# Antimicrobial consumption and resistance in adult hospital inpatients in 53 countries: results of an internet-based global point prevalence survey



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# First web-based Global Point Prevalence Survey of Antimicrobial Consumption and Resistance (GLOBAL-PPS) in 53 Countries : results on hospitalized adults

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**Abstract**

**Background**

The Global Point Prevalence Survey (Global-PPS) established an international network of hospitals to measure antimicrobial prescribing and resistance worldwide.

**Methods**

Using a standardized surveillance method, detailed data were collected in 2015 from 335 hospitals (H) in 53 countries (C): Europe (25C;215H); Africa (5C;12H), Asia (15C;56H), Americas (6C;43H), Oceania (2C;9H) for all inpatients receiving an antimicrobial on the day of the survey. We report findings for adult inpatients.

**Findings**

Out of 100,591 inpatients, 86,776 were admitted to adult wards (n=3,315); of which 34.4% (n=29,891 patients) received at least one antimicrobial. Among 48,436 antimicrobials in the entire survey, 41,213 were used in adult wards of which 89.6% antibacterial agents (ATC J01) for systemic use.

The top three antibiotics included penicillin beta-lactamase inhibitor combinations (highest in Western Europe:33.3% and Northern Europe:28.6%); third-generation cephalosporins (highest in Eastern Europe:49.4% and Western and Central Asia:25.0%); and fluoroquinolones (highest in Northern America:19.1%). Carbapenems were most frequently prescribed in Latin America and Western and Central Asia (9.0%). Among 19.8% patients with targeted treatment, 5.9% (range:2.8% in Africa to 15.2% in Latin America) received an antibiotic targeting a multidrug resistant organism. Latin America and East and Southern Asia reported the highest number of patients having at least one healthcare associated infection (11.9% and 10.1% respectively). Overall, the reason for treatment was recorded in 76.9% and a stop/review date in 38.3% of antimicrobial prescriptions. Local antibiotic guidelines were missing in 19.2% of recorded diagnosis and guideline compliance was 77.4%.

**Interpretation**

This Global-PPS demonstrated that worldwide surveillance can be accomplished with voluntary participation. It uniquely provided quantifiable measures to assess and compare quantity and quality of antibiotic prescribing and resistance in hospitalized patients worldwide (www.global-pps.com). These data serve to improve quality of antibiotic prescribing through education and practice changes. The Global-PPS is particularly useful for Low-Middle-Income-Countries for which no tools are available to monitor antibiotic prescribing in hospitals.

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## Research in context

### Evidence before this study

Surveillance systems monitoring antimicrobial use and resistance are the cornerstone to successfully implement sustainable antimicrobial stewardship programmes. They are needed to enhance decision-making and assess the impact of interventions. A Point Prevalence Survey (PPS) is a well demonstrated method which has shown its applicability and benefit in European hospitals and beyond.

### Added value of this study

The project, called the Global-PPS, assessed the prevalence of antimicrobial use and resistance worldwide. The Global-PPS offered a simple protocol and tool for data entry and immediate feedback enabling direct benchmarking with other (primary, secondary or tertiary care) hospitals and wards (e.g. Intensive Care, haematology/oncology, transplant, pneumology, surgery), by country and region. Hospitals in Low and Middle Income Countries (LMIC) were for the first time able to measure and compare antimicrobial use patterns at local and regional level. The Global-PPS allows to share best practises and raise awareness of inappropriate antimicrobial prescribing. Tangible quantifiable quality indicators were offered to improve antibiotic prescribing at hospital level. Participants became part of a unique and strong network supporting them in the process of data collection, -entry, -analysis, communication of their results.

### Implications of all the available evidence

The WHO has developed the Global Antimicrobial Surveillance System (GLASS) that provides countries with a standardized approach for collecting, analyzing, and sharing data on AMR. The Global-PPS can complement this by providing a validated method for measuring the quality of antimicrobial prescribing and the impact of interventions to improve antimicrobial prescribing. Governments can use this to support the antimicrobial stewardship framework as part of their WHO National Action Plans, whereas the Interagency Coordination Group (IACG) on AMR of the United Nations could use it for international mapping of antimicrobial prescribing and resistance in hospitals, and for building a sustainable hospital surveillance framework, focusing on LMIC.

## Introduction

The need for information and data related to the quantity and quality of antimicrobial prescribing has been identified as one of the key barriers in the successful development and implementation of antimicrobial stewardship programmes internationally.[1] Surveillance systems to monitor antimicrobial use and resistance are needed to enhance decision-making and assess the impact of interventions.[2, 3] Moreover, audit and feedback of prescribing practices complements and enhances[4] other core stewardship interventions.[5, 6]

The Global Point Prevalence Survey of Antimicrobial Consumption and Resistance (Global-PPS) was developed to further build on three point-prevalence surveys (PPS) carried out by the European Surveillance of Antimicrobial Consumption (ESAC) project between 2006 and 2009.[7, 8] Several studies on the applicability and benefits of a PPS of antimicrobial use demonstrated their value in a range of European hospitals.[8-11] The ESAC-PPS methodology was adapted for the European Centre for Disease Prevention and Control (ECDC) PPS of healthcare-associated infections and antimicrobial use in acute care hospitals (ECDC-PPS)[12] as well as for the Antibiotic Resistance and Prescribing in European Children (ARPEC-PPS) project that focused on antimicrobials administered to paediatric and neonatal patients worldwide.[13-16]

Following the 4$^{th}$ World Healthcare-Associated Infections and Antimicrobial Resistance Forum on,[2] bioMérieux decided to support a project to assess the international prevalence of antimicrobial use and resistance, called the Global-PPS, prioritizing countries with limited resources, support and expertise.[17]

We report on the first Global-PPS conducted in 2015. The current paper describes antibiotic prescribing practises among hospitalized patients admitted to adult wards only (hereafter called “adult inpatients”), in order to determine the variation in quantity and quality of antimicrobial prescribing and resistance rates across continents.

## Materials and methods

Countries and hospitals

Any hospital was welcome to join the ad hoc Global-PPS network. Promotion of the study was done through existing ESAC- and ARPEC-PPS hospital networks, during the 2014 ECCMID congress (http://2014.eccmid.org/), through the aid of bioMérieux subsidiaries and members of the HAI/AMR Forum.[17]

The Global-PPS was first piloted in October-November 2014 in 33 hospitals worldwide. Key amendments following this pilot included improvements to the Global-PPS software tool, not protocol amendments. The full Global-PPS was conducted between January and September 2015. The data of hospitals successfully participating in the pilot Global-PPS (n=18) were transferred for inclusion in the full Global-PPS data-set for final analysis. As such, we finally included 335 hospitals from 53 countries belonging to the five United Nation (UN) regions (Africa, Americas, Asia, Europe and Oceania).[18] Depending on the number of hospitals participating, countries were grouped into UN sub-regions. For the Americas, Latin America and the Caribbean (hereafter called Latin America because of lack of data on the Caribbean) and Northern America were defined. For Asia, Southern, Eastern and South-eastern Asia (hereafter called East and Southern Asia) on one side and Western and Central Asia on the other side were grouped together**.** For Europe, four sub-regions (i.e. Eastern, Northern, Southern, Western) were defined.[18] Details on the participating countries and the number and type of hospitals is available as supplementary material (Appendix I). Hospitals were classified according to primary, secondary, tertiary (including infectious diseases hospitals) and paediatric hospitals, as previously defined by the European Centre for Disease Prevention and Control (ECDC).[19] Overall, five main ward types were defined for adult and paediatric wards separately: medical wards; surgical wards; intensive care units; haematology/oncology wards and transplant (bone marrow transplant/solid) medical wards. For adult wards we also specified pneumology medical wards. Neonatal wards included neonatal intensive care units and general neonatal medical wards.

## Data collection

As detailed in the protocol (Appendix II), each ward had to be surveyed once within the fixed time period. The one-day cross sectional PPS included all inpatients admitted in the ward at 8:00 am the day of the survey. Data collection was performed using a ward (recording of denominators) and a patient (recording of numerators) paper form. Definitions on the different variables are available as supplementary material in appendix II and III. In summary, for each patient receiving at least one antimicrobial, mandatory data included information on patient characteristics, received antimicrobial agents and details on the diagnosis and indication according to predefined lists (Appendix III). Four main types of indications categorized into two major categories were used. The first included therapeutic antimicrobial prescribing for community-acquired (CAI) and health-care associated infections (HAI). A HAI was defined as an infection whereby symptoms started 48 hours after admission to the hospital. The second category included antimicrobial prescribing for surgical and medical prophylaxis. Retrospective information on surgical prophylaxis was captured in the previous 24 hours of the surgery indicating 1 dose, multiple doses in 1 day or multiple doses for more than one day. Additional antimicrobial quality indicators included 1) the diagnosis being documented in the patient's notes at the start of treatment; 2) the antibiotic prescription (choice) being compliant with local guidelines and 3) if a stop or review date of the antimicrobial prescription was documented in the notes. Additionally, empiric or targeted treatment (based upon microbiology data from a relevant clinical specimen (e.g., blood, sputum, etc.,) [excluding screening tests]) was recorded. If the treatment choice was determined by available microbiology data, the participant could indicate if it targeted one of the 9 multidrug-resistant organisms as described in Table 6 and appendix III. Finally, information included whether biomarker data (C-reactive protein (CRP), procalcitonin (PCT) or any other biomarker) were used in supporting the decision to prescribe. Denominators included the total number of patients present on the ward census at 8 am.

Antimicrobials included antibiotics for systemic use (J01), antimycotics (J02) and antifungals (D01B) for systemic use, drugs to treat tuberculosis (J04A), oral antibiotics prescribed as intestinal anti-infectives (A07AA; e.g. oral vancomycin), nitroimidazole derivatives (P01AB), neuraminidase inhibitors (J05AH) and antimalarials (P01B). All antimicrobials were online automatically classified according to the standardized and internationally recognized WHO Anatomical Therapeutic Chemical (ATC) classification system classifying drugs based on their main therapeutic use (WHO, version 2014).[20]

The protocol (supplementary material, appendix III) mentioned that no discussion or personal judgment on the appropriateness, or lack thereof, of antibiotic prescribing should be entertained during the survey. Data were inputted into the freely available Global-PPS program, a web-based application for data-entry, validation and reporting. A helpdesk and several supplementary documents such as a frequently asked questions (FAQ) list were freely available to support the participants.

Data validation included several online in-built checks providing errors and warnings that had to be managed by the user in order to download a real-time feedback report (see discussion: study strengths). Since total inpatient inclusion at the hospital level was requested but not mandatory, the participants had to report whether they surveyed the whole hospital or not (i.e. a check on completeness of data). The software was further designed to avoid missing and erroneous data-entry in the numerator such as inconsistencies between the indication and the diagnosis (e.g. an antibiotic given for prophylactic use but prescribed for sepsis), extremely high total daily dose, double entry of the same substance; as well as denominator error avoidance (see also appendix II, data validation). In addition, all hospitals with an overall antibiotic prevalence of more than 70% were individually contacted in order to confirm the described prevalence.

All data were completely anonymized within the database and safeguarded at the University of Antwerp, Belgium. However, all data remained the property of the hospital. Since participation was exclusively on a voluntary basis, results were not intended to be representative for a country or region. Depending on the countries' legal requirements, hospitals had to comply with local ethical approval. A data privacy excerpt document was available for this purpose. Informed consent was not needed because the survey did not require direct involvement or contact with the patient, treatment nor other intervention.

Data analysis

For the final analyses, 303 hospitals were eligible for inclusion: 22 pediatric hospitals (see appendix I) as well as another three hospitals which did not report data on adult wards were removed from analyses. Also another 7 hospitals were excluded due to unsolved denominator issues.

This paper focusses on prescribing patterns of antibiotics for systemic use (ATC J01) and is reported as 1) the number of treated patients, 2) the number of therapies and 3) the number of prescriptions. Therapy was defined as one treatment (received at least one antibiotic) per diagnosis. A prescription was defined as the use of one substance in one route of administration. Antimicrobial prescribing rates are expressed as a percentage of the patients on antimicrobials, or as a percentage of all antibiotic or antimicrobial prescriptions (proportional use), means and/or ranges aggregated at UN regional level,[18] by ward type and indication. We ranked the number of antibiotics accounting for 90% and 75% of (antibiotic) drug utilization (DU90% and DU75%). Antibiotic resistance patterns are expressed as the proportion of patients receiving at least one antibiotic targeting at least one resistant micro-organism out of all patients for which an antimicrobial result (targeted treatment) was available.

## **Results**

General overview

The final 2015 Global-PPS dataset included 45 primary care (6,264 patients, 6.2%), 131 secondary care (34,571 patients, 34.4%), 111 tertiary care (51,051 patients, 50.8%), 22 pediatric hospitals (4,091 patients, 4.1%) as well as 19 infectious diseases or specialized hospitals (4,614 patients, 4.6%) (see Appendix I). The number of beds of participating hospitals ranged from 16 to 2,500 beds (82 hospitals fell below P25=153 beds; P50=293 beds; P75=520 beds; 33 hospitals fell above P90=817 beds of which 19 had a bed capacity of >1,000 beds). We collected data on 100,591 patients admitted to 4,031 wards of which 3,315 adult wards accounting for 86,776 patients. Overall, 52.6% of treated patients were males (range 45.6% in Northern America to 57.3% in Eastern Europe).

Out of 48,436 antimicrobial prescriptions, 41,213 were prescribed on adult wards. Antibacterials for systemic use (ATC code J01) represented 89.6% (N=43,391), followed by antimycotics and antifungals for systemic use (J02 and D01BA, 4.3%, N=2,073), drugs to treat tuberculosis (J04A, 2.3%, N=1136), nitroimidazole derivatives (P01AB, 1.9%, N=929), antibiotics prescribed as intestinal anti-infectives (A07AA, 1.6%, N=781) and neuraminidase inhibitors (J05AH, 0.3%, N=126).

Antimicrobial use rates among participating hospitals varied between continents (range: 31.9% in Europe to 50.0% in Africa) and ward types (range: 29.0% in medical wards to 77.0% in transplant (BMT/solid) medical wards) (Table 1).

## Antibiotic drug utilization

In total, 36,792 antibacterials for systemic use were used in patients admitted to adult wards on the day of the survey, including 139 different agents (Table 2). The DU90% for East and Southern Asia comprised 31 antibacterials, while this was much lower for Africa and for Eastern Europe (15 and 13 respectively). The combination of penicillins with a beta-lactamase inhibitor were the most commonly prescribed class (20.1%, mainly amoxicillin with beta-lactamase inhibitor (11.4%) and piperacillin with beta-lactamase inhibitor (7.7%) of total use of antibiotics). The second and third most commonly prescribed antibiotics were third-generation cephalosporins (14.1%, mainly ceftriaxone (11.0%)) and fluoroquinolones (12.3%, mainly ciprofloxacin (6.8%) and levofloxacin (4.1%)). Complementary to Table 2, a supplementary figure (appendix IV) shows the most commonly prescribed subgroups of antibiotics by UN region.

### Antibiotic prescribing by indication

The top 5 indications accounted for 45.9% of treated patients. Pneumonia was overall the most common indication (19.2% of all treated patients). The next most common reasons were skin and soft tissue infections (9.0%), intra-abdominal infections (7.0%), lower urinary tract infections (cystitis, 6.0%) and upper urinary tract infections (pyelonephritis, 4.7%). Table 3 summarizes the most common indications for treatment in patients admitted to adult wards, by UN region.

### Therapeutic prescribing

Table 4 compares the number of prescribed antibacterials (J01) by indication and type of treatment. Overall, most antibiotics were prescribed for community-acquired infections (CAI) (45.6%). Targeted prescribing was more common for HAI (36.9%).

The overall prevalence of adult inpatients treated with antibacterials (J01) for at least one HAI was 8.4% (n=7,278). Lowest rates were found in Eastern Europe (2.8%), followed by Southern Europe (7.5%), Western Europe (7.7%), Western and Central Asia (8.7%), Northern Europe (8.8%), Oceania (8.9%), Northern America (9.6%), East and Southern Asia (10.1%) and Latin America (11.9%). The most frequent reported indications *(*see online Appendix III, page 7, supplementary data collection forms for type of indication) were non-intervention related or other HAI (4.2%), followed by post-operative surgical site infections (1.6%).

The most prescribed antibiotics for a HAI were penicillins with a beta-lactamase inhibitor (24.8%) of which piperacillin and beta-lactamase inhibitor accounted for 14.6% (highest use in Northern Europe; 24.2% and Northern America; 15.2%) and amoxicillin and beta-lactamase inhibitor for 8.9% (highest use in Western Europe; 17.7% and Northern Europe; 11.9%). Fluoroquinolones were the second most prescribed (12.8%), with highest use in Eastern Europe (24.4%; mainly ciprofloxacin, 15.9% and moxifloxacin, 7.3%), Northern America (18.9%; mainly levofloxacin, 11.8% and ciprofloxaxin, 7.0%) and lowest in Northern Europe (5.2%). Carbapenems, mainly meropenem, were the third most frequently prescribed antibiotic class accounting for 12.2% of worldwide antibiotic use for a HAI with highest use observed for Western and Central Asia, Africa and Latin America (all 20%). The fourth most frequently prescribed were glycopeptides (mainly vancomycin) with highest use in Latin and Northern America (18.1% and 13.8% of total antibiotic use for HAI, respectively) (Figure 1).

The most commonly prescribed antibiotics for CAI were penicillins with a beta-lactamase inhibitor (29.2%) of which amoxicillin and beta-lactamase inhibitor accounted for 16.3% (highest use in Western Europe; 33.8% and Northern Europe; 14.5%) and piperacillin and beta-lactamase inhibitor for 7.7% (highest use in Northern Europe; 14.0% and Northern America; 12.7%). Third-generation cephalosporins were second most common prescribed (15.5%, mainly ceftriaxone) with highest rates observed in Eastern Europe, Latin America and Western and Central Asia (52.0%, 30.1%, 27.0% of total antibiotic use for treatment of CAI). Fluoroquinolones ranked third (14.0%) and were frequently prescribed for a CAI in Northern America (20.1%, mainly levofloxacin) and Southern Europe (19.0%, mainly ciprofloxacin). Figure 2 shows the most commonly prescribed antibiotics to treat a CAI, by region.

Prophylactic prescribing

On average, 26.6% (range: 16.6% in Northern America to 41.5% in Eastern Europe) of adult patients receiving antibiotics were administered at least one antibiotic for prophylaxis. The overall mean prevalence of surgical prophylaxis was 17.8% (Table 4). Cefazolin was the most commonly prescribed antibiotic for surgical prophylaxis (27.5%) with highest prescribing rates observed for Oceania (64.5% of total surgical prophylactic prescribing), Northern America (62.4%) and Western Europe (57.7%). Ceftriaxone was most commonly prescribed in Eastern Europe, Southern Europe and Africa (39.5%, 28.0% and 27.7% respectively). Prolonged surgical prophylaxis (>1 day) was very common in all regions, ranging from 40.6% in Oceania to 85% and 86.3% in Southern and Eastern Europe.

The overall mean prevalence of medical prophylaxis was 7.4% (Table 4). Many different antibiotics were used for medical prophylaxis with sulfamethoxazole/trimethoprim being predominant worldwide (highest use in Oceania and East and Southern Asia, 63.4% and 56.0% of total medical prophylactic prescribing respectively). Ceftriaxone was most commonly prescribed in Eastern Europe, Southern Europe and Western and Central Asia (54.2%, 16.9% and 16.9% respectively).

Quality indicators of antibiotic prescribing

Table 5 provides an overview of all selected antimicrobial quality indicators by region. The stop/review date was poorly documented (overall 38.3% of antimicrobial prescriptions).

Antibiotic treatment based on microbiology data

Among 29,891 treated patients, 1,769 (19.8%) received a targeted antibacterial (J01) treatment (range: 7.8% in Eastern Europe to 26.5% in Latin America), 5.9% of whom received the treatment targeting at least one multidrug-resistant organism (Table 5). Overall, 60% of these patients received antibiotics targeting gram negative bacteria (GNB) with highest proportional numbers observed in Eastern Europe. Only in Northern America, a higher proportion of patients received targeted treatment against Grampositive bacteria. Table 6 shows the prevalence of patients receiving targeted treatment against resistant bacteria by UN region.

**Discussion**

We demonstrated the feasibility of conducting the Global-PPS, which focused on antibiotic prescribing and resistance, with a simple and affordable method on an international scale. Many hospitals were able to assess antibiotic prescribing patterns and collect information on antibiotic resistance in their hospital for the first time. This is essential for developing antimicrobial stewardship programs. Other PPSs have been conducted successfully in High Income Countries (HIC) of the European Union and the United States of America[21, 22], but this simple Global-PPS tool also allowed the participation of a large number of hospitals in Low and Middle Income Countries (LMIC) to collect information on antimicrobial use and resistance.

We found substantial differences in the prevalence of antibiotic prescribing between and within regions or countries with the highest prevalence found in Africa (50.0%; country range 27.8%-74.7%) and the lowest in Eastern Europe (27.4%; country range 23.7%-27.8%). The overall prevalence for Europe (31.9%; range: 23.7% in Bulgaria to 62.0% in the Former Yugoslav Republic of Macedonia (results not show)) was comparable with the weighted prevalence of previous PPS in Europe in 2011-2012 (32.6%; range: 21.4% in France to 54.7% in Greece)[21], but lower as compared to the PPS conducted in 183 US hospitals in 2011 (49.9%; CI 49.0%-50.9%).[22] Amoxicillin with beta-lactamase inhibitor was found to be the most frequently prescribed antibiotic in this survey, which is related to its high prescribing rates in Western Europe (25.6%), mainly represented by Belgian hospitals (Table 2). Except for Western Europe, this is in line with the ECDC-PPS in 2011-2012 whereby this agent represented on average 11.% of all antimicrobial agents.[21] The third-generation cephalosporins, mainly ceftriaxone, ranked second, and this was due to the high prescribing rates observed in Asia, Latin America, Southern and Eastern Europe; both for CAI and HAI. The high use of ceftriaxone in these regions of the world may indicate that at least a proportion of this prescribing may be inappropriate. Fluoroquinolones ranked third among antibiotics prescribed during this global PPS, due to the high use of levofloxacin in hospitals in Northern America and East and Southern Asia (mainly for pneumonia in both cases), and the high use of ciprofloxacin, mainly for cystitis in Western Europe and various indications elsewhere in Europe. Striking differences of levofloxacin use were found in the Americas (12.8% in Northern America versus 1.2% in Latin America) and Asia (7.4% in East and Southern Asia versus <1.0% in Western and Central Asia) (Table 2). There may be differences in cost or access to fluoroquinolones that preclude their use in certain locations which may vary substantial, among and within countries. We also speculate that these differences could be due to marketing strategies and/or regulation of antibiotics in these regions. Remarkably high vancomycin use was noted in Northern and Latin American hospitals. This high vancomycin use can be explained by high MRSA rates reported for American hospitals,[23] which is in line with the high percentage of patients with targeted treatment against MRSA infections in this Global-PPS (table 6). Carbapenems (mainly meropenem) were widely prescribed in Latin America and Asia. These high prescribing rates are most likely due to the high rates of infections caused by ESBL-producing Gram-negative bacteria, which has been reported in previous surveillance studies,[24-26] and which is in line with the observed rates in our Global-PPS (table 6).

The most frequent indication for antibiotic therapy worldwide was pneumonia, followed by urinary tract infections (UTI), combining upper and lower UTI's. We need more in-depth analyses to find out the proportion of healthcare associated ESBL UTI's. There appeared to be high proportion of prophylaxis for a range of indications, but unusually high prophylactic use for gastro-intestinal infections in Western and Central Asia. Further research is warranted in order to understand the reasons for this.

Our study investigated five antibiotic quality indicators to identify areas of inappropriate antibiotic prescribing. These can easily be used to set benchmarks for quality improvement of antibiotic use in hospitals.[10]

The first indicator referred to the documentation of the reason for prescription in the patient notes. This indicator ensures communication of diagnosis and treatment among clinicians and other healthcare providers, allows prescription stop or review dates and other interventions such as de-escalation. In Northern and Western Europe, America and Oceania, the outcome of this indicator is comparable to the 2009 ESAC-PPS conducted among European adults (80%).[8] Lower scores were found for Eastern (64%) and Southern European (70%), African (70%) and Asian hospitals (73%).

The second indicator refers to the formal procedure for a physician or other staff member to review the appropriateness of an antimicrobial administered at or after 48 hours from the initial order (post-prescription review).[27] It refers to the existence of a policy or agreed intervention preventing unnecessarily long antibiotic courses and ensures that the chosen antibiotic and its route of administration is still appropriate. Such a policy has an impact on selection pressure, prevention of adverse effects such a drug related toxicity and ecological damage leading to *C.difficile* infection. In less than one third of antimicrobials prescribed in Southern Europe, Western and Central Asia and Oceania, a stop/review data was recorded. In other areas, less than half of all prescriptions included a stop/review date. These data indicate the need to perhaps target this review process as a key intervention and measure its impact by repeated PPS.[10]

The third quality indicator referred to parental administration which was highest in Western and Central Asia, Latin America, Eastern and Southern Europe (>80% of patients on antibiotics). Broad-spectrum antibiotics are commonly administered in these regions (such as third generation cephalosporins) for which broad-spectrum antibacterial oral equivalents are often lacking. The switch from intravenous to oral antibiotics has many well-known advantages such as reduction in catheter-related complications, less healthcare costs and earlier hospital discharge. This is recognised as a key metric for stewardship processes in hospitals.[27, 28] On the other hand, it is not known to what extent different antibiotic administration routes have an impact on antimicrobial resistance.[29]

The fourth quality indicator referred to the existence and adherence to antibiotic treatment guidelines. In Western and Central Asia, local guidelines were not available in 40% of antibiotic prescriptions, especially for medical prophylaxis in the absence of a clear diagnosis. In one of the African countries, 11% of patients were treated with antibiotics for which the diagnosis was unknown, contrary to guidelines for LMIC which state that "an appropriate treatment must be preceded by diagnoses that ensures the correct clinical path".[30] This involves the existence of a clinical microbiology laboratory and antimicrobial stewardship involvement in for example daily laboratory rounds.[31] Guideline compliance referred only to the choice of drug for therapeutic or prophylactic use. Overall mean compliance to guidelines reached 77% and was less than 70% in Latin America, Western and Central Asia and Africa. Next to developing and updating local treatment guidelines, adherence to guidelines may improve clinical outcome in terms of mortality, as well as treatment duration and length of hospital stay.[32] A recent systematic review and meta-analysis showed that guideline-adherent empirical therapy was associated with a significant relative risk reduction for mortality of 35%.[6] The reason for this relatively lower level of compliance is uncertain and probably multi-factorial. It may reflect current local resistance patterns, uncertainty avoidance and fear of failure. Our data provide hospitals/countries with information to pursue further detailed investigation at country and/or hospital level.

The fifth quality indicator concerned prolonged surgical prophylaxis commonly seen during this PPS and in line with previous studies conducted in Europe.[21] Especially in Southern and Eastern Europe, mean prolonged surgical prophylaxis was very high (85% and 86.3%). It is well-known that surgical antibiotic prophylaxis for most indications for >24 hours does not prevent development of post-operative infections. Instead, it increases the risk of antimicrobial resistance and side effects.[33] Evidence showed that, in the absence of preoperative infection or severe complications, prolonged or surgical postoperative antibiotic prophylaxis patients is unnecessary.[34]

Study strengths and limitations

The strength of our study lies in the uniformity of data-collection, the simplicity of the protocol and data collection templates, the assurance of data quality (data completeness and validation process through web-based tool), the opportunity for real-time educational feedback of results to participating centres comparing their results to national and regional results, and the consistency and reproducibility of data.[9] Although we had to rely on the participants professionalism and motivation to provide valid data, we implemented strict online checks to avoid erroneous or incomplete data. Minimal training was required and most hospitals successfully participated in the Global-PPS with the online supporting materials (e.g. FAQ), helpdesk support and the online e-learning course (www.futurelearn.com/courses/point-prevalence-surveys) developed by the British Society for Antimicrobial chemotherapy [BSAC]. Thanks to the simple protocol and tool for data entry and feedback, we successfully included hospitals from low-middle income countries (n=8) and upper middle income countries (n=17, see appendix I). The study, conducted on a voluntary basis and often carried out with limited resources (financial, IT and manpower), provided a good utility value for the time commitment (see "evaluation of the 2015 Global-PPS" at www.global-pps.com/documents). It enforces the creation of clinical prescriber buy in, particularly if the data accrued is fed back to the prescribers,[35] the development of a sustainable network and the construction of a huge database allowing the production of various analyses and publications at international, regional and local levels. This Global-PPS not only contributes to continued world-wide awareness about antibiotic use and resistance, but it also helps participants in setting targets to improve antibiotic prescribing (see examples at www.global-pps.be/dissimination, including several communications from country networks as well as stand-alone hospitals), thereby driving improved prescribing behavior.[10]

The limitations of this study are inherent to the epidemiological method of a cross-sectional survey whereby the main purpose is to describe prescribing patterns in hospitals.[13] The overall rates provided average figures without correcting for patient case mix, disease incidence or prevalence of different types of infections, variations in resistance levels, institutional factors, differences in climates and seasons etc., which can all influence antibiotic use patterns. For that reason, one need to be very cautious in interpreting and comparing the reported prevalence rates.

Although we observed substantial differences in the prevalence of antibiotic prescribing between and within regions or countries, we are not representative for most of these countries and regions. For instance, Northern Europe was mainly presented by the UK, while Western European data included most Belgian hospitals thanks to the coordination by the Belgian Antibiotic Policy Coordination Committee (BAPCOC) at federal level.[36] Western European results might therefore be biased due to typical Belgian prescribing practices (e.g. the high use of amoxicillin with beta-lactamase inhibitor). We hope that if in the future, countries could participate with a representative number of hospitals, which would allow more meaningful analysis at country and regional level.

Future considerations

The Global-PPS was repeated in 2017 with increased participation of additional countries and hospitals. We focused again on LMIC because it is the only tool available for measuring antibiotic prescribing in hospitals in these countries, often demonstrating the highest prevalence of antibiotic prescribing and resistance. We aim to carry out repeated PPS at hospital or ward level (yearly or quarterly) to measure the impact of antibiotic stewardship interventions. Governments can use the Global-PPS tool to support the antimicrobial stewardship framework as part of their WHO National Action Plan. Indeed, in some countries (Saudi Arabia, The Philippines, Belgium), the Global-PPS was endorsed by the Ministries of Health, inviting many hospitals to participate in the 2017 PPS. The Interagency Coordination Group (IACG) on AMR of the United Nations could use the Global-PPS tool for international mapping of antimicrobial prescribing and resistance in hospitals, and for building a sustainable hospital surveillance framework, focusing on LMIC. The Global-PPS could compliment the Global Antimicrobial Resistance

Surveillance System (GLASS) of the WHO.[3] Ultimately, we aim to develop appropriate benchmarking standards, including quantifiable quality targets; but recognizing the significant pitfalls for using these quantitative data for benchmarking[37]. Currently, we are developing an educational framework and training programme for healthcare professionals working on hospital antibiotic stewardship in LMIC

Conclusion

The Global-PPS provided a comprehensive assessment of the prevalence's of antibiotic use and resistance internationally, using a simple and user-friendly tool. As such, hospitals from LMIC's were for the first time able to measure antimicrobial use patterns. We found substantial differences among hospitals in the quantity as well as the quality of antibiotic prescribing worldwide. These results will help hospitals and countries to improve hospital antibiotic prescribing and to define antibiotic stewardship objectives.

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**Contributions:**

PZ, VJ, DN, HG and AV had substantial contributions to the conception and the design of the work;

Data management and analysis was carried out by AV;

HG, PZ and AV contributed to the interpretation of data for the work;

AV drafted the work and all co-authors revised it critically for important intellectual content;

All authors gave the final approval of the version to be published.

**Declarations of interests**

Mark Miller, Isabelle Caniaux and Marie-Françoise Gros are bioMérieux employees.

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**Ethics committee approval**

This study was a completely anonymized audit of current antimicrobial prescribing practices and resistance. No unique identifiers were entered onto the database. Every patient record was given a unique not identifiable survey number which was automatically generated by the Global-PPS computer program specifically designed for anonymous data-entry. Formal ethical approval for this study depended on the country and was taken care of by each participating hospital if required.

**Table 1. N adult patients on antimicrobial use (%) by region and ward type, year 2015.**

| | | | Medical Ward | | Surgical Ward | | Intensive Care Unit | | Haemato-onco ward | | Pneumology ward | | Transplant (BMT/solid) | | Total adult wards | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **UN-region** | **N countries** | **N hospitals** | N admitted patients | Prevalence of antimicrobial use (%) | N admitted patients | Prevalence of antimicrobial use (%) | N admitted patients | Prevalence of antimicrobial use (%) | N admitted patients | Prevalence of antimicrobial use (%) | N admitted patients | Prevalence of antimicrobial use (%) | N admitted patients | Prevalence of antimicrobial use (%) | N admitted patients | Prevalence of antimicrobial use (%, country range) |
| **Europe** | **25** | **215** | **29663** | **26.1** | **18078** | **33.3** | **2954** | **59.2** | **1947** | **40.6** | **1878** | **52.0** | **192** | **74.5** | **54712** | **31.9 (23.7-62.0)** |
| Eastern Europe | 2 | 8 | 778 | 11.6 | 1381 | 33.2 | 107 | 67.3 | 11 | 9.1 | 105 | 30.5 | | | 2382 | 27.4 (23.7-27.8) |
| Northern Europe | 5 | 36 | 4959 | 29.8 | 2371 | 37.7 | 370 | 55.9 | 242 | 49.6 | 101 | 53.5 | 51 | 60.8 | 8094 | 34.4 (29.0-37.8) |
| Southern Europe | 13 | 53 | 6443 | 32.6 | 5475 | 40.0 | 1010 | 64.1 | 646 | 33.6 | 561 | 60.2 | 52 | 76.9 | 14187 | 39.0 (27.2-62.0) |
| Western Europe | 5 | 118 | 17483 | 23.4 | 8851 | 28.0 | 1467 | 56.0 | 1048 | 43.1 | 1111 | 49.7 | 89 | 80.9 | 30049 | 28.1 (25.1-37.1) |
| **Africa** | **5** | **12** | **619** | **49.9** | **1101** | **49.0** | **64** | **64.1** | | | | | | | **1798** | **50.0 (27.8-74.7)** |
| **Asia** | **15** | **56** | **8517** | **35.0** | **6912** | **36.1** | **1098** | **59.1** | **1003** | **53.0** | | | | | **18088** | **38.6 (22.4-85.7)** |
| East & Southern Asia | 6 | 29 | 6644 | 33.0 | 5663 | 34.2 | 702 | 65.5 | 847 | 54.0 | 409 | 46.2 | 146 | 86.3 | 14411 | 37.2 (29.6-78.5) |
| Western & Central Asia | 9 | 27 | 1873 | 42.0 | 1249 | 44.7 | 396 | 47.7 | 156 | 48.1 | | | | | 3677 | 43.8 (22.4-85.7) |
| **Oceania** | **2** | **9** | **1781** | **29.8** | **604** | **52.5** | **76** | **69.7** | **46** | **54.3** | | | | | **2516** | **37.0 (33.3-38.5)** |
| **Americas** | **6** | **43** | **5547** | **32.2** | **2707** | **40.2** | **992** | **57.4** | **294** | **46.9** | | | **80** | **66.3** | **9662** | **37.8 (30.9-44.8)** |
| Latin America | 4 | 19 | 1942 | 31.8 | 1571 | 37.3 | 468 | 55.1 | 92 | 28.3 | | | 41 | 65.9 | 4122 | 36.8 (32.5-43.4) |
| Northern America | 2 | 24 | 3605 | 32.4 | 1136 | 44.2 | 524 | 59.4 | 202 | 55.4 | 34 | 58.8 | 39 | 66.7 | 5540 | 38.6 (30.9-44.8) |
| **Total** | **53** | **335** | **46127** | **29.0** | **29402** | **35.6** | **5184** | **59.0** | **3298** | **45.1** | **2344** | **51.3** | **421** | **77.0** | **86776** | **34.4 (22.4-85.7)** |

Prevalence rates are calculated for and within each ward by region

Empty cells: No cases or too few cases which are counted in ‘total adult wards’ only

East & Southern Asia includes Southern, Eastern & South-eastern Asia

| Eastern Europe % (n=708; 2C) | | Northern Europe % (n=3536; 5C) | | Southern Europe % (n=6837; 12C) | | Western Europe % (n=9485, 5C) | | Africa % (n=1213, 4C) | | East & Southern Asia % (n=6781, 6C) | | Western & Central Asia % (n=2084, 9C) | | Oceania % (n=1226, 2C) | | Latin America % (n=2170, 4C) | | Northern America % (n=2752, 2C) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ceftriaxone | 36.3 | Amoxicillin/β-lact. inh. | 14.4 | Ceftriaxone | 19.6 | Amoxicillin/β-lact. inh. | 25.6 | Ceftriaxone | 19.3 | Amoxicillin/β-lact. inh. | 7.9 | Ceftriaxone | 20.2 | Cefazolin | 10.8 | Ceftriaxone | 14.4 | Levofloxacin | 12.8 |
| Ciprofloxacin | 9.6 | Piperacillin/β-lact. inh. | 14.2 | Ciprofloxacin | 10.3 | Piperacillin/β-lact. inh. | 8.4 | Metronidazole | 17.4 | Levofloxacin | 7.4 | Metronidazole | 8.3 | Ceftriaxone | 8.3 | Metronidazole | 9.5 | Piperacillin/β-lact. inh. | 11.8 |
| Amoxicillin/β-lact. inh. | 9.0 | Amoxicillin | 8.1 | Cefazolin | 8.2 | Cefazolin | 7.1 | Ciprofloxacin | 10.3 | Ceftriaxone | 7.3 | Ciprofloxacin | 7.0 | Amoxicillin/β-lact. inh. | 8.1 | Vancomycin | 9.5 | Ceftriaxone | 11.2 |
| Cefotaxime | 8.8 | Metronidazole | 6.0 | Metronidazole | 6.5 | Ciprofloxacin | 7.0 | Cefuroxime | 9.9 | Piperacillin/β-lact. inh. | 7.1 | Cefuroxime | 6.4 | Piperacillin/β-lact. inh. | 7.8 | Cefazolin | 6.1 | Vancomycin | 10.6 |
| Cefazolin | 6.6 | Doxycycline | 5.3 | Amoxicillin/β-lact. inh. | 6.0 | Ceftriaxone | 5.0 | Amoxicillin/β-lact. inh. | 9.6 | Cefazolin | 6.8 | Meropenem | 5.5 | Metronidazole | 7.4 | Ciprofloxacin | 5.9 | Cefazolin | 8.0 |
| Cefuroxime | 4.8 | Ciprofloxacin | 5.2 | Piperacillin/β-lact. inh. | 5.8 | Cefuroxime | 4.4 | Amoxicillin | 5.4 | Sulfa/trimethoprim | 6.1 | Piperacillin/β-lact. inh. | 5.5 | Sulfa/trimethoprim | 5.9 | Sulfa/trimethoprim | 5.4 | Ciprofloxacin | 6.1 |
| Cefoperazone, comb. | 3.4 | Flucloxacillin | 4.7 | Gentamicin | 4.6 | Sulfa/trimethoprim | 3.6 | Clindamycin | 4.3 | Meropenem | 5.7 | Vancomycin | 4.1 | Flucloxacillin | 5.1 | Piperacillin/β-lact. inh. | 5.3 | Metronidazole | 5.5 |
| Metronidazole | 2.5 | Clarithromycin | 4.6 | Levofloxacin | 3.6 | Meropenem | 3.5 | Levofloxacin | 3.1 | Cefuroxime | 5.4 | Cefazolin | 4.1 | Amoxicillin | 4.6 | Meropenem | 4.8 | Meropenem | 5.2 |
| Gentamicin | 2.0 | Gentamicin | 4.2 | Vancomycin | 3.1 | Moxifloxacin | 3.2 | Sulfa/trimethoprim | 2.6 | Metronidazole | 4.2 | Amoxicillin/β-lact. inh. | 3.3 | Doxycycline | 4.6 | Cefotaxime | 4.2 | Azithromycin | 3.3 |
| Levofloxacin | 2.0 | Meropenem | 4.1 | Cefuroxime | 2.9 | Levofloxacin | 3.0 | Azithromycin | 2.2 | Vancomycin | 4.2 | Azithromycin | 3.0 | Cefuroxime | 4.3 | Cefalotin | 2.8 | Cefepime | 3.3 |
| Meropenem | 2.0 | Teicoplanin | 3.5 | Meropenem | 2.7 | Amoxicillin | 2.9 | Ertapenem | 1.6 | Ciprofloxacin | 3.8 | Amoxicillin | 3.0 | Vancomycin | 3.6 | Imipenem & enz. inh. | 2.8 | Sulfa/trimethoprim | 2.9 |
| Amikacin | 1.7 | Cefuroxime | 3.4 | Amoxicillin | 2.5 | Vancomycin | 2.9 | Meropenem | 1.3 | Ampicillin/β-lact. inh. | 3.3 | Imipenem & enz. inh. | 3.0 | Ciprofloxacin | 3.3 | Clindamycin | 2.7 | Doxycycline | 2.1 |
| Cefepime | 1.6 | Trimethoprim | 2.6 | Clindamycin | 2.2 | Metronidazole | 2.6 | Ampicillin | 1.2 | Clindamycin | 2.0 | Cefotaxime | 2.4 | Cefalexin | 3.2 | Amikacin | 2.4 | Clindamycin | 1.7 |
| | | Ceftriaxone | 2.6 | Amikacin | 2.2 | Clindamycin | 2.5 | Gentamicin | 1.0 | Cefmetazole | 1.9 | Gentamicin | 2.1 | Azithromycin | 2.7 | Gentamicin | 2.3 | Cefalexin | 1.5 |
| | | Sulfa/trimethoprim | 2.0 | Sulfa/trimethoprim | 2.0 | Flucloxacillin | 1.9 | Amikacin | 0.9 | Cefepime | 1.7 | Cefepime | 2.0 | Meropenem | 2.6 | Clarithromycin | 2.1 | Amoxicillin/β-lact. inh. | 1.5 |
| | | Benzylpenicillin | 1.8 | Ampicillin | 1.7 | Ceftazidime | 1.5 | | | Cefoperazone, comb. | 1.5 | Colistin | 1.7 | Benzylpenicillin | 1.9 | Colistin | 1.9 | Linezolid | 1.5 |
| | | Vancomycin | 1.5 | Imipenem & enz. inh. | 1.6 | Clarithromycin | 1.4 | | | Clarithromycin | 1.4 | Ampicillin | 1.5 | Roxithromycin | 1.9 | Ampicillin | 1.8 | Amoxicillin | 1.4 |
| | | Clindamycin | 1.2 | Ceftazidime | 1.3 | Temocillin | 1.3 | | | Cefcapene | 1.4 | Sulfa/trimethoprim | 1.4 | Gentamicin | 1.5 | Cloxacillin | 1.8 | | |
| | | Cefalexin | 1.0 | Azithromycin | 1.1 | Azithromycin | 1.3 | | | Teicoplanin | 1.3 | Ampicillin, comb. | 1.4 | Cefaclor | 1.5 | Ceftazidime | 1.6 | | |
| | | | | Cefepime | 1.0 | Cefepime | 1.1 | | | Azithromycin | 1.2 | Moxifloxacin | 1.4 | Clindamycin | 1.4 | Ertapenem | 1.4 | | |
| | | | | Ertapenem | 0.8 | Nitrofurantoin | 1.1 | | | Ampicillin | 1.1 | Amikacin | 1.3 | | | Levofloxacin | 1.2 | | |
| | | | | Clarithromycin | 0.8 | | | | | Ceftazidime | 1.0 | Ceftazidime | 1.0 | | | Azithromycin | 1.0 | | |
| | | | | | | | | | | Amoxicillin | 0.9 | Ceftizoxime | 0.9 | | | | | | |
| | | | | | | | | | | Imipenem & enz. inh. | 0.9 | | | | | | | | |
| | | | | | | | | | | Gentamicin | 0.9 | | | | | | | | |
| | | | | | | | | | | Cefotiam | 0.8 | | | | | | | | |
| | | | | | | | | | | Amikacin | 0.7 | | | | | | | | |
| | | | | | | | | | | Cefditoren | 0.6 | | | | | | | | |
| | | | | | | | | | | Cloxacillin | 0.6 | | | | | | | | |
| | | | | | | | | | | Doxycycline | 0.6 | | | | | | | | |
| | | | | | | | | | | Minocycline | 0.6 | | | | | | | | |

**Table 2. Most Prescribed Antibiotics (ATC J01; 5th level) to adult inpatients by UN Region, ranked at overall drug utilization 90% (DU90%), year 2015.**

**Grey lines provides drug utilization up to 75% (DU75%) by UN Region; C=countries**

**East & Southern Asia includes Southern, Eastern & South-eastern Asia**

| Diagnosis code | Eastern Europe % (n=646 patients) | Northern Europe % (n=2791 patients) | Southern Europe % (n=5452 patients) | Western Europe % (n=8414 patients) | Africa % (n=870 patients) | East & Southern Asia % (n=5402 patients) | Western & Central Asia % (n=1626 patients) | Oceania % (n=967 patients) | Latin America % (n=1554 patients) | Northern America % (n=2139 patients) | Total % (n=29861 patients) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| LRTI | 15.2 | 28.2 | 14.3 | 23.3 | 10.3 | 16.2 | 14.8 | 19.0 | 16.5 | 21.1 | 19.2 |
| Skin & Soft Tissue | 13.5 | 9.1 | 6.7 | 8.0 | 16.2 | 8.2 | 7.9 | 15.6 | 12.5 | 11.6 | 9.0 |
| Intra-abdominal | 1.2 | 8.3 | 5.6 | 7.1 | 3.8 | 7.8 | 5.2 | 9.1 | 10.2 | 7.4 | 7.0 |
| Lower UTI | 0.5 | 6.7 | 4.3 | 8.1 | 2.4 | 3.5 | 4.6 | 8.5 | 5.5 | 11.2 | 6.0 |
| Upper UTI | 4.6 | 5.9 | 4.3 | 4.9 | 1.4 | 4.5 | 5.3 | 3.6 | 6.0 | 4.3 | 4.7 |
| Proph Bone Joint | 7.6 | 2.4 | 6.3 | 4.7 | 6.6 | 4.4 | 3.1 | 6.1 | 4.1 | 3.5 | 4.7 |
| URTI (Bronchitis) | 5.6 | 3.5 | 4.5 | 7.3 | 0.7 | 1.1 | 5.2 | 3.0 | 1.8 | 2.9 | 4.2 |
| Proph Gastro-intestinal | 6.3 | 1.8 | 8.1 | 2.4 | 2.8 | 4.3 | 8.2 | 1.7 | 5.3 | 1.7 | 4.2 |
| Med Proph in general | 2.8 | 2.3 | 5.0 | 2.7 | 2.9 | 5.9 | 1.2 | 5.0 | 3.9 | 3.5 | 3.8 |
| Unknown | 0.8 | 3.5 | 2.7 | 2.9 | 11.4 | 3.0 | 2.0 | 1.9 | 1.7 | 4.0 | 3.1 |
| Proph Obstetrics/Gyn. | 3.9 | 2.5 | 4.4 | 0.9 | 9.8 | 4.4 | 3.8 | 1.3 | 2.9 | 2.6 | 3.0 |
| Bone Joint infection | 3.4 | 2.2 | 1.6 | 3.5 | 3.0 | 2.4 | 3.3 | 3.7 | 2.6 | 3.4 | 2.8 |
| Sepsis | 0.2 | 3.9 | 2.1 | 2.3 | 3.8 | 2.8 | 4.5 | 0.7 | 2.6 | 3.8 | 2.7 |
| Proph UTI | 5.3 | 2.0 | 3.4 | 2.8 | 1.7 | 1.5 | 4.5 | 2.6 | 2.8 | 1.3 | 2.6 |
| Gastro-intestinal | 4.8 | 1.5 | 2.3 | 2.3 | 2.4 | 2.3 | 4.4 | 1.4 | 1.7 | 2.9 | 2.4 |

**Table 3. Top 10 most recorded reasons to treat adult inpatients with at least one antibacterial for systemic use (ATC J01), year 2015.**

**Patients recorded with more than one diagnoses will be counted according to the number of diagnosis,**

**Patients not treated by antibacterials for systemic use (J01), but treated with other antimicrobials (eg antimalarials) are not included in this table.**

East & Southern Asia includes **Southern, Eastern & South-eastern Asia**

LRTI= Pneumonia or LRTI (lower respiratory tract infections); Skin & Soft Tissue: Cellulitis, wound including surgical site infection, deep soft tissue not involving bone e.g., infected pressure or diabetic ulcer, abscess; Intra-abdominal= Intra-abdominal sepsis including hepatobiliary, intra-abdominal abscess *etc*.; Lower UTI= Lower urinary tract infection, cystitis; Upper UTI=upper urinary tract infection including catheter related urinary tract infection, pyelonephritis; Proph Bone Joint=Prophylaxis for SST, for plastic or orthopaedic surgery (Bone or Joint); URTI (bronchitis)= Acute Bronchitis or exacerbations of chronic bronchitis; Proph Gastro-intestinal= Surgery of the Gastro-Intestinal tract, liver or biliary tree, GI prophylaxis in neutropaenic patients or hepatic failure , Med Proph in general=Drug is used as Medical Prophylaxis in general, without targeting a specific site; Unknown=Completely Unknown Indication; Proph Obstretrics/Gyn.= Prophylaxis for Obstetric or Gynaecological surgery; Bone joint Infection: Septic arthritis (including prosthetic joint), osteomyelitis, Sepsis= sepsis, sepsis syndrome or septic shock with no clear anatomic site, Proph UTI= Prophylaxis for urological surgery (SP) or recurrent Urinary Tract Infection (MP); Gastro-intestinal = Gastro intestinal infections (salmonellosis, *Campylobacter*, parasitic, *C.difficile*, etc.).

| | | Therapeutic use | | | | Prophylactic use | |
|---|---|---|---|---|---|---|---|
| | | Therapeutic use | | | | Antibiotics for Medical Prophylaxis (%) | Antibiotics for Surgical Prophylaxis (%) |
| | Total N antibiotics (J01) | Antibiotics for a CAI % | Targeted prescribing for a CAI % | Antibiotics for a HAI % | Targeted prescribing for a HAI % | | |
| Eastern Europe | 708 | 46.5 | 12.2 | 11.6 | 34.1 | 23.7 | 17.5 |
| Northern Europe | 3536 | 56.3 | 14.1 | 25.1 | 20.4 | 5.8 | 9.5 |
| Southern Europe | 6837 | 36.7 | 16.6 | 20.6 | 41.3 | 8.2 | 29.2 |
| Western Europe | 9485 | 51.0 | 27.1 | 28.3 | 43.4 | 5.9 | 12.0 |
| Africa | 1213 | 57.4 | 19.5 | 9.5 | 33.9 | 3.5 | 23.2 |
| East & Southern Asia | 6781 | 36.9 | 22.2 | 27.7 | 31.7 | 9.8 | 21.3 |
| Western & Central Asia | 2084 | 44.8 | 13.4 | 20.9 | 36.8 | 7.7 | 23.2 |
| Oceania | 1226 | 53.3 | 23.1 | 23.6 | 38.4 | 7.6 | 12.6 |
| Latin America | 2170 | 41.4 | 19.1 | 34.9 | 44.1 | 5.6 | 16.0 |
| Northern America | 2752 | 52.2 | 22.8 | 26.1 | 31.2 | 5.1 | 8.6 |
| **Total** | **36792** | **45.6** | **20.9** | **25.2** | **36.9** | **7.4** | **17.8** |

**Table 4. Antibiotic use (ATC J01) by indication and type of treatment (targeted versus empiric) for adult inpatients by region, year 2015.**

**CAI= Community Acquired Infection; HAI=Hospital Acquired Infection.**

**Overall, 486 antibiotics were recorded with 'another' indication; 1009 antibiotics with unknown indication; these are not listed in the table.**

East & Southern Asia includes **Southern, Eastern & South-eastern Asia**

| | Denominators | | | | | Antimicrobial/Antibiotic quality indicators | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| REGION | N treated patients | N antimicrobial prescriptions | N antibiotic (J01) prescriptions | N patients with targeted treatment | N patients with targeted treatment against resistant organisms | Targeted treatment§ % patients | % patients treated with ABs targeting resistant organisms | Reason in notes* % | Stop/review date documented* % | Parenteral RoA° % patients | % antibiotic prescriptions for which guidelines were available°° | % antibiotic prescriptions compliant to local guidelines+ | % of antibiotic prescriptions for which no guidelines were available++ |
| Eastern Europe | 653 | 747 | 708 | 51 | 42 | 7.8 | 6.4 | 64.3 | 50.5 | 87.6 | 79.8 | 85.7 | 19.2 |
| Northern Europe | 2783 | 3880 | 3536 | 396 | 80 | 14.2 | 2.9 | 81.4 | 51.6 | 62.2 | 90.0 | 83.4 | 6.5 |
| Southern Europe | 5534 | 7674 | 6837 | 838 | 292 | 15.1 | 5.3 | 69.5 | 29.1 | 80.0 | 60.5 | 70.8 | 29.6 |
| Western Europe | 8458 | 10612 | 9485 | 2204 | 469 | 26.1 | 5.5 | 80.5 | 40.3 | 64.0 | 81.0 | 78.7 | 10.1 |
| Africa | 899 | 1502 | 1213 | 131 | 25 | 14.6 | 2.8 | 70.4 | 36.6 | 62.7 | 49.5 | 67.9 | 26.7 |
| East & Southern Asia | 5363 | 7607 | 6781 | 938 | 287 | 17.5 | 5.4 | 74.6 | 43.5 | 71.8 | 76.4 | 81.5 | 21.4 |
| Western & Central Asia | 1612 | 2252 | 2084 | 236 | 153 | 14.6 | 9.5 | 72.8 | 19.8 | 85.2 | 53.4 | 66.3 | 40.5 |
| Oceania | 932 | 1411 | 1226 | 218 | 63 | 23.4 | 6.8 | 85.1 | 27.0 | 60.5 | 87.4 | 73.2 | 11.7 |
| Latin America | 1518 | 2403 | 2170 | 403 | 231 | 26.5 | 15.2 | 81.4 | 40.3 | 84.4 | 76.5 | 64.1 | 19.9 |
| Northern America | 2139 | 3125 | 2752 | 511 | 127 | 23.9 | 5.9 | 84.9 | 39.6 | 73.1 | 77.3 | 85.8 | 18.5 |
| **Grand Total** | **29891** | **41213** | **36792** | **5926** | **1769** | **19.8** | **5.9** | **76.9** | **38.3** | **71.4** | **74.3** | **77.4** | **19.2** |

**Table 5. Overview of antimicrobial/antibiotic quality indicators for adult inpatients by region, year 2015.**

§ % patients receiving at least one antibiotic for systemic use (ATC J01), selection has been made for therapeutic antibiotic use only (HAI and CAI). Calculation= N patients with targeted treatment/N treated patients.

* Including all antimicrobials. Denominator=N antimicrobial prescriptions

° % patients receiving at least one parenteral antibiotic for systemic use (ATC J01). Denominator=N treated patients

°° % prescriptions for which guidelines were available refers to the antibiotic choice (not route, dose, duration) and is calculated as compliance to guidelines Yes and No/ compliance with local guidelines Yes and No + those for which no local guidelines for the specific indication were available (not applicable) + those not indicated (NI) where information is lacking because the indication is unknown

+ Denominator used is “all antibiotic (J01) prescriptions for which guidelines were available”

++ Denominator used are all antibiotic (J01) prescriptions

ABs=antibiotics for systemic use (ATC J01)

East & Southern Asia includes Southern, Eastern & South-eastern Asia

| | **N patients received a targeted treatment*** | N patients with targeted treatment against resistant organisms | **% pat MRSA** | **% pat MRCoNS** | **% pat VRE** | **% pat ESBL** | **% pat 3rd gen cep** | **% pat CRE** | **% pat ESBL non fermenter** | **% pat CR non fermenter** | **% pat other MDRO** |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Eastern Europe | **53** | 42 | 7.5 | 1.9 | | 37.7 | 5.7 | | 15.1 | 20.8 | 3.8 |
| Northern Europe | **435** | 80 | 5.3 | 0.7 | 1.6 | 6.0 | 0.9 | 0.2 | 0.2 | 1.8 | 2.3 |
| Southern Europe | **1021** | 292 | 5.0 | 2.2 | 2.9 | 8.4 | 1.5 | 2.1 | 2.8 | 3.6 | 4.9 |
| Western Europe | **2472** | 469 | 3.4 | 1.8 | 0.2 | 7.1 | 3.0 | 0.4 | 0.5 | 0.6 | 2.8 |
| Africa | **170** | 25 | 1.2 | 0.6 | | 5.3 | 0.6 | | 1.8 | 2.4 | 2.9 |
| East & Southern Asia | **1070** | 287 | 6.2 | 2.8 | 0.9 | 6.5 | 3.6 | 2.1 | 1.7 | 3.6 | 2.4 |
| Western Central Asia | **266** | 153 | 9.8 | 1.1 | 0.8 | 13.9 | 3.8 | 3.0 | 6.8 | 7.5 | 15.0 |
| Oceania | **227** | 63 | 4.8 | 1.8 | 1.8 | 6.6 | 2.6 | 0.4 | 11.5 | 1.8 | 0.9 |
| Latin America | **450** | 231 | 10.4 | 4.9 | 1.3 | 19.1 | 4.4 | 4.0 | 2.4 | 1.1 | 4.4 |
| Northern America | **586** | 127 | 7.8 | 2.0 | 1.4 | 4.3 | 2.9 | | 1.4 | 5.1 | 3.1 |
| **Total** | **6750** | **1769** | **5.3** | **2.1** | **1.1** | **8.1** | **2.8** | **1.2** | **2.0** | **2.6** | **3.6** |

**Table 6. Prevalence rate of adult inpatients (%) receiving a targeted antibiotic (ATC J01) treatment by region and resistance profile of the organism, year 2015.**

* denominator = number of patients receiving a targeted treatment

Targeted treatment = based upon microbiological result. Microbiology result can be any culture and/or sensitivity result from a relevant clinical (e.g., blood, sputum, etc.,) [but not screening] specimen as well as any other microbiology result like for example Legionella Urinary Antigen.

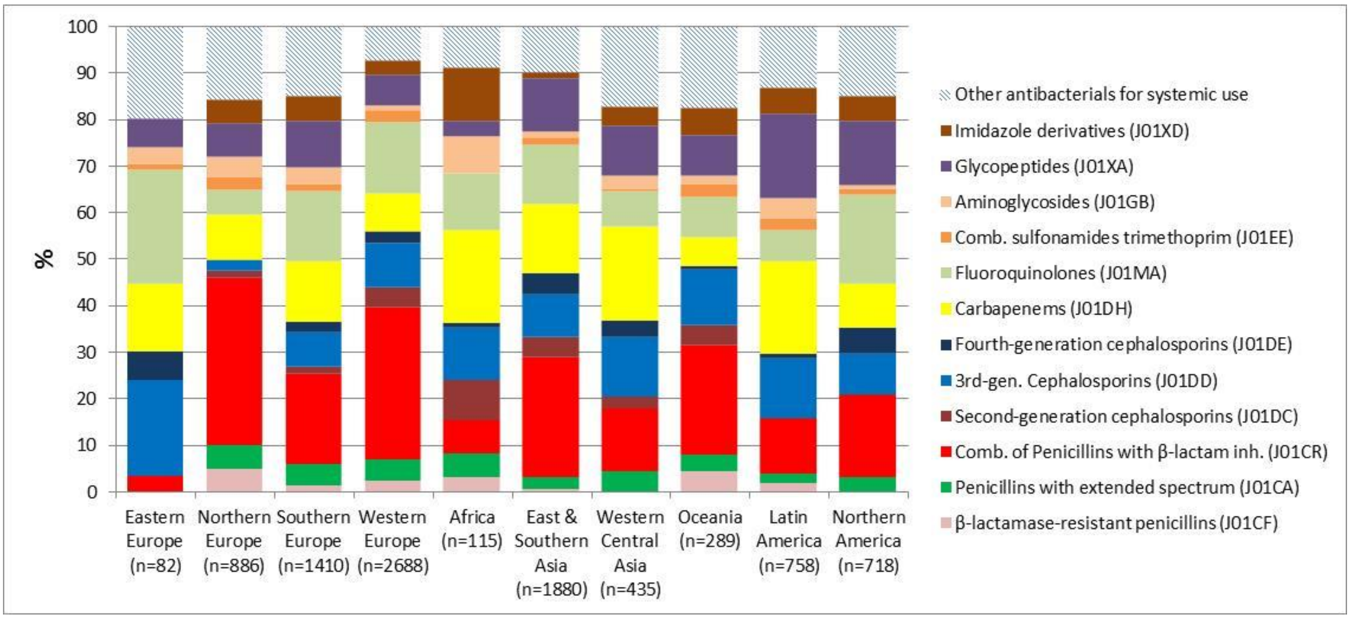
If the treatment was based on microbiology data, participants could report whether the treatment choice was based on one of the following 9 micro-organisms:

MRSA=meticillin-resistant *Staphylococcus aureus*, MRCoNS=meticillin-resistant coagulase-negative staphylococci, VRE=vancomycin-resistant enterococci, ESBL=Enterobacteriaceae producing extended-spectrum beta-lactamase, $3^{rd}$ gen cep=$3^{rd}$ generation cephalosporin resistant Enterobacteriaceae non-ESBL producing or ESBL status unknown, CRE=carbapenem-resistant Enterobacteriaceae, ESBL non-fermenter= ESBL-producing non-fermenter Gram-negative bacilli, CR non-fermenter=carbapenem-resistant non-fermenter Gram-negative bacilli, Other MDRO=other multi-drug resistant organisms

Note: a patient can be counted twice depending on the number of targeted antibiotics administered for more than one resistant micro-organism.

East & Southern Asia includes Southern, Eastern & South-eastern Asia

**Figure 1. Proportion of prescribed antibiotics for systemic use (ATC4 level, N=9,261) for a HAI among adult inpatients by region, year 2015**

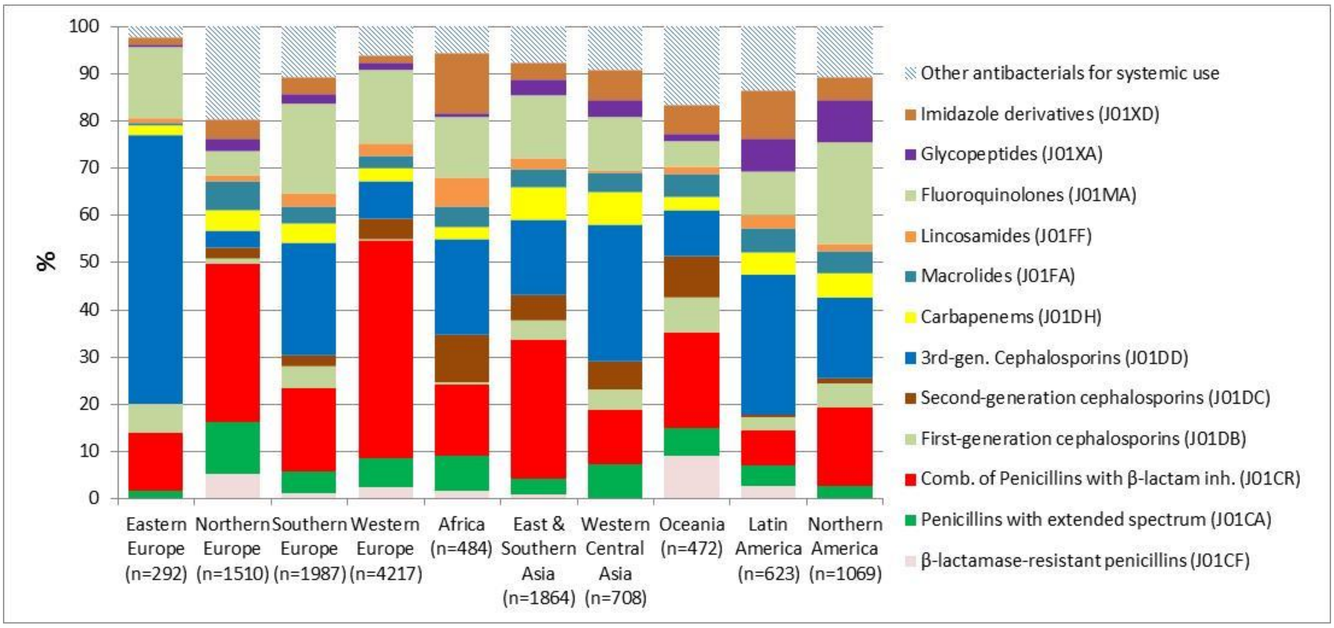



Not colored striped part of stacked bar represents other antibacterial subgroups

N=number of reported antibiotics for systemic use at regional level

East & Southern Asia includes Southern, Eastern & South-eastern Asia

**Figure 2. Proportion of prescribed antibiotics for systemic use (ATC4 level, N=13,226) for a CAI among adult inpatients by region, year 2015**




Not colored striped part of stacked bar represents other antibacterial subgroups

N=number of reported antibiotics for systemic use at regional level

East & Southern Asia includes Southern, Eastern & South-eastern Asia

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