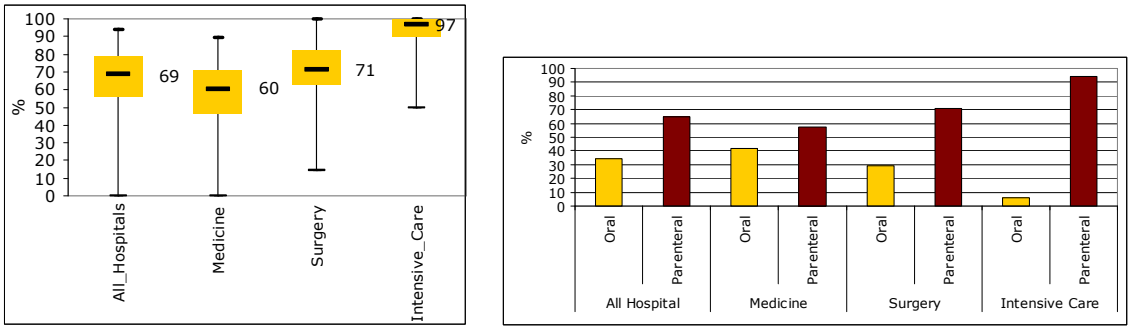


Figure 8 Distribution of percentage of parenteral therapies among hospitals (left), distribution of the oral and parenteral routes of administration split by specialty

In ICUs, most of the therapies were parenteral except for the sulphonamides and trimethoprim class (J01E). In medicine and surgery, the percentage of parenteral therapies was similar for penicillins, cephalosporins, aminoglycosides, quinolones, and other antibacterials. However, the percentage of parenteral therapies of macrolides was higher in surgery (48%) than in medicine (29%) (Fig. 9).

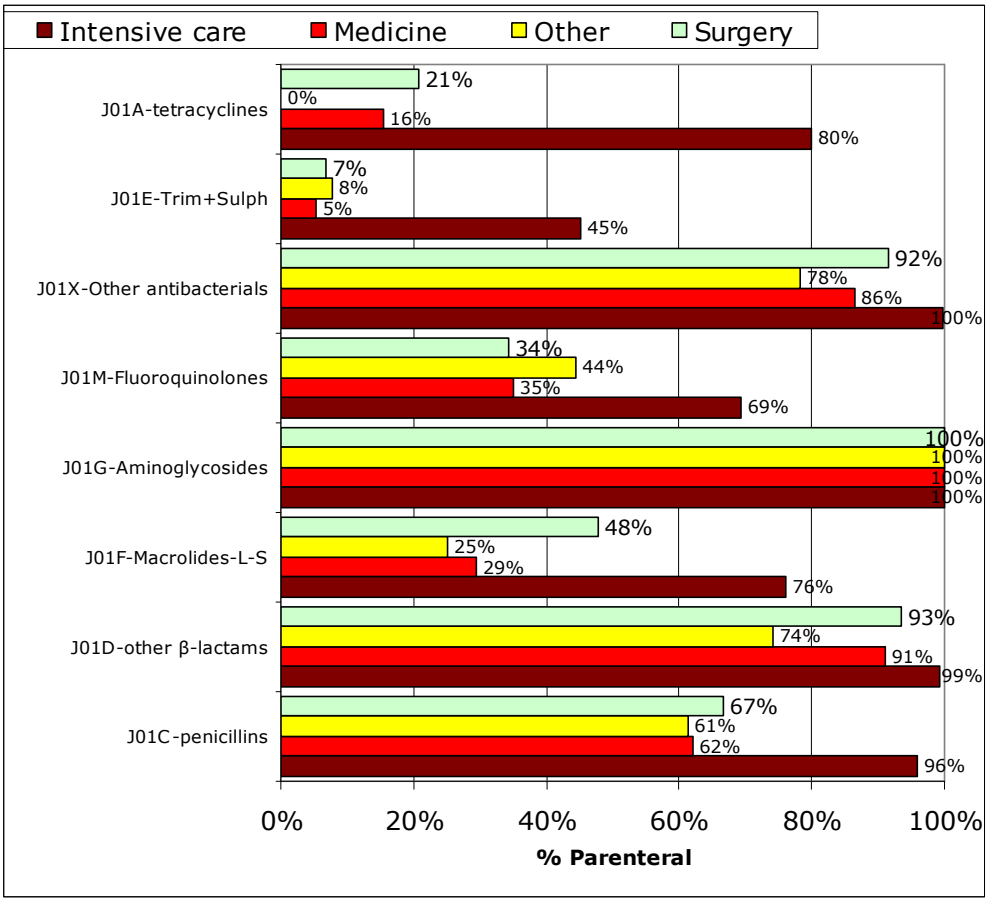


Figure 9 Proportion of parenteral therapies split by specialty

3.4. DU75

Table 3 shows the average number of drugs (ATC 5 level) used per hospital in the survey (27). It also shows that co-amoxiclav (J01CR02) had the highest use overall but ciprofloxacin (J01MA02) was used in more hospitals. Overall 18 drugs composed the DU75.

Table 3 Number of used antimicrobials in hospitals and list of molecules within DU75

ATC	Min	Average	25th percentile	Median	75th percentile	Max	Number of:	
No. of Molecules	6	27	19	27	35	46	Hospitals	Rx
Order of drugs within DU75								
J01CR02	0	14.1%	5.0%	14.2%	20.5%	40.4%	69	2067
J01MA02	0	8.7%	4.7%	8.2%	11.9%	25.0%	71	1207
J01CR05	0	5.4%	1.4%	4.6%	8.4%	22.4%	59	843
J01DC02	0	5.6%	0.0%	2.4%	7.8%	44.4%	55	830
J01XD01	0	5.0%	1.9%	4.7%	7.3%	18.8%	65	760
J01DD04	0	4.6%	0.0%	1.6%	5.4%	56.7%	55	631
J01XA01	0	3.0%	0.6%	2.6%	4.3%	11.1%	58	547
J01GB03	0	3.2%	0.5%	2.2%	4.5%	17.4%	58	455
J01DB04	0	3.1%	0.0%	0%	5.0%	24.1%	36	426
J01FA09	0	2.7%	0.0%	1.3%	4.7%	10.0%	50	425
J01CF05	0	2.9%	0.0%	1.2%	5.6%	12.5%	39	393
J01DH02	0	2.2%	0.0%	1.7%	3.2%	8.5%	53	390
J01EE01	0	2.1%	0.0%	1.5%	3.0%	9.7%	53	387
J01CA04	0	3.4%	0.6%	1.9%	4.3%	25.0%	58	364
J02AC01	0	2.3%	0.1%	1.4%	2.8%	22.2%	55	347
P01AB01	0	2.4%	0.1%	1.8%	3.2%	12.5%	55	339
J01FF01	0	2.0%	0.0%	1.0%	2.9%	12.9%	53	314
J01MA12	0	1.9%	0.0%	0.0%	1.0%	42.9%	33	284

4. Indication

Community acquired infections accounted for more than half (52%) of the indications for antimicrobial use (Fig. 10). However, huge variations were observed among the hospitals (Fig. 11).

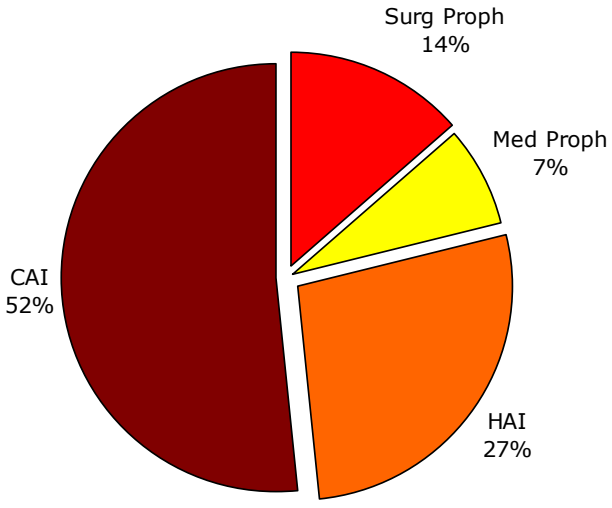


Figure 10 Proportion of different types of indication

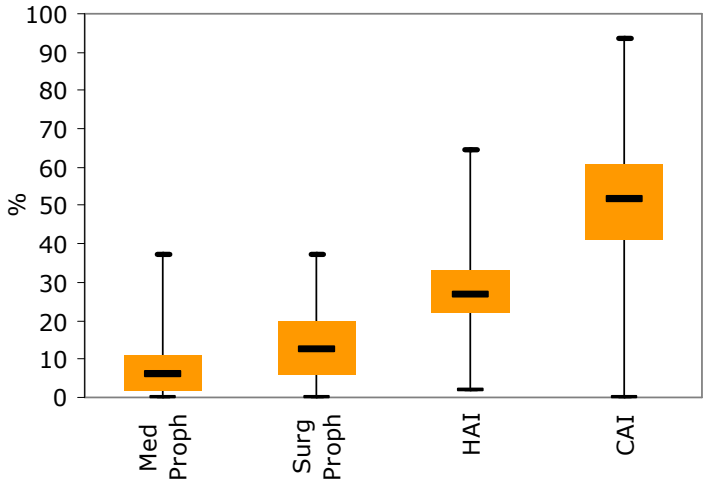


Figure 11 Range of proportions for the different indications

4.1. Prophylaxis

Amongst prophylaxis (Fig. 12), the proportion of surgical prophylaxis was 68% (range: 0-100), whereas the proportion of medical prophylaxis represented 32% (range: 0-100).

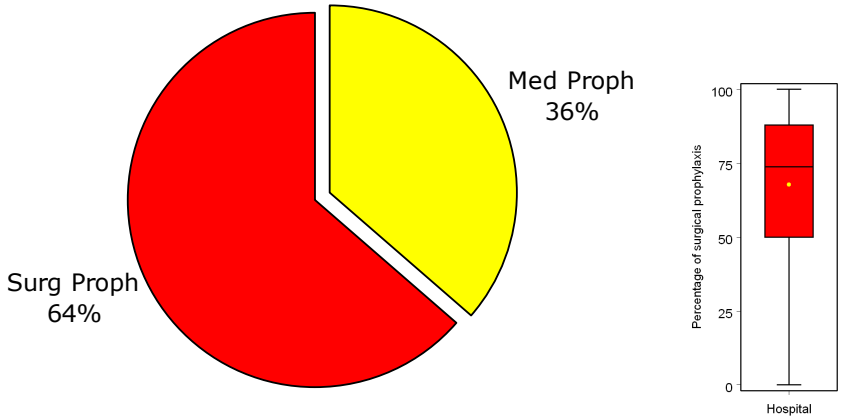


Figure 12 Proportion of medical/surgical prophylaxis

4.1.1. Surgical prophylaxis therapies at the ATC4 level

Figure 13 shows that combination of penicillins with β-lactamase inhibitors (20.3%) were the most utilised class for surgical prophylaxis, followed by 1st, 2nd and 3rd generation cephalosporins respectively. The combination of cephalosporins plus the anti-anaerobic imidazole derivatives (J01XD) (shown in yellow) were also frequently used.

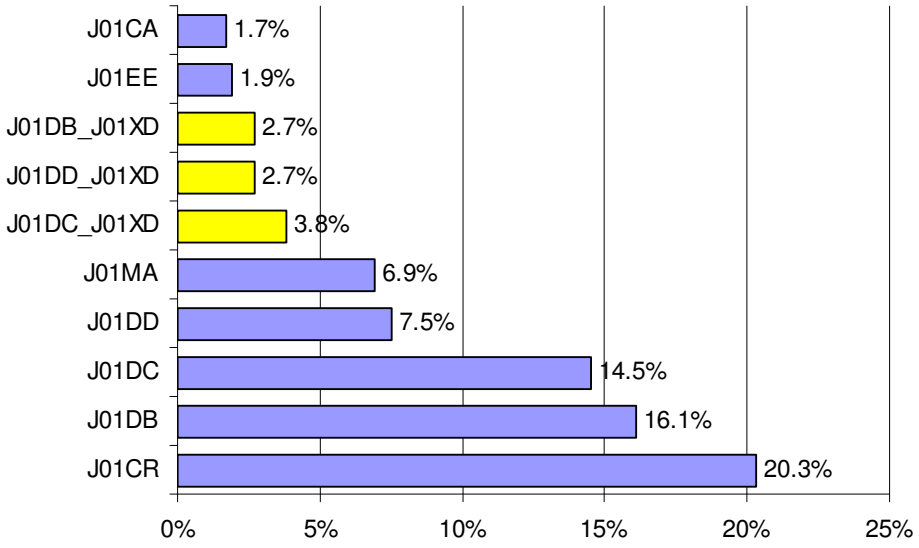


Figure 13 Top 10 surgical prophylaxis agents aggregated at ATC4 level

4.1.2. Duration of surgical prophylaxis

The duration of antibiotic prophylaxis for surgery was more than 1 day in 54% of all prescribed therapies. Huge variations were observed among hospitals (range: 0-100). The proportion for one day and single dose was 23% for both(Fig. 14).

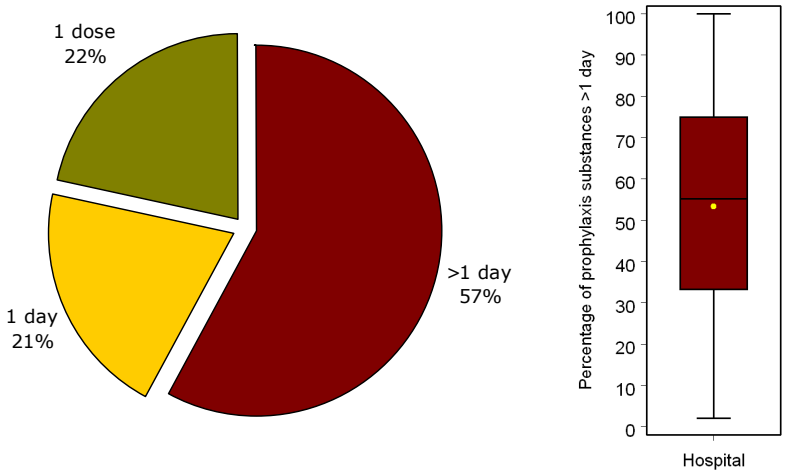
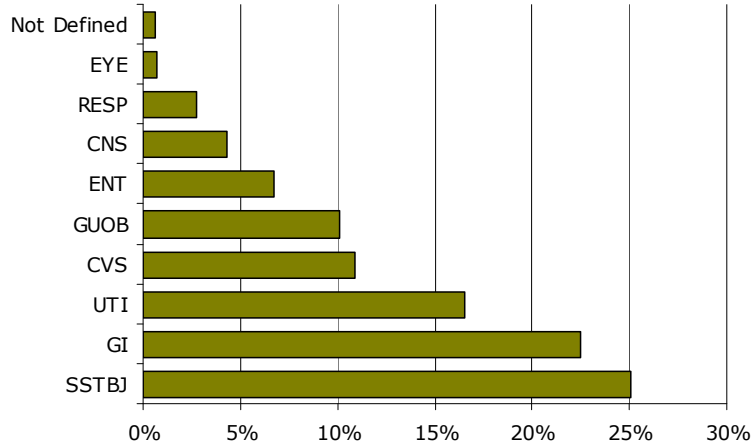


Figure 14 Proportion of duration of surgical prophylaxis (left), distribution of percentage of the surgical prophylaxis > 1 day (right)

4.1.3. Sites

Figure 15 shows that the most frequent site for surgical prophylaxis was skin-soft-tissue-bone-joint, followed by, gastro-intestinal and urology.

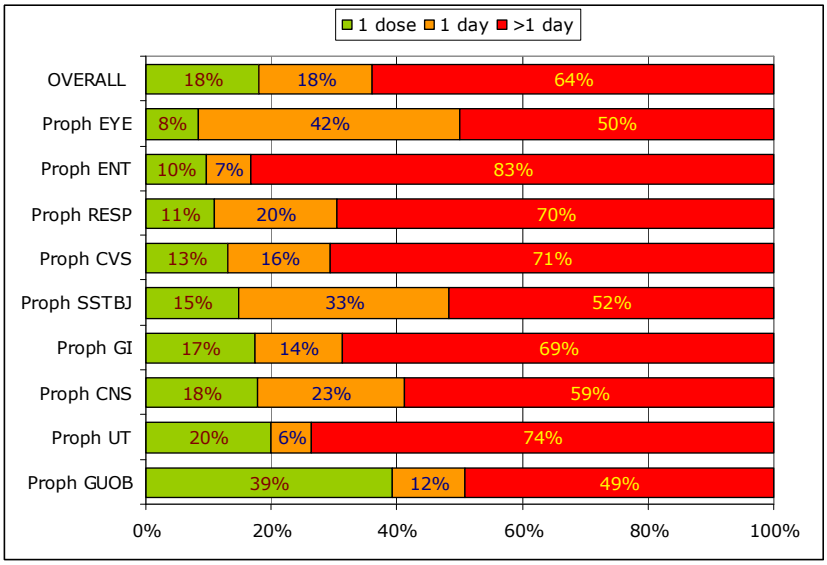


Site	Description
CNS	Central-nervous system
EYE	Ophthalmic
ENT	Otolaryngology
RESP	Respiratory
CVS	Cardiovascular system
GI	Gastro-intestinal tract
SSTBJ	Skin, soft-tissue, Bone and joint
UTI	Urinary tract
GUOB	Gynae and obstetrics
Not Defined	Site not defined (including systemic infections)

Figure 15 Proportion of surgical prophylaxis by site

4.1.4. Duration of Surgical Prophylaxis by Site

Prolonged surgical antibiotic prophylaxis (>1 day) was highest for otolaryngology (ENT) and respiratory tract. On the contrary, single doses of antibiotics were commonly given in gynaecology and obstetrics (GUOb) (Fig.16). Single dose prophylaxis was least frequently used in ophthalmology.



Prophylaxis Site	Description
Proph CNS	Central-nervous system
Proph EYE	Ophthalmic
Proph ENT	Otolaryngology
Proph RES	Respiratory
Proph CVS	Cardiovascular system
Proph GI	Gastro-intestinal tract
Proph SBJ	Skin, soft-tissue, Bone and joint
Proph UT	Urinary tract
Proph GUOB	Gynae and obstetrics

Figure 16 Duration of surgical prophylaxis split by site

4.2. Infection

For the treatment of infections (Fig. 17), the proportion of treatment of hospital acquired infections was 35% (range: 0-100) compared to the proportion of treatment of community acquired infections which was 64% (range: 0-100).

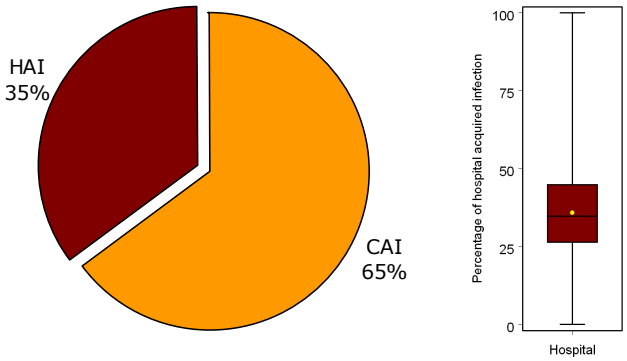


Figure 17 Proportion of Hospital acquired infections

4.2.1. Therapies given to treat infection at ATC4 level

Figure 18 shows that the penicillins with beta-lactam inhibitors (J01CR), fluoroquinolones (J01MA), and third generation cephalosporins (J01DD) were all frequently prescribed in the treatment of both HAI and CAI. However, the proportion of certain antimicrobials was higher to treat CAI than HAI, e.g. macrolides (J01FA, HAI: 1%; CAI: 3%). The proportion of hospital-specific-agents was higher to treat HAI, e.g. carbapenems (J01DH, HAI: 6%; CAI: 3%).

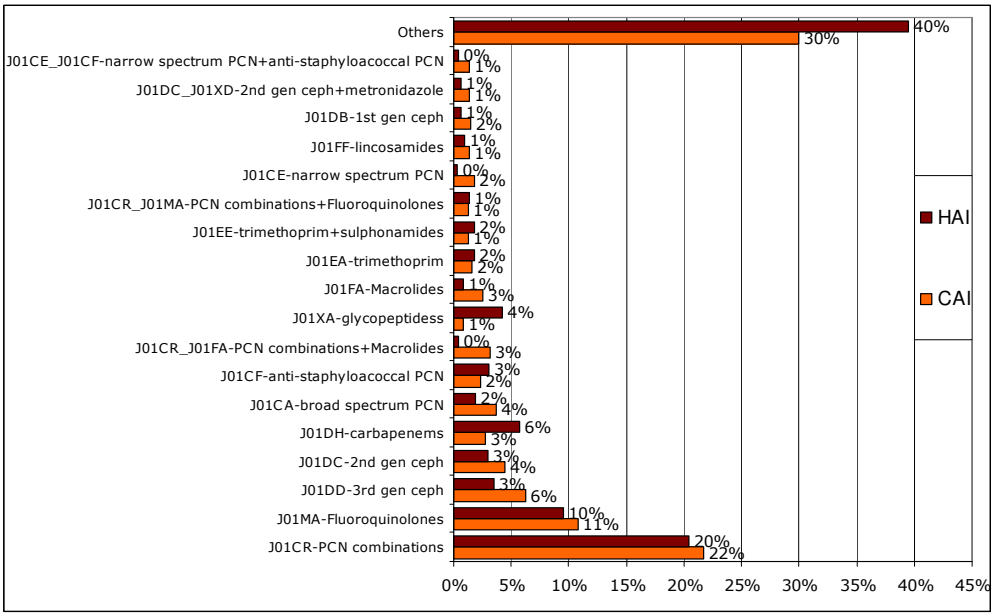


Figure 18 Proportion of therapies given to treat of HAI/CAI aggregated at ATC 4 level

4.2.2. Anatomical sites

The most common anatomical site for therapy was the respiratory tract (HAI: 26.1% CAI: 31.9%). Figure 19 shows that UTI's and SSTBJ were also frequently treated.

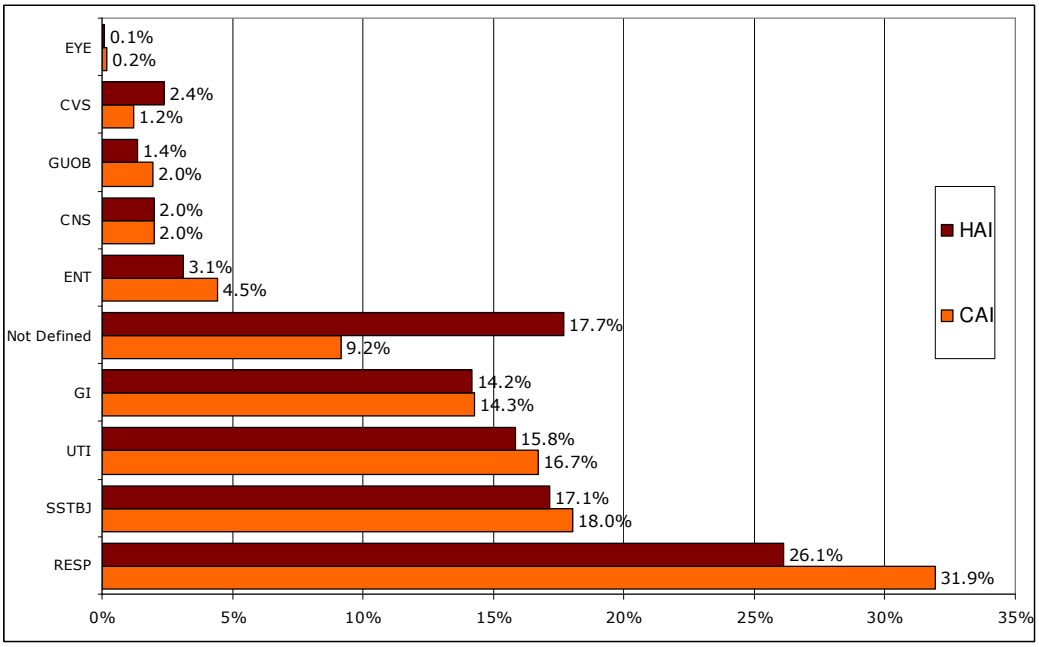


Figure 19 Proportion of HAI/CAI infections split by site

4.2.3. Types of hospital acquired infections

"Other hospital acquired infection" was the most common (42%) of all hospital acquired infections whilst "*Clostridium difficile* infection" was the least frequent (5%, Fig. 20).

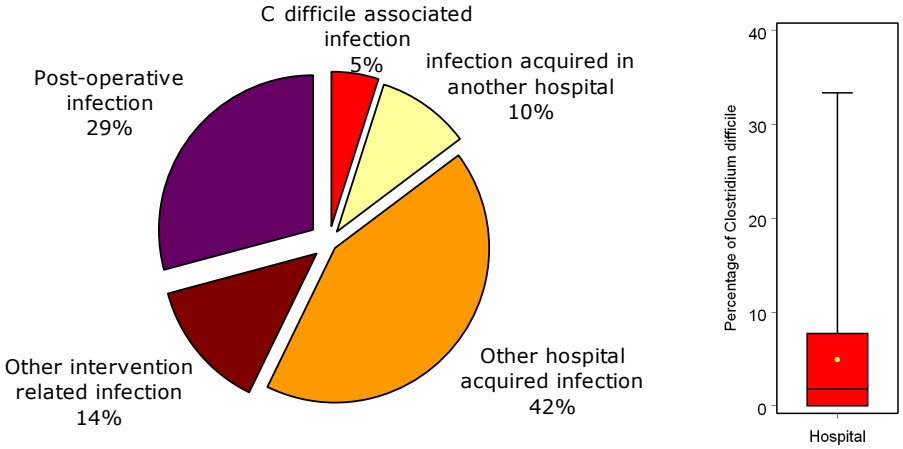


Figure 20 Proportion of types of hospital acquired infections (left), distribution of percentage of *Clostridium difficile* infection among hospital acquired infections (right)

4.2.4. Other hospital acquired infections

The proportion of antimicrobials for "other hospital acquired infection" like most HAI (with the exception of "*Clostridium difficile* infection") showed a greater proportion of hospital-specific drugs like glycopeptides and carbapenems (Fig. 21).

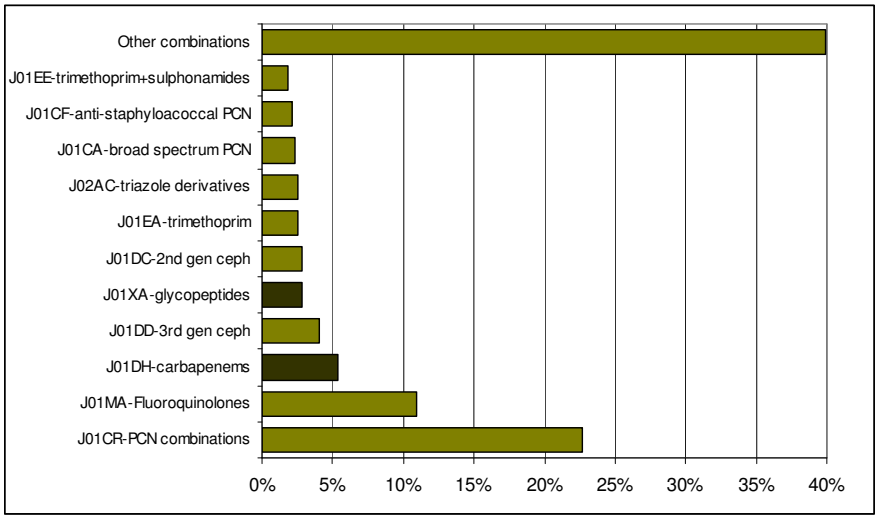
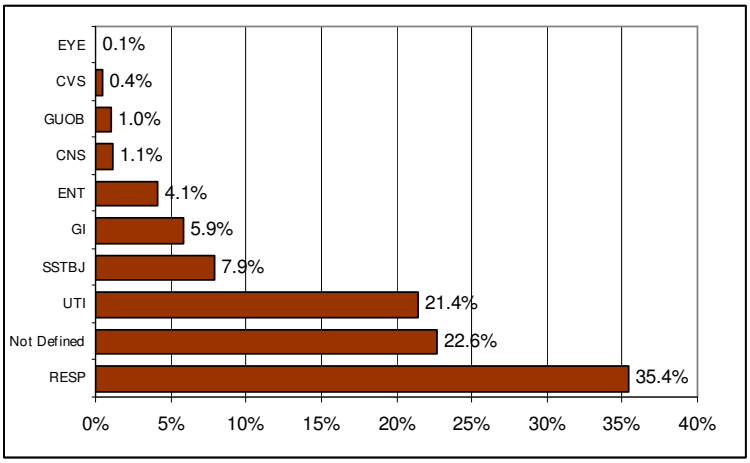


Figure 21 Proportion of 'other hospital acquired infection aggregated at ATC4 level

Regarding the sites, the proportions of undefined site for "other hospital acquired infection" was exceptionally high (Fig. 22). As for the rest of the indications, the respiratory tract was the most frequently infected site.



Site	Description
CNS	Central-nervous system
EYE	Ophthalmic
ENT	Otolaryngology
RESP	Respiratory
CVS	Cardiovascular system
GI	Gastro-intestinal tract
SSTBJ	Skin, soft-tissue, Bone and joint
UTI	Urinary tract
GUOB	Gynae and obstetrics
Not Defined	Site not defined (including systemic infections)

Figure 22 Proportion of other hospital acquired infections split by site

5. Specific diagnoses detail (Top 3 diagnoses)

The top 3 diagnoses accounted for 35.8% of all indications, pneumonia (17.8%), skin & soft tissue infections (10.6%) and intra-abdominal infections (7.3%). Figure 23 shows that penicillins (J01C) were followed by the other beta-lactams (J01D) as the most commonly prescribed drugs in the treatment of the three most common diagnoses. The other β-lactams ranked first in intra-abdominal infections.

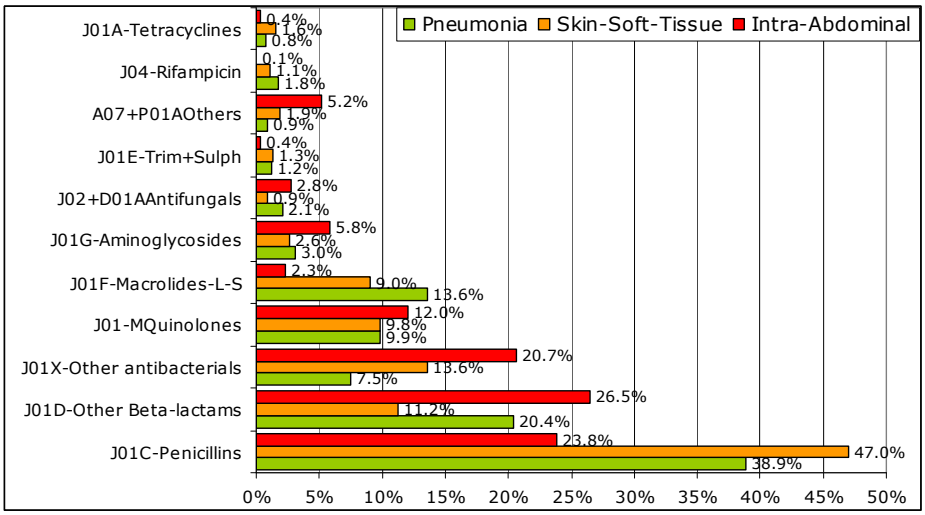


Figure 23 Proportion of therapy for the top 3 diagnoses aggregated at ATC3 level

6. Combination Therapy

Overall, 37 ATC4 groups were used as monotherapy options. The number of combinations used was 618. However, only eight combinations, all of which were dual therapy, featured within the DU75. Figure 24 shows these combinations (including their overall ranking). The respective proportion of multiple-therapies accounted for 31.1% of all treated patients. J01DC_J01XD and J01DD_J01XD were mainly used for CAI and surgical prophylaxis.

J01CR_J01FA was mainly used for CAP; J01CR_J01MA and J01CA_J01GB were used in both CAI and HAI; J01DH_J01XA was almost exclusively used in HAI. The apparently illogical combination J01CR_J01XD was mainly used in CAI.

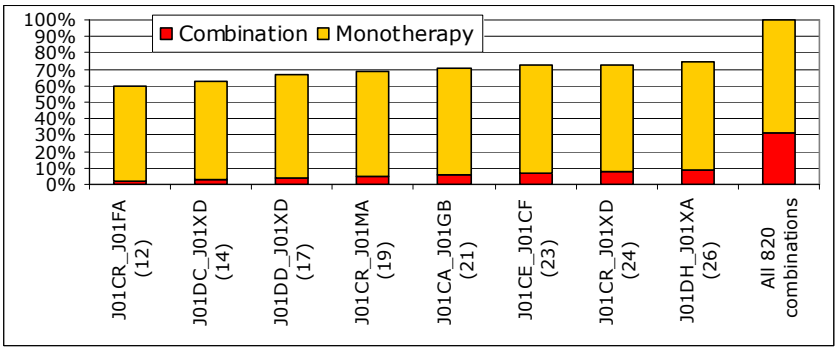


Figure 24 Proportion (and ranking) of combination therapy.

DISCUSSION AND CONCLUSION

ESAC-PPS was the only survey of antimicrobial prescriptions involving hospitals across the continent (Europe). Very few studies compare hospital antibiotic use between different countries and in such studies countries belong to a particular region, as the study by Vlahovic-Palcevski and colleagues (2007) evaluated hospitals from Baltic countries.[2] Another study by de With and colleagues (2006), described consumption in South-Western Germany.[3] This highlights the lack of availability and therefore, the need for pan-European information on hospital antimicrobial use. Furthermore, point-prevalence surveys were performed either in solitary or regional networks of hospitals mainly concentrating on prescriptions for healthcare-associated infections. [4-17]

This was the third hospital PPS performed by ESAC where data collection using online submission with automatic reporting was used.[8,18] In addition, this was the second PPS which utilised the in-house developed Web-PPS software, this time on a larger scale than in 2008. Some hospitals used a Portable Digital Assistant (PDA) for data entry thus making the PPS more rapid to perform. Data from the PDA was then extracted and uploaded into Web-PPS.

ESAC PPS results, throughout the 3 surveys, were consistent in the fact that approximately 30% of hospitalised patients were treated with antibiotics. Another consistency was the excessively prolonged duration of surgical antibiotic prophylaxis for more than one day (>50%). This practice is against any evidence-based literature which recommends a single dose giving peri-operative antibiotic cover with very few exceptions which never exceed the 24 hour period of cover.[19] Surgical prophylaxis was therefore identified by ESAC as a key quality performance indicator within the surgical departments.

Secondly, also prevalence and/or proportion of HAI was identified as a quality indicator for all hospital specialties, since most HAI are preventable through effective infection control programmes/bundles. Hospitals could compare HAI rates within similar areas of practice within the same institution, region or country. In addition, the individual hospital could monitor trends against time in order to assess any changes in any performance indicator. However, one must only compare hospitals with similar patient characteristics, otherwise hospitals which act as referral centres for sicker patients might be erroneously classified as 'poor performers' whilst the higher proportion of HAI would be expected.

ICUs from different hospitals tend to have differing case mix. However, these tend to have similar trends incompatible with the 'general wards' within the same hospital. Thus if the use of hospital specific antibiotics (e.g., carbapenems and glycopeptides) is high in the general wards it is an indicator of either prevalence of resistant strains or inappropriate prescribing of second or third line agents. [20,21] The difference between ICUs and the general ward was also highlighted by the different drugs used within the same category. For example, one would expect that in an ICU the use of piperacillin-tazobactam (J01CR05) would be higher than that of co-amoxiclav (J01CR02) and vice versa for the general ward.

A lower use of antimicrobial agents that are associated with an increased risk of *Clostridium difficile* infections such as ciprofloxacin, cephalosporins, clindamycin, co-amoxiclav, especially id associated with a greater proportion of narrower spectrum antimicrobials, such as amoxicillin, doxycycline, metronidazole, trimethoprim and flucloxacillin would be indicative of good practice for the particular hospital. If such a pattern is observed, it needs to be sustained and improved further. If the trend is in the opposite direction the particular hospital would have a more difficult task to reverse the situation.

In the ESAC PPS 2009 the types of drugs used in combination were evaluated. A total of 618 different combinations (at ATC4 level) were used. Combinations such as cephalosporins with an imidazole derivative were commonly used for CAI and surgical prophylaxis, the latter being in line with guidelines.[19] Similarly, the combination of a β-lactam plus macrolide for CAP is appropriate.[22] The combination of a carbapenems with a glycopeptide was, as expected, almost exclusively used in HAI. However, 'apparently illogical combinations', such as metronidazole with another drug having sufficient anti-anaerobic activity, e.g. co-amoxiclav, piperacillin-tazobactam or a carbapenems, were often used. Thus this was yet another quality indicator.

ESAC PPS 2009 has shown that the web-based PPS methodology could be used in almost 200 hospitals and, therefore, with an appropriate Information-Technology and Clinical helpdesk(s) the methodology could be applied anywhere. Recently, interest in Web-PPS methodology has been expressed from North America, Oceania and North Africa. The ESAC PPS methodology identified various key quality indicators which should alert outlier hospitals to instigate programmes for improvement in the particular areas concerned. ESAC shall not support any further PPS, however, the methodology can be transferred to third parties with minimal restrictions. In addition, 3 European spin-offs shall utilise amended versions of the ESAC Web-PPS, namely: Antibiotic Resistance and Prescribing in European Children (ARPEC) network,[23] funded by DG SANCO, which has an entire work-package based on ESAC methodology; the European Point Prevalence Survey of Healthcare Associated Infections and Antibiotic use in Long-Term Care Facilities (HALT), funded by ECDC and; the ECDC point prevalence survey on healthcare-associated-infections and antimicrobial use which will be piloted in 2010 and rolled out across all Europe in 2011 is the final European surveillance network which shall adapt ESAC methodology.[24]

Finally, it should be emphasised that antibiotic prescribing depends not only on prescribers' knowledge, but also on their attitude, and behaviour.[25] Thus any programme for improvement of prescribing must target issues of behaviour and attitude and not rely only on knowledge and education in order to be successful.

In conclusion, the results have confirmed the feasibility of the web-based PPS methodology developed by ESAC across countries in almost 200 hospitals. Process indicators for quality improvement, which can be monitored by this methodology, have been identified. The methodology is in the process of being adapted to also survey healthcare-associated infections, in an ECDC PPS on both antimicrobial use and healthcare-associated infections. This PPS shall be piloted in 2010 and a full-scale European-wide survey is planned for 2011.

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LIST OF FIGURES

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APPENDICES

Appendix 1: The data collection Form

ESAC Point Prevalence Survey 2009

Date of survey						
Auditor code						
Department	**Name**					
	Code (optional)					
Mixed department	**Y**	☐		**N**	☐	
Speciality: tick the box corresponding to the specialty of the department. In case of mixed-department, tick all the encountered specialities	**Medicine**		**Surgery**	**Intensive Care**		**Other** Please specify
	☐		☐	☐		☐
Denominator: total number of patients in the department at 8am. In case of mixed department, fill the total number of patients corresponding to each of the encountered specialities.						

Patient Form

Department	Speciality[a]	Full Patient Identifier[b]	Survey Number[c]	Age[d] Year	Age[d] Month	Sex

[a]Specify only when the department is a mixed department. (M: medicine, S: surgery, IC: intensive care, O: other)
[b] For example 10 digits unique hospital number to allow local linkage to patient records for more detailed audit. This identifier will not be included in the ESAC on-line database.
[c]A unique but non-identifiable number for each patient entered in the survey by this hospital. This number will be given by the ESAC WebPPS program after the patient has been recorded in the ESAC on-line database.
[d]If the patient is more than 2 years old, specify only the number of years, otherwise only the number of months.

Essential Fields							
Drug	Unit Dose[1]	Doses per day[2]	Route[3]	Diagnosis (site)[4]	Indication[5]	Local guidelines compliance[6] (Y/N/NA/NI)	Reason in notes[7] (Y/N)
1							
2							
3							
4							
5							

[1]Dose per administration in grams: for combination see annex 3.
[2]Provide fractions of doses if necessary, e.g. every 16h = 1.5 doses per day, every 36h = 0.67 doses per day, every 48h = 0.5 doses per day
[3]Parenteral (injections), oral, rectal, inhalation (or **P**, **O**, **R**, **I**, respectively)
[4]See diagnoses groups list (Annex 1)
[5]See Indication codes (Annex 2)
[6]Treatment in compliance with local guidelines (Y: Yes/N: No/NA: Not assessable, NI: no information)
[7]A diagnosis or indication for treatment was recorded in the notes at the start of antibiotic treatment (Yes or No)

Diagnosis Group: by anatomical site of infection treated or prevented (prophylaxis).

Site	Codes	Examples
CNS	Proph CNS	Prophylaxis for CNS (neurosurgery, meningococcal)
	CNS	Infections of the Central Nervous System
EYE	Proph EYE	Prophylaxis for eye operations
	EYE	Endophthalmitis
ENT	Proph ENT	Prophylaxis for Ear, Nose or Throat (surgery or medical)
	ENT	Infections of ear, mouth, nose, throat or larynx
RESP	Proph RES	Pulmonary surgery, prophylaxis for respiratory pathogens
	Bron	Acute bronchitis or exacerbations of chronic bronchitis
	Pneu	Pneumonia
CVS	Proph CVS	Cardiac or vascular surgery, endocarditis prophylaxis
	CVS	Cardiovascular infections: endocarditis, vascular graft
GI	Proph GI	Surgery of the GI tract, liver or biliary tree, GI prophylaxis in neutropenic patients or hepatic failure
	GI	GI infections (salmonellosis, antibiotic associated diarrhoea)
	IA	Intra-abdominal sepsis including hepatobiliary
SSTBJ	Proph SBJ	Prophylaxis for plastic or orthopaedic surgery (bone or joint)
	SST	Cellulitis, wound, deep soft tissue not involving bone
	BJ	Septic arthritis (including prosthetic joint), osteomyelitis
UTI	Proph UT	Prophylaxis for urological surgery, recurrent UTI
	Cys	Lower UTI
	Pye	Upper UTI
GUOB	Proph GyOb	Prophylaxis for obstetric or gynaecological surgery
	OBGY	Obstetric or gynaecological infections, STD in women
	GUM	Prostatitis, epididymo-orchitis, STD in men
Not Defined	BAC	Bacteraemia (not endocarditis) with no clear anatomical site
	SIRS	Systemic inflammatory response with no clear anatomic site
	UND	Completely un-defined site with no systemic inflammation

Appendix 2: List of PPS 2009 antimicrobials at the ATC level 4

Code	Name
A07AA	Antibiotics
D01BA	Antifungals for systemic use
J01AA	Tetracyclines
J01BA	Amphenicols
J01CA	Penicillins with extended spectrum
J01CE	Beta-lactamase sensitive penicillins
J01CF	Beta-lactamase resistant penicillins
J01CG	Beta-lactamase inhibitors
J01CR	Combinations of penicillins, incl. β-lactamase inhibitors
J01DB	First-generation cephalosporins
J01DC	Second-generation cephalosporins
J01DD	Third-generation cephalosporins
J01DE	Fourth-generation cephalosporins
J01DF	Monobactams
J01DH	Carbapenems
J01EA	Trimethoprim and derivatives
J01EB	Short-acting sulfonamides
J01EC	Intermediate-acting sulfonamides
J01ED	Long-acting sulfonamides
J01EE	Combinations of sulfonamides and trimethoprim, incl. derivatives
J01FA	Macrolides
J01FF	Lincosamides
J01FG	Streptogramins
J01GA	Streptomycins
J01GB	Other aminoglycosides
J01MA	Fluoroquinolones
J01MB	Other quinolones
J01RA	Combinations of antibacterials
J01XA	Glycopeptide antibacterials
J01XB	Polymyxins
J01XC	Steroid antibacterials
J01XD	Imidazole derivatives
J01XE	Nitrofuran derivatives
J01XX	Other antibacterials
J02AA	Antibiotics
J02AB	Imidazole derivatives
J02AC	Triazole derivatives
J02AX	Other antimycotics for systemic use
J04AA	Aminosalicylic acid and derivatives
J04AB	Antibiotics
J04AC	Hydrazides
J04AD	Thiocarbamide derivatives
J04AK	Other drugs for treatment of tuberculosis
J04AM	Combinations of drugs for treatment of tuberculosis
J04BA	Drugs for treatment of lepra
P01AB	Nitroimidazole derivatives
D01BA	Antifungals for systemic use

Appendix 3: Distribution of the treated patients/100 patients at the ATC4 level in European hospitals

- All specialties

atc4	Class	Average	Minimum	25th Percentile	Median	75th Percentile	Maximum
J01AA	Tetracyclines	0.42	0	0	0.14	0.67	3.65
J01CA	Penicillins with extended spectrum	1.79	0	0.58	1.34	2.48	7.43
J01CE	Beta-lactamase sensitive penicillins	1.09	0	0	0.46	1.47	6.63
J01CF	Beta-lactamase resistant penicillins	1.49	0	0.3	1.15	2.16	5.88
J01CR	Combinations of penicillins, incl. beta-lactamase inhibitors	8.5	0	4.82	8.88	11.63	20.81
J01DB	First-generation cephalosporins	1.49	0	0	0.7	2.16	6.58
J01DC	Second-generation cephalosporins	2.51	0	0.39	1.45	3.87	12.77
J01DD	Third-generation cephalosporins	3.43	0	0.89	2.1	3.86	21.74
J01DE	Fourth-generation cephalosporins	0.1	0	0	0	0	1.15
J01DH	Carbapenems	1.81	0	0.3	1.24	2.41	14.49
J01EA	Trimethoprim and derivatives	0.6	0	0	0	0.93	5.88
J01EE	Combinations of sulfonamides and trimethoprim, incl. derivatives	0.82	0	0	0.59	1.06	4.62
J01FA	Macrolides	1.57	0	0.35	1.16	2.15	6.31
J01FF	Lincosamides	0.82	0	0	0.55	1.03	4.7
J01GB	Other aminoglycosides	2.09	0	0.56	1.54	2.71	11.84
J01MA	Fluoroquinolones	4.86	0	2.78	4.49	6.32	13.16
J01XA	Glycopeptide antibacterials	1.73	0	0.31	1.29	2.45	13.04
J01XB	Polymyxins	0.12	0	0	0	0	1.47
J01XD	Imidazole derivatives	2.19	0	0.87	1.84	3.05	13.04
J01XE	Nitrofuran derivatives	0.32	0	0	0	0.42	2.94
J01XX	Other antibacterials	0.29	0	0	0	0.39	2.46

- Intensive care units

atc4	Class	Average	Minimum	25th Percentile	Median	75th Percentile	Maximum
J01AA	Tetracyclines	1.47	0	0	0	0	50
J01CA	Penicillins with extended spectrum	3.28	0	0	0	5.56	29.41
J01CE	Beta-lactamase sensitive penicillins	3.75	0	0	0	0	100
J01CF	Beta-lactamase resistant penicillins	2.07	0	0	0	3.13	16.67
J01CR	Combinations of penicillins, incl. beta-lactamase inhibitors	13.19	0	0	12.58	19.35	75
J01DB	First-generation cephalosporins	2.18	0	0	0	2.17	46.15
J01DC	Second-generation cephalosporins	3.61	0	0	0	3.7	40
J01DD	Third-generation cephalosporins	8.97	0	0	4.55	12.77	60
J01DE	Fourth-generation cephalosporins	1.21	0	0	0	0	50
J01DH	Carbapenems	11.12	0	0	6.9	18.52	50
J01EA	Trimethoprim and derivatives	0.35	0	0	0	0	14.29
J01EE	Combinations of sulfonamides and trimethoprim, incl. derivatives	0.43	0	0	0	0	6.52
J01FA	Macrolides	2.9	0	0	0	2.5	50
J01FF	Lincosamides	1.82	0	0	0	0	33.33
J01GB	Other aminoglycosides	8.8	0	0	5.26	13.33	50
J01MA	Fluoroquinolones	6.36	0	0	3.7	8.16	60
J01XA	Glycopeptide antibacterials	6.38	0	0	3.28	9.38	33.33
J01XB	Polymyxins	0.24	0	0	0	0	5.56
J01XD	Imidazole derivatives	6.87	0	0	3.23	8.75	60
J01XE	Nitrofuran derivatives	0	0	0	0	0	0
J01XX	Other antibacterials	1.44	0	0	0	0	25

- Medicine units

atc4	Class	Average	Minimum	25th Percentile	Median	75th Percentile	Maximum
J01AA	Tetracyclines	0.45	0	0	0	0.69	4
J01CA	Penicillins with extended spectrum	2.05	0	0.29	1.43	2.9	9.03
J01CE	Beta-lactamase sensitive penicillins	1.21	0	0	0.59	1.54	12
J01CF	Beta-lactamase resistant penicillins	1.36	0	0	1.01	2.11	5.88
J01CR	Combinations of penicillins, incl. beta-lactamase inhibitors	8.6	0	3.89	8.71	11.92	24.27
J01DB	First-generation cephalosporins	0.52	0	0	0	0.65	5.88
J01DC	Second-generation cephalosporins	1.8	0	0	0.8	2.56	12.55
J01DD	Third-generation cephalosporins	3.45	0	0.87	1.93	4.71	20.86
J01DE	Fourth-generation cephalosporins	0.1	0	0	0	0	1.92
J01DH	Carbapenems	1.27	0	0	0.67	1.85	8.33
J01EA	Trimethoprim and derivatives	0.7	0	0	0	0.93	5.88
J01EE	Combinations of sulfonamides and trimethoprim, incl. derivatives	1.01	0	0	0.58	1.21	7.69
J01FA	Macrolides	2.05	0	0.38	1.41	2.82	9.85
J01FF	Lincosamides	0.71	0	0	0.34	1.14	8
J01GB	Other aminoglycosides	1.46	0	0	0.8	1.9	10.68
J01MA	Fluoroquinolones	4.91	0	2.16	4.54	6.77	18.18
J01XA	Glycopeptide antibacterials	1.32	0	0	0.93	2.3	5.49
J01XB	Polymyxins	0.11	0	0	0	0	1.94
J01XD	Imidazole derivatives	1.09	0	0	0.7	1.54	4.86
J01XE	Nitrofuran derivatives	0.38	0	0	0	0.49	2.94
J01XX	Other antibacterials	0.17	0	0	0	0	1.56

- Others

atc4	Class	Average	Minimum	25th Percentile	Median	75th Percentile	Maximum
J01AA	Tetracyclines	0.03	0	0	0	0	0.55
J01CA	Penicillins with extended spectrum	0.31	0	0	0	0	5.26
J01CE	Beta-lactamase sensitive penicillins	0.8	0	0	0	0	9.52
J01CF	Beta-lactamase resistant penicillins	0.53	0	0	0	0	3.45
J01CR	Combinations of penicillins, incl. beta-lactamase inhibitors	5.62	0	0	1.33	3.45	27.45
J01DB	First-generation cephalosporins	0.13	0	0	0	0	2.27
J01DC	Second-generation cephalosporins	2.46	0	0	0	0	20
J01DD	Third-generation cephalosporins	0.12	0	0	0	0	1.96
J01DE	Fourth-generation cephalosporins	0	0	0	0	0	0
J01DH	Carbapenems	0.2	0	0	0	0	3.45
J01EA	Trimethoprim and derivatives	0.13	0	0	0	0	1.59
J01EE	Combinations of sulfonamides and trimethoprim, incl. derivatives	0.1	0	0	0	0	1.75
J01FA	Macrolides	2.52	0	0	0	0	33.33
J01FF	Lincosamides	0	0	0	0	0	0
J01GB	Other aminoglycosides	0.45	0	0	0	0	7.69
J01MA	Fluoroquinolones	2.1	0	0	0	0.55	25
J01XA	Glycopeptide antibacterials	0.2	0	0	0	0	3.45
J01XB	Polymyxins	0	0	0	0	0	0
J01XD	Imidazole derivatives	0.83	0	0	0	0	7.69
J01XE	Nitrofuran derivatives	0.1	0	0	0	0	1.65
J01XX	Other antibacterials	0	0	0	0	0	0

- Surgery units

atc4	Class	Average	Minimum	25th Percentile	Median	75th Percentile	Maximum
J01AA	Tetracyclines	0.28	0	0	0	0.29	3.82
J01CA	Penicillins with extended spectrum	1.35	0	0	0.45	1.67	11.25
J01CE	Beta-lactamase sensitive penicillins	0.68	0	0	0	0.65	6.45
J01CF	Beta-lactamase resistant penicillins	1.75	0	0	0.83	2.32	12.96
J01CR	Combinations of penicillins, incl. beta-lactamase inhibitors	8.56	0	3.38	8.57	11.88	27.11
J01DB	First-generation cephalosporins	2.98	0	0	1.35	4.55	18.1
J01DC	Second-generation cephalosporins	3.69	0	0	1.65	5.26	17.19
J01DD	Third-generation cephalosporins	2.91	0	0	1.25	3.39	36.36
J01DE	Fourth-generation cephalosporins	0.05	0	0	0	0	1.16
J01DH	Carbapenems	1.54	0	0	0.66	1.96	12.21
J01EA	Trimethoprim and derivatives	0.4	0	0	0	0	3.57
J01EE	Combinations of sulfonamides and trimethoprim, incl. derivatives	0.78	0	0	0	1.14	13.22
J01FA	Macrolides	0.77	0	0	0	1.02	9.68
J01FF	Lincosamides	1.05	0	0	0.29	1.64	7.64
J01GB	Other aminoglycosides	2.33	0	0	1.34	3.05	13.64
J01MA	Fluoroquinolones	4.86	0	2.08	4.07	6.38	16.13
J01XA	Glycopeptide antibacterials	1.58	0	0	0.89	2.11	9.91
J01XB	Polymyxins	0.02	0	0	0	0	1.23
J01XD	Imidazole derivatives	3.77	0	1.61	3.17	5.42	18.18
J01XE	Nitrofuran derivatives	0.18	0	0	0	0	1.85
J01XX	Other antibacterials	0.37	0	0	0	0.32	5.79

Appendix 4: List of participating hospitals

The total number of hospitals registered in the WebPPS was 193. Sixteen hospitals either did not upload their data or their data were not validated or had no patients on antibiotics. This left a total 177 hospitals with valid antimicrobial use data, a sample of 75 hospitals was used in this report.

Hospital Name	Country code
LKH Klagenfurt	AT
Elisabethinen Hospital	AT
LKH Freistadt	AT
LKH Rohrbach	AT
LKH Kirchdorf	AT
Meduni Salzburg	AT
LKH Feldkirch	AT
Erasme Hospital	BE
CHU Brugmann	BE
Universitair Ziekenhuis Brussel	BE
Cliniques Universitaires Saint Luc	BE
hopital ixelles etterbeek	BE
UZ Antwerpen	BE
AZ Heilige Familie	BE
Sint-Jozefkliniek	BE
Heilig Hartziekenhuis	BE
AZ St. Dimpna	BE
Virga Jesseziekenhuis	BE
UZ Gent	BE
AZ Sint Lucas	BE
AZ Jan Palfijn AV	BE
AZ Zusters van Barmhartigheid	BE
AZ Jan Portaels	BE
Ziekenhuis Inkendaal	BE
AZ Groeninge	BE
clinique notre dame de grâce	BE
Cliniques Universitaires de Mont-Godinne	BE
CHR de Namur	BE
University Multipurpose Hospital for Active Treatment Aleksandrovska	BG
Hôpitaux Universitaires de Genève	CH
Centre Hospitalier Universitaire Vaudois	CH
Limasssol General Hospital	CY
Lefkosia General Hospital	CY
Teaching hospital Hradec Kralove	CZ
St.Ann Teaching Hospital Brno	CZ
University Hospital Olomouc	CZ
Zlin	CZ
Krajská nemocnice T. Bati, a.s.	CZ
Opava	CZ
Roskilde Hospital	DK
Vejle Sygehus	DK
West Tallinn Central Hospital	EE
East Tallinn Central Hospital	EE
Tartu University Hospital	EE
Warrington and Halton Hospitals NHS Foundation Trust	EN
University Hospital of South Manchester	EN
North Manchester General Hospital	EN
Salford Royal NHS Foundation Trust	EN

Hospital Name	Country code
Blackpool Fylde and Wyre NHS Foundation Trust	EN
Royal Liverpool and Broadgreen University Hospital Trust	EN
Wirral University Teaching Hospital NHS Foundation Trust	EN
York Hospitals NHS Foundation Trust	EN
Barnsley NHS Foundation Trust	EN
Sheffield Teaching Hospitals NHS Foundation Trust	EN
Airedale NHS Trust	EN
Leeds Teaching Hospitals NHS Trust	EN
Calderdale and Huddersfield NHS Trust	EN
Chesterfield Royal NHSFT	EN
Sherwood Forest Hospitals NHS Foundation Trust	EN
University Hospitals of Leicester	EN
United Lincolnshire Hospitals NHS Trust	EN
Princess Royal Hospital	EN
Dudley Group of Hospitals	EN
Peterborough and Stamford Hospitals NHS Foundation Trust	EN
Papworth Hospital NHS Foundation Trust	EN
Cambridge University Hospitals NHS Foundation Trust	EN
Norfolk and Norwich University Hospital NHS Foundation Trust	EN
Luton & Dunstable Hospital	EN
East and North Hertfordshire NHS Trust	EN
West Hertfordshire Hospitals NHS Trust	EN
Southend university Hospital	EN
Basildon and Thurrock University Hospitals	EN
Mid Essex Hospital Services NHS Trust	EN
Essex Cardiothoracic Centre	EN
St George’s Healthcare NHS Trust	EN
Chelsea and Westminster NHS Foundation Trust	EN
Royal Brompton and Harefield NHS Trust	EN
University College London Hospitals NHS Foundation Trust	EN
Imperial College Healthcare NHS Trust	EN
Whittington Hospital	EN
King's College Hospital	EN
Hometon University Hospital	EN
Barnet & Chase Farm Hospital NHS Trust	EN
South London Healthcare Trust - Queen Elizabeth, Woolwich	EN
Royal Free Hampstead NHS Trust	EN
North Middlesex University Hospital	EN
The Hillingdon Hospital NHS Trust	EN
Heatherwood & Wexham Park NHS Trust	EN
Buckinghamshire Hospitals NHS Trust	EN
East Surrey Hospital, Surrey and Sussex Healthcare Trust	EN
St Richards Hospital	EN
Portsmouth Hospital NHS Trust	EN
Southampton University Hospitals NHS Trust	EN
Winchester & Eastleigh Healthcare NHS Trust	EN
St Mary's Hospital	EN
Medway Foundation NHS Trust	EN
Heart of England NHS Foundation Trust	EN
Hospital Universitari Bellvitge	ES
Hospital Son Dureta	ES
Vaasa central hospital	FI
CH Dron	FR
CHU Besançon	FR
CMC Ares	FR
Centre Hospitalier de la côte Basque	FR

Hospital Name	Country code
Clinical Hospital Centre Zagreb	HR
University Hospital for Infectious Diseases	HR
Clinical Hospital Centre Split	HR
University Hospital Szeged	HU
Midland Regional Hospital Tullamore	IE
Cavan General Hospital	IE
Galway University Hospitals	IE
Portiuncula Hospital	IE
Mayo General Hospital	IE
Mid-Western Regional Hospital Ennis	IE
MidWestern Regional Hospital Nenagh	IE
Mid-Western Regional Hospital Limerick	IE
Tallaght Hospital	IE
St. James's Hospital	IE
Connolly Hospital Blanchardstown	IE
Beacon Hospital	IE
ST.Vincents University Hospital	IE
Our Ladys Childrens Hospital	IE
Mater Misericordiae University Hospital	IE
St Vincents private hospital	IE
St. Luke's General Hospital Carlow/Kilkenny,	IE
Waterford Regional Hospital	IE
Wexford general hospital	IE
Cork University Hospital	IE
Mercy University Hospital	IE
South Infirmary Victoria University Hospital	IE
Mallow General Hospital	IE
Haemek Medical Center	IL
Azienda Sanitaria ULSS 18 Rovigo	IT
Azienda ospedaliero Universitaria di Udine	IT
Liepaja Regional hospital	LV
P. Stradins Clinical University hospital	LV
Mater Dei Hospital	MT
South Eastern HSC Trust	NI
Antrim Area Hospital	NI
WHSCT	NI
Craigavon Area Hospital	NI
Aker University Hospital	NO
Asker and Baerum Hospital	NO
Hospital Infante D. Pedro E.P.E.	PT
S. Francisco Xavier Hospital	PT
Samara Regional Hospital for War Veterans	RU
Smolensk Regional Hospital	RU
Smolensk District Children's Clinical Hospital	RU
Aberdeen Royal Infirmary	SC
Woodend General Hospital	SC
Dr Gray's Hospital	SC
Royal Cornhill Hospital	SC
Royal Aberdeen Childrens Hospital	SC
Aberdeen Maternity Hospital	SC
Ninewells Hospital	SC
Royal Victoria Hospital	SC
Arbroath Infirmary	SC
Queen Margaret Hospital	SC
Victoria Hospital	SC

Hospital Name	Country code
Cameron Hospital	SC
Borders General Hospital	SC
Royal Infirmary Edinburgh	SC
Astley Ainslie	SC
Western General Hospital	SC
Perth Royal Infirmary	SC
Stirling Royal Infirmary	SC
St John's Hospital at Howden	SC
Golden Jubilee National Hospital	SC
NHS Dumfries and Galloway	SC
Crosshouse Hospital	SC
East Ayrshire Community Hospital	SC
Victoria Infirmary	SC
Monklands Hospital	SC
The Ayr Hospital	SC
Davidson Cottage Hospital	SC
Caithness General Hospital	SC
Raigmore Hospital	SC
Lorn and Isles Hospital	SC
Belford Hospital	SC
Balfour Hospital	SC
Gilbert Bain Hospital	SC
Montfield Hospital	SC
GH Brezice	SI
General Hospital Jesenice	SI
Splošna bolnišnica Izola	SI
General Hospital Novo mesto	SI
University Medical Center	SI
Conwy Denbighshire NHS Trust	WL
University Hospital of Wales	WL
Llandough Hospital	WL
Rookwood Hospital	WL
West Wing	WL
Royal Gwent Hospital	WL

Appendix 5 Overview of most common errors in ATC/DDD lists

Drug	ATC code	RoA	Comment-Issue	Suggestion
Errors that can be corrected for:				
Anidulafungin	J02AX06	P	Though only available as 'P' some institutions listed it as 'O'	Can be converted to P and utilized in analyses.
Metronidazole	J01XD01	P	Often listed for both O & P	Metronidazole ATC misclassification should be corrected for RoA and utilized in analyses.
	P01AB01	O/R	Often unknown as the O/R ATC code	
Co-amoxiclav	J01CR02	P/O	Since the amoxicillin part is to be taken into account, some data was inputted as J01CA04. J01CR02 has a different DDD for P	Should be corrected for ATC/DDD and utilized in analyses..
Vancomycin	A07AA09	O	Vancomycin P was sometimes classified as A07AA09 instead of J01XA01.	Unless the institutions use the parenteral formulation orally (for C. difficile therefore correctly labeled as A07AA09) this should be corrected for (J01XA01) and utilized in the analyses.
Errors that cannot be corrected for:				
Benzylpenicillin	J01CE01	P	Often listed as O. The oral penicillin is V (phenoxymethyl-) [J01CE02] not G (benzyl-). This could possibly be that 'Penicillin' (V or G) were interchanged OR that the RoA inputted incorrectly.	Cannot be used for analyses.
Neomycin	J01GB05	O	Though only available as 'P' some institutions listed it as 'O'	One cannot ascertain which is right 'RoA' or 'ATC'. Cannot be used for analyses.
Amikacin	J01GB06	P	Often mixed with J01GB05 (neomycin)	
Combination penicillins	J01CE30	O/P	This ATC code is very generic. Therefore this is a limitation within the ATC classification. Various misnomers could be hypothesized including J01CR. Corrections eventually available, if ROA should be determinable for some combinations	Cannot be used for analyses. If so, usable after addiction
J04AM group		O/P	Neither the RoA nor the actual constituents are known. The ATC classification has a lacuna in this context.	Cannot be used for analyses. Also DDD are not available