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Identification of targets for quality improvement in antimicrobial prescribing: the web-based ESAC Point Prevalence Survey 2009

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Objectives: Since electronic prescribing is limited to few hospitals, point prevalence surveys, such as the standardized European Surveillance of Antimicrobial Consumption point prevalence survey (ESAC PPS), are an alternative tool for monitoring prescribing and helping to identify performance indicators and prescribing trends. The main objective of this study was to identify and assess targets for quality improvement.

Methods: Each hospital had to carry out the survey within 2 weeks. Each department had to be surveyed in 1 day. Data collected, for all inpatients, included age and gender. For patients on systemic antimicrobial treatment, the antimicrobial/s, infection/prophylaxis site, reason in medical notes and guideline compliance were also collected. A central database using a web-based tool (WebPPS) developed in-house was used for data entry.

Results: Combination of two or more antimicrobials accounted for 30% of use. Surgical prophylaxis was prolonged (>1 day) in 53% of cases. 'Intensive care' had higher proportions of treated patients (53% versus 29%), combination therapy (49% versus 31%), hospital-acquired infections (49% versus 31%) and parenteral administration (91% versus 61%). 'Reason in notes' was documented in 76%, and 'guideline compliance' occurred in 62% of patients.

Conclusions: The ESAC PPS provided useful information on the quality of prescribing, which identified a number of targets for quality improvement. These could apply to specific departments or whole hospitals. Intensive care, which has different characteristics, should not be compared with general wards with respect to combination therapy, hospital-acquired infections or parenteral proportion. The study confirmed that the ESAC PPS methodology can be used on a large number of hospitals at regional, national, continental or global level.

Keywords: antimicrobial consumption, hospitals, Europe, point prevalence surveys

Introduction

Until the turn of the century there were limited reliable data on antimicrobial utilization in hospitals.[1] However, a temporal relationship between antimicrobial use and resistance had already been demonstrated.[2,3] The use of certain antimicrobials is also associated with higher levels of resistance, e.g. quinolones are more prone to generate resistance compared with β-lactams.[4,5] These data highlight the importance of surveillance of antimicrobial use, even at the patient level. The best way to monitor prescribing would be through monitoring electronic prescribing in hospitals. However, to date, this is a rare luxury available only in a limited number of countries/hospitals.[6] Therefore, point prevalence surveys (PPSs) are a practical surveillance tool for this purpose.[7] PPSs can identify targets for quality improvement for particular clinical departments, as well as changes in prescribing trends over time. The European Surveillance of Antimicrobial Consumption (ESAC) PPS is a standardized methodology on the quality of antimicrobial use within hospitals.[8]

The main objectives of the extensive ESAC 2009 Hospital PPS were to confirm targets for quality improvement that had already been identified in the previous two smaller PPSs and possibly identify others in view of the larger sample of hospitals.

Such targets for quality improvement should, in turn, be utilized by the individual participating hospitals, or even at a national level, in order to improve deficient areas of practice. Furthermore, the feasibility of carrying out the survey in a larger sample of hospitals was being evaluated. The number of participating hospitals increased to 172, compared with the 20 hospitals of 2006 and 50 hospitals of 2008, by the time the data were extracted for analysis.

Methods

Hospitals and countries

The ESAC Hospital Care National Representatives who each recruited two hospitals to perform the PPS in 2008 were asked to add as many more hospitals as possible for the 2009 PPS. The 2009 PPS was performed in 172 hospitals from 25 European countries based on a simplified version of the protocol of the 2006 PPS.[8] The 25 countries that took part in the 2009 PPS were Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, England, Estonia, France, Hungary, Ireland, Israel, Italy, Latvia, Malta, Northern Ireland, Norway, Portugal, Russian Federation, Scotland, Slovenia, Spain, Switzerland and Wales. Thus six of the countries that participated in PPS 2006 did not participate in PPS 2009; however, the participation of another 11 countries resulted in a net increase of 5 countries participating in PPS 2009.[8]

The WebPPS software

A new web application, WebPPS, was specifically developed by ESAC for data entry, automated feedback and reporting for the participating hospitals. This was first piloted during PPS 2008 and was used on the larger hospital sample in PPS 2009. Data were entered locally into the application. Upon finalization and validation of data entry the hospital could extract a report for all hospitals with validated data. If more than two hospitals validated their data from a specific country, there was also the option to create a report for the specific country. Either of the above-mentioned reports can be rerun even now for all hospitals that had validated their data.

WebPPS is a web application developed in Java where data are backed up in a Postgresql database for which free software has been used. Essentially, the program 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.

Hospital categorization

The hospitals had to fill in a questionnaire and classify themselves as primary, secondary, tertiary care or specialized hospitals. Whilst there is natural overlap in the different types of healthcare there are distinctions between primary (e.g. general practice and basic district hospital services), secondary (district hospitals with basic specialty functions such as obstetrics) and tertiary healthcare (specialized care, usually on referral from primary or secondary medical care personnel, with facilities for special investigations and treatment). In addition they had to declare whether they were teaching hospitals. Teaching hospitals could be both those linked to universities providing only undergraduate training, those providing specialization training or both.

Data collection

Data on antibiotic use were collected by dedicated team/s, comprising infectious diseases specialists, microbiologists, pharmacists and infection control nurses, for all inpatients within a maximum of two consecutive weeks. Most of the hospitals carried out the survey between May and June 2009. However, the Belgian hospitals carried out the survey in November 2009. Furthermore, reminders were sent to those hospitals who had carried out the survey, entered but did not validate their data. In order to be included in the survey, patients had to be admitted in the hospital for at least 24 h before the survey and still present at 0800 on the day of survey. For surgical patients, administration of prophylactic antimicrobials was checked for the previous day to code the duration of prophylaxis as either one dose, 1 day or >1 day. The number of patients in each ward was used as denominator. Depending on the number of beds, hospitals decided to complete the survey on either one or more days. However, all beds in each department had to be completed in a single day. For each patient treated with systemic antimicrobials, information was collected on age, gender, antimicrobial agent/s (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 and whether the indication was actually documented in medical records. Whenever the reasons for treatment were not documented, the ward doctors in charge of the patient's care were contacted in order to obtain such information. Compliance with local guidelines was also requested but not assessed centrally.

Antimicrobial use was reported as the number of treated patients and the number of therapies. Therapy was defined as the use of one substance by one route of administration. Data were entered on the central database (based at the University of Antwerp, Belgium) using the web-based tool developed internally, WebPPS. This was done locally, within the hospital, after completing paper forms in the wards.

Statistical analysis

A simulation method was used to select 30 samples of 74 hospitals with not more than 5 hospitals per country in order to determine whether the results would change. If the results were significantly different, this would have implied an over-representation of countries with high participation. The Kruskal–Wallis one-way analysis of variance by rank, a non-parametric method for testing equality of population medians between groups, was used to determine whether there was any significant difference in population and or indicators (*P* value for all was consistently close to 1, i.e. non-significant). The outcome showed no significant difference between any of the samples and the total data set, therefore it was decided to carry out the analysis using all 172 hospitals. The *z*-test was used to determine whether differences in proportions between sets of data for different departments were large enough to be statistically significant.

Results

Hospital overview

Twenty-five countries participated in the ESAC PPS 2009 with 172 hospitals including 21 primary, 89 secondary, 57 tertiary and 5 specialized hospitals. The median number of hospitals per country was 3 (range 1–45). Since hospital participation was exclusively on a voluntary basis the number of hospitals was not intended to be representative. Teaching hospitals amounted to 76 (44.2%).

Patient demographics and overview of prescribing

A total of 73060 patients were enrolled, of whom 21194 (29.0%) were prescribed 29665 antimicrobial therapies. Intensive care

Table 1. Overview of patients and indicators by department

Parameter description	Department				All hospital
	intensive care	medical	other	surgical	
Number of hospitals	153	169	57	162	172
Number of included patients (range)	3894 (2–310)	43 577 (14–1781)	2323 (3–251)	23 242 (17–2771)	73 060 (2–680)
Number of treated patients (%)	2068 (53.1)	11 690 (26.8)	251 (10.8)	7188 (30.9)	21 197 (29.0)
Number of prescriptions	3425	16 155	345	9740	29 665
Parenteral therapy, % (range)	90.8 (0–100)	50.3 (0–100)	46.1 (0–100)	67.3 (0–77.8)	60.5 (0–67.6)
Reason in notes, %[a]	79.0	78.9	69.9	69.4	75.7
Guidelines compliant, %[a]	66.8	64.3	54.2	56.1	62.0
Combination therapy, % (range)	48.6 (0–100)	30.2 (0–100)	29.9 (0–100)	30.4 (11.1–100)	32.1 (0–94.4)

Note values and percentages refer to actual overall values for the complete data set.
[a]Range for reason in notes and guideline compliance was 0–100% for all specialties.

departments had the highest proportion of treated patients, often receiving more than one agent.

The majority of patients received monotherapy [median of 68.9% of patients; interquartile range (IQR) 61.5%–77.1%]. Data for proportion of treated patients, parenteral route of administration, inclusion of reason in patient notes, compliance with local guidelines and combination therapy for the different department categories, are summarized in Table 1.

Route of administration

A mean of 60.5% of antimicrobials were administered via the parenteral route. The proportion of parenteral use differed considerably in the participating hospitals and specialties (Figure 1). The parenteral proportion was significantly higher ($P < 0.0001$) in intensive care with respect to the three other categories. The reason for starting antibiotics was a key factor in the selection of the route of administration. Medical prophylaxis had the only relevant proportion (3.3%) of inhaled treatment, mainly for the respiratory site (e.g. for cystic fibrosis) with the oral route being predominant (64.4%). In surgical prophylaxis, parenteral

administration was used in 82% of cases. Community-acquired infection (CAI) and hospital-acquired infection (HAI) had similar proportions of oral therapy, 42.5% and 36.6%, respectively, with the rest almost exclusively parenteral. Fluoroquinolones (J01MA) (68.6% oral) and penicillins (J01C) (35.9% oral) are available for both oral and parenteral use. The most used fluoroquinolone, ciprofloxacin, had only 29.7% parenteral use, whilst co-amoxiclav, the most used penicillin, had 52.6% parenteral use.

Reason in notes

The reason for which antimicrobials were prescribed was recorded in three-quarters of the patients' medical records. This varied in the different hospitals with a median of 80.0% (IQR, 69.9%–87.7%). Analysing the same data by specialty yielded a significantly higher inclusion of reason in notes for 'Intensive care' and 'Medical' departments with respect to 'Other' and 'Surgical' departments ($P < 0.0001$). Neither the difference between 'Intensive care' and 'Medical' departments, nor the difference between 'Other' and 'Surgical' departments
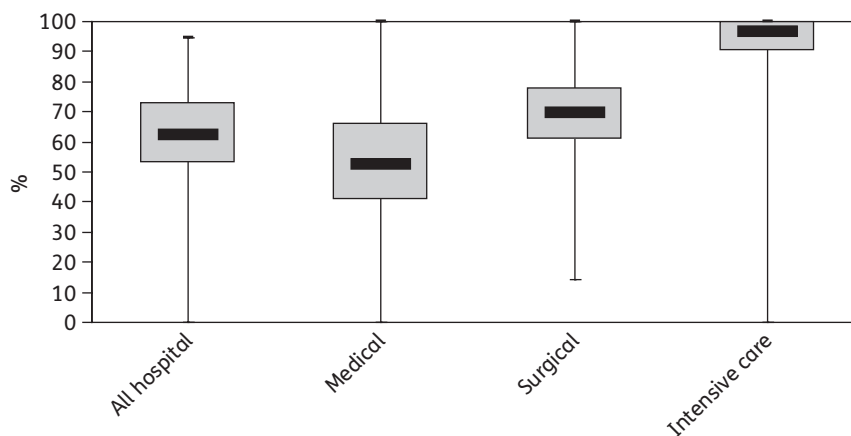

Figure 1. Box and whisker plot showing the proportion (and range) of parenteral antimicrobials within participating hospitals and the respective specialties.

was significant. The reason was more frequently included in patients' notes when the indication was infection (80.8%) as opposed to prophylaxis (54.2%). There was no significant difference between the type of infection (CAI 81.8%; HAI 79.2%) or type of prophylaxis (surgical 55.0%; medical 53.3%).

Compliance with local guidelines

The overall compliance with local guidelines was 62.8%. The difference between departments, once again, showed that 'Intensive care' had, significantly, the best compliance rate followed by 'Medical' ($P=0.0061$), 'Surgical' ($P<0.0001$) and 'Other' ($P<0.0001$) departments, respectively.

Antimicrobial use by Anatomical Therapeutic Chemical (ATC) classification

Stratifying at the second level of the WHO ATC classification (ATC-2), 89.7% of the prescribed antibiotics were antibacterials—J01. Systemic antifungals—J02—was the second class in 'Intensive care' (5.6%) whilst minimally used in 'Surgical' departments (1.2%). The 'other antimicrobials', mainly oral/rectal metronidazole were second in both 'Medical' and 'Other' departments (5.2%, 7.9%).

At ATC level 3 (ATC-3) penicillins were the most used class (J01C: 35.0%), followed by the other β-lactams (J01D: 17.1%) and 'other antibacterials' (J01X: 12.6%). The most utilized class, at ATC level 4 (ATC-4), was the penicillins/β-lactamase inhibitors (J01CR: 22.1%) followed by the fluoroquinolones (J01MA: 9.1%). At ATC level 5 (ATC-5), amoxicillin/β-lactamase inhibitor was the most used substance [J01CR02: 15.0% (7.9% parenteral; 7.1% oral)]. Differences between the different specialties especially between 'Intensive care' departments and the other categories were observed. 'Intensive care' had a higher use of piperacillin/β-lactamase inhibitor (J01CR05) whilst all other specialties mainly used amoxicillin/β-lactamase inhibitor (J01CR02).

Antimicrobial use by indication

The penicillin/β-lactamase inhibitor ATC-4 category was prevalent in most indications. Amoxicillin/β-lactamase inhibitor (J01CR02) was the most common antimicrobial for surgical prophylaxis (20.0%) and CAI (17.8%) while piperacillin/β-lactamase inhibitor (J01CR05) was most common in HAI (11.5%). For medical prophylaxis different antimicrobials were used. Sulphonamides, namely co-trimoxazole—J01EE01 (14.5%)—was the most utilized antimicrobial followed by the triazole derivatives—J02AC, mainly fluconazole—J02AC01 (18.6%).

Antimicrobial use by diagnostic site of infection

The top four indication sites accounted for >75% of cases. The respiratory tract was the most common site (27.2%), followed by skin, soft-tissue, bone, joint (SSTBJ) (19.0%), gastrointestinal tract (GIT) (17.2%) and urinary tract (12.9%). The four most utilized antimicrobials were co-amoxiclav (20.0% of respiratory), flucloxacillin (19.9 of SSTBJ), parenteral metronidazole (18.0% of GIT) and trimethoprim (18.8% of urinary tract infections). The most utilized antimicrobial was different for the different indications. However, co-amoxiclav ranked second in the other three sites indicating that its use is not limited to specific sites.

Antimicrobial use for surgical prophylaxis

The top five antibiotics for surgical prophylaxis were amoxicillin/β-lactamase inhibitor (20.0%), cefuroxime (17.1%), cefazolin (12.4%) metronidazole (10.4%) and gentamicin (6.9%). However, metronidazole was hardly ever used as a single agent (only 16 patients), but mainly combined with cefuroxime 129 times (32.6%). Amoxicillin/β-lactamase inhibitor was the most used for all sites whilst cefuroxime and cefazolin were mostly used in SSTBJ, metronidazole in GIT and gentamicin for urinary tract operations.

Prophylaxis was generally prolonged, in the majority of cases for >1 day, for all operation sites (Figure 2). For the most used
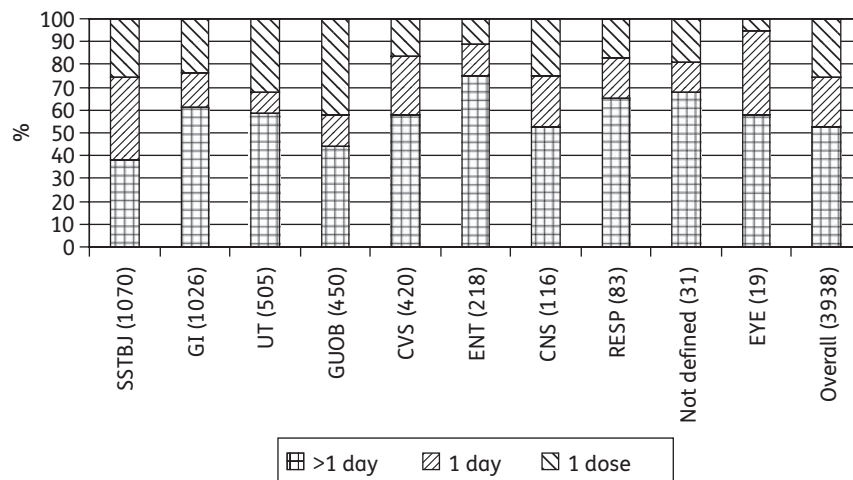

Figure 2. Duration of surgical prophylaxis by operation site. The number of cases for each of the categories is shown in brackets. Categories: SSTBJ, skin, soft tissue, bone and joint; GI, gastrointestinal; UT, urinary tract; CVS, cardiovascular system; GUOB, gynaecology and obstetrics; ENT, otorhinolaryngology; RESP, respiratory; EYE, ophthalmic.

Table 2. Top antimicrobial combinations and respective indications for which they were used

Combination	Aetiology	Main site	Main diagnosis	Number	Combination, %
Co-amoxiclav + clarithromycin	CAI	Resp	CAP	289	91
Benzylpenicillin + flucloxacillin	CAI	SSTBJ	SST	163	94
Cefuroxime + metronidazole	CAI	GI	IA	89	42
	Surg proph	GI	ProphGI	55	26
Amoxicillin + clarithromycin	CAI	Resp	CAP	105	75
Co-amoxiclav + metronidazole	CAI	GI	IA	29	35
	Surg proph	GI	ProphGI	18	22
Ceftriaxone + metronidazole	CAI	GI	IA	29	47
	Surg proph	GI	ProphGI	18	29
Piperacillin/tazobactam + metronidazole	Surg proph	GI	ProphGI	31	56

Abbreviations: CAI, community-acquired infection; Surg proph, surgical prophylaxis; CAP, community-acquired pneumonia; IA, intra-abdominal; ProphGI, prophylactic gastrointestinal; SST, skin and soft tissue; Resp, respiratory; GI, gastrointestinal; SSTBJ, skin and soft tissue or bone and joint.
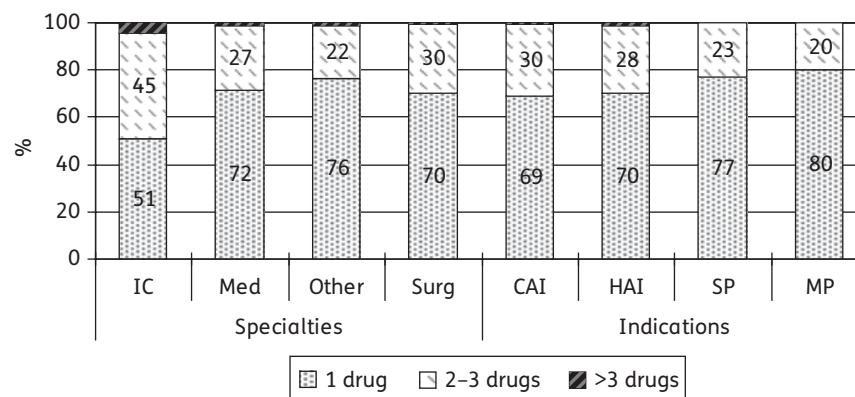

Figure 3. Differences between specialties and indications, respectively, in the use of monotherapy and combination therapies. Specialties: IC, intensive care; Med, medicine; Other, other departments; Surg, surgical departments. Indications: CAI, community-acquired infection; HAI, hospital-acquired infection; SP, surgical prophylaxis; MP, medical prophylaxis.

antimicrobial, co-amoxiclav, >1 day duration was used in 59.3% of cases. Ceftriaxone, which has a long half-life, was used for >1 day in 73.0% of cases. Alternatives to prolonged prophylaxis included gentamicin, used as a single dose 74.6% of the time, and flucloxacillin, used for 1 day in 51.5% of cases.

HAI

HAI accounted for 30.7% of all antimicrobial therapies. The proportion was highest in 'Intensive care' (48.9%), 30% in 'Surgery' and 27% in both 'Medical' and 'Other' departments. Hospital-specific antimicrobials such as glycopeptides and carbapenems were more utilized in 'Intensive care'. Respiratory infections (26.8%) were the most common HAI in 'Intensive care' (38.5%) and 'Medical' (29.7%) departments, urinary tract infections (23.4%) were the most common in 'Other' departments whilst SSTBJ HAIs (32.7%) were the most common in 'Surgical' departments.

Combination therapy

Combination therapy was used in 6794 (32.1%) patients. Table 2 highlights the most frequently used combinations and the

respective aetiologies and sites. Figure 3 highlights the fact that monotherapy prevailed across the different departments and indications. However, 'Intensive care' showed a significantly higher proportion of combination therapy ($P < 0.0001$). The difference between the other departments was not significant.

Discussion

The ESAC PPS is a proven success because the number of participating hospitals, from the 20 of the pilot PPS (2006), increased to 50 (2008) and reached 172 hospitals in 2009. It took the surveillance programme in the USA a quarter of a century to increase from 19 to 230 hospitals.[9] This fact proves that our objective of evaluating the feasibility of carrying out the survey in a larger sample of hospitals was achieved successfully. The great variation in antibiotic stewardship initiatives across Europe highlights an urgent need for standardization and agreement on the principles and key components.[10] Southern Europe is a region requiring more work on this matter.[11]

Various indicators have been established with respect to antibiotic prescribing. Amelioration in these indicators is desired in order to improve patient outcomes. When PPSs are carried out

repeatedly these can help verify any changes in targeted area/s of practice, previously identified as performance indicators. One of these indicators is the switch from intravenous to oral therapy when the patient improves. Patients with an appropriate early switch to oral therapy have a shorter length of hospital stay, and require less nursing time.[12,13] This form of benchmarking is more appropriate for comparison of repeated PPSs within the same hospital since the case mix would tend to be more or less stable. On the other hand different hospitals might have a very different case mix and therefore a different need for parenteral therapy.

Another indicator that can be monitored by PPS is guideline compliance, an indicator that is applicable to any area of practice and not exclusively to antibiotics.[14–16] In our study the compliance was relatively low at 62% with slightly better results for 'Intensive care'. However, ESAC could not assess the answers given by the hospitals. The answers to this parameter could be biased by the surveyors' perspective.

The inclusion of the reason why therapy was started in the patient's medical notes (Reason in notes) is an indicator not previously well documented in the literature. ESAC PPS has identified this parameter as a key performance indicator. It allows intelligibility and statement of practice, as well as facilitating measurement of prescribing quality. Whatever the baseline compliance (median 80%, IQR 70%–88%, in this study) there is room for improvement especially for the less compliant outliers. Once again, 'Intensive care' was the better performing department, along with the 'Medical' department. The facts that patients are sicker and the nurse-to-patient (and doctor-to-patient) ratios are higher in 'Intensive care' may possibly contribute to higher documentation of the indication/reason why a patient is prescribed any pharmacological agents including antimicrobials. The lower documentation rate observed in surgical departments could mainly be due to the fact that, most of the time, the indication is excessively prolonged surgical antimicrobial prophylaxis.

HAIs represent a serious public health problem.[17] The prevalence of HAI is also another performance indicator that is often overlooked.[18] Surveillance of HAI, which has been identified as a clinical performance indicator, has been ongoing in the USA since 1970.[9] 'Intensive care', as expected, had the highest prevalence of HAI with almost half of the treated patients being treated for an HAI, not necessarily acquired within the 'Intensive care' setting. In fact, 8.0% of HAIs were imported from another hospital and not just a different department within the same hospital. Therefore, one has to factor this in, in order to minimize potential bias, since in such cases the HAI cannot be attributed to the surveyed hospital. This is more relevant when the PPS aims to benchmark the hospitals.

Most antimicrobial combinations are clinically justified, e.g. the use of a β-lactam plus a macrolide for community-acquired pneumonia.[19,20] However, the combination of metronidazole with either co-amoxiclav, piperacillin/tazobactam or carbapenems indicates an anti-anaerobe overkill, which is not clinically warranted.[21] In this study, such combinations accounted for 8.5% of combination and 2.7% of all therapies.

Empirical treatment requires a wide spectrum of cover; however, in a PPS there is always a mixture of newly prescribed therapies and cases where the culture and susceptibility results are available and therefore therapy should have been changed accordingly. The antimicrobial selection for particular indications was therefore, identified as another target for quality improvement. In general, a higher proportion of narrow-spectrum agents suggests a better performance than a higher proportion of broad-spectrum second-line antimicrobials.[22] In the case of hospital-specific antimicrobials this is much less of a bias issue. An elevated use of hospital-specific antimicrobials either in the general wards or for CAI is another quality indicator that should be targeted. The tendency is that countries with high antibiotic use also have high use of hospital-specific antimicrobials.[23] A study in Latvia recorded an increase in the use of antimicrobial agents including an increase in the proportion of hospital-specific antimicrobials.[24] It is probable that this trend would be observed elsewhere unless specific antibiotic stewardship measures are implemented.

Another area of concern was the excessively prolonged duration of surgical antibiotic prophylaxis for >1 day. Surgical prophylaxis should cover the peri-operative period only and a single dose is usually enough unless there is extensive blood loss or the procedure is prolonged.[25]

Individual hospitals could decide to prioritize and focus on specific departments in order to improve selected quality indicators. However, better-performing departments should not be neglected in order to ensure they maintain the level of practice and also as a benchmark for other departments. Any benchmarking has to be done either by observing trends within the same hospital/units or by comparing similar types of hospital, especially for oral-to-parenteral ratio, since tertiary referral centres would be expected to have a higher use of parenteral therapy compared with primary hospitals. The fact that there is no international standardized hospital categorization system is a major limitation in comparing hospitals, especially from different countries, ensuring they have a similar case mix. However, for duration of surgical prophylaxis, compliance with guidelines or documentation of the reason for starting therapy in notes should not be affected by the type of hospital.

This study confirms the findings of the first ESAC PPS that a web-based method for PPS offers a standardized instrument that can identify targets for quality improvement.[8] Furthermore, this study identified performance indicators not identified in the previous ESAC PPSs. These include the proportions of HAIs, guideline compliance and combination therapy. The WebPPS is also a dynamic tool that, besides providing a standardized methodology, is also adaptable to different research and/or surveillance questions enabling the PPS organizers to modify the software to fit their needs. The WebPPS developed by ESAC has now been modified to include HAI surveillance, in addition to antimicrobial use, for the European Centre for Disease Prevention and Control (ECDC) PPS. The antimicrobial part is based on the ESAC PPS whilst the HAI part is based mainly on Improving Patient Safety in Europe/Hospital in Europe Link for Infection Control through Surveillance (IPSE/HELICS) and CDC/National Healthcare Safety Network (CDC/NHSN) case definitions.[26]

In conclusion, ESAC developed a web-based application (WebPPS), which was used successfully across Europe. Areas of practice where improvement is required can be identified using the WebPPS PPS tool. Hospitals can audit and feed back the results instigating improvement in practice. The ESAC WebPPS software is also available for other countries outside Europe.

Some European hospitals now have access to an amended WebPPS tool for a combined PPS on HAI and antimicrobial use. This new PPS protocol and WebPPS tool is currently being piloted and will be rolled out for a representative European PPS on HAI and antimicrobial use in 2011.

Transparency declarations

None to declare.

Disclaimer

The information contained in this publication does not necessarily reflect the opinion of ECDC.

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