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

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Summary

Background The Global Point Prevalence Survey (Global-PPS) established an international network of hospitals to measure antimicrobial prescribing and resistance worldwide. We aimed to assess antimicrobial prescribing and resistance in hospital inpatients.

Methods We used a standardised surveillance method to collect detailed data about antimicrobial prescribing and resistance from hospitals worldwide, which were grouped by UN region. The internet-based survey included all inpatients (adults, children, and neonates) receiving an antimicrobial who were on the ward at 0800 h on one specific day between January and September, 2015. Hospitals were classified as primary, secondary, tertiary (including infectious diseases hospitals), and paediatric hospitals. Five main ward types were defined: medical wards, surgical wards, intensive-care units, haematology oncology wards, and medical transplantation (bone marrow or solid transplants) wards. Data recorded included patient characteristics, antimicrobials received, diagnosis, therapeutic indication according to predefined lists, and markers of prescribing quality (eg, whether a stop or review date were recorded, and whether local prescribing guidelines existed and were adhered to). We report findings for adult inpatients.

Findings The Global-PPS for 2015 included adult data from 303 hospitals in 53 countries, including eight lower-middle-income and 17 upper-middle-income countries. 86 776 inpatients were admitted to 3315 adult wards, of whom 29 891 (34·4%) received at least one antimicrobial. 41 213 antimicrobial prescriptions were issued, of which 36 792 (89·3%) were antibacterial agents for systemic use. The top three antibiotics prescribed worldwide were penicillins with β-lactamase inhibitors, third-generation cephalosporins, and fluoroquinolones. Carbapenems were most frequently prescribed in Latin America and west and central Asia. Of patients who received at least one antimicrobial, 5926 (19·8%) received a targeted antibacterial treatment for systemic use, and 1769 (5·9%) received a treatment targeting at least one multidrug-resistant organism. The frequency of health-care-associated infections was highest in Latin America (1518 [11·9%]) and east and south Asia (5363 [10·1%]). Overall, the reason for treatment was recorded in 31 694 (76·9%) of antimicrobial prescriptions, and a stop or review date in 15 778 (38·3%). Local antibiotic guidelines were missing for 7050 (19·2%) of the 36 792 antibiotic prescriptions, and guideline compliance was 77·4%.

Interpretation The Global-PPS showed that worldwide surveillance can be accomplished with voluntary participation. It provided quantifiable measures to assess and compare the quantity and quality of antibiotic prescribing and resistance in hospital patients worldwide. These data will help to improve the quality of antibiotic prescribing through education and practice changes, particularly in low-income and middle-income countries that have no tools to monitor antibiotic prescribing in hospitals.

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Introduction

The paucity of information and data about the quantity and quality of antimicrobial prescribing is a key barrier to the successful development and implementation of antimicrobial stewardship programmes internationally.[1] Surveillance systems to monitor antimicrobial use and resistance are needed to improve decision making and assess the effect of interventions.[2,3] Furthermore, auditing of, and feedback on, prescribing practices complements and improves[4] other core stewardship interventions (eg, empirical therapy according to guidelines).[5,6]

The Global Point Prevalence Survey (Global-PPS) of Antimicrobial Consumption and Resistance was developed after the fourth World Healthcare-Associated Infections and Antimicrobial Resistance Forum. Its aim was to assess the international prevalence of antimicrobial use and resistance, with an emphasis on countries with low resources, support, and expertise.[7] The project built

Research in context

Evidence before this study

We did not do a systematic search of published work to establish the usefulness of the Global Point Prevalence Survey. Surveillance systems monitoring antimicrobial use and resistance are the cornerstones of successful implementation of sustainable antimicrobial stewardship programmes. They improve decision making and enable assessment of the effects of interventions. A point prevalence survey is a well established method that is applicable and beneficial in European hospitals and beyond.

Added value of this study

In the Global Point Prevalence Survey, we assessed the prevalence of antimicrobial use and resistance worldwide. The study protocol was easy to follow, and we provided a simple tool for data entry and immediate feedback, enabling direct benchmarking with other hospitals and wards by country and region. Hospitals in low-income and middle-income countries could for the first time measure and compare antimicrobial use patterns at a local and regional level. The Global Point Prevalence Survey allowed sharing of best practice, raised awareness of inappropriate antimicrobial prescribing, and provided tangible, quantifiable quality indicators to improve antibiotic prescribing at hospital level.

Implications of all the available evidence

The Global Point Prevalence Survey complements WHO's Global Antimicrobial Surveillance System (which provides a standardised approach for collection, analysis, and sharing of data for antimicrobial resistance) by providing a validated method for measuring the quality of antimicrobial prescribing and the effect of interventions to improve prescribing. Governments can use this tool to support antimicrobial stewardship frameworks as part of their WHO National Action Plans, and the UN's Interagency Coordination Group on Antimicrobial Resistance could use it for international mapping of antimicrobial prescribing and resistance in hospitals, and to build a sustainable hospital surveillance framework with a focus on low-income and middle-income countries.

on the findings of three point prevalence surveys done by the European Surveillance of Antimicrobial Consumption Network between 2006 and 2009.[8,9] Several studies[9–12] of the applicability and benefits of point prevalence surveys of antimicrobial use showed their value in a range of European hospitals. Additionally, the European Surveillance of Antimicrobial Consumption Network's methods were adapted for the European Centre for Disease Prevention and Control point prevalence survey of health-care-associated infections and antimicrobial use in acute care hospitals,[13] and for the Antibiotic Resistance and Prescribing in European Children project, which focused on antimicrobials administered to paediatric and neonatal patients worldwide.[14–17]

In this Article, we report the first Global-PPS, which was done in 2015, with a focus on antibiotic prescribing practices for patients admitted to adult hospital wards (ie, adult inpatients), to establish the variation in quantity and quality of antibacterial prescribing and resistance across continents.

Methods

Study design and setting

We did a cross-sectional audit of antimicrobial prescribing practices and resistance at hospitals around the world. All hospitals admitting inpatients worldwide were welcome to join the Global-PPS, which was promoted through existing European Surveillance of Antimicrobial Consumption and Antibiotic Resistance and Prescribing in European Children hospital networks and at the 2014 European Congress of Clinical Microbiology and Infectious Diseases, with help from bioMérieux subsidiaries and members of the Hospital-Acquired Infection/Antimicrobial Resistance Forum.[7]

For more on the **European Congress of Clinical Microbiology and Infectious Diseases** see http://2014.eccmid.org/

The Global-PPS was piloted in 33 hospitals worldwide from Oct 1, 2014, to Nov 30, 2014. Several key amendments were made to the study after this pilot, including software improvements (no protocol amendments were made), before the full Global-PPS was done between Jan 1, 2015, and Sept 30, 2015. Data from hospitals that successfully participated in the pilot study were included in the final data analysis.

Hospitals in participating countries were grouped by UN region (ie, Africa, Americas, Asia, Europe, and Oceania),[18] which were broken into subregions depending on the number of hospitals participating. The Americas region was divided into Latin America and the Caribbean (hereafter called Latin America because of an absence of data for the Caribbean) and North America. Asia was divided into two groups: east and south Asia (which includes south, east, and southeast Asia), and west and central Asia. Europe was divided into four subregions: eastern Europe, northern Europe, southern Europe, and western Europe.[18] Hospitals were classified as primary, secondary, tertiary (including infectious diseases hospitals), and paediatric hospitals, as previously defined by the European Centre for Disease Prevention and Control.[19] Overall, five main ward types were defined for adult and paediatric wards: medical wards, surgical wards, intensive-care units, haematology oncology wards, and medical transplantation (bone marrow or solid transplants) wards. For adult wards, we also included pneumology medical wards, whereas for children, neonatal intensive-care units and neonatal medical wards were included.

All study data were completely anonymised, and no unique identifiers were recorded. Furthermore, the survey did not require direct contact with patients. Thus,

patient consent was not required. Each patient record was given a unique but non-identifiable survey number, which was automatically generated. The need for ethics approval for this study varied by country, and was taken care of by participating hospitals on an individual basis if required. A data privacy excerpt document was available for this purpose.

Data collection

Hospital-based doctors, pharmacists, and nurses were responsible for completing the Global-PPS. They were asked to do a 1-day survey, during which all wards had to be audited once. All inpatients who were on the ward at 0800 h were included. Total ward inclusion at the hospital level was requested but not mandatory (appendix). Data collection was done with two forms, one for ward-level data (ie, recording of denominators, such as the total number of inpatients on the ward) and one for patient-level data (recording of numerators; appendix). For each patient receiving at least one antimicrobial, we gathered data about patient characteristics, the antimicrobials received, their diagnosis, and the therapeutic indication according to predefined lists (appendix). Two major categories—treatment and prophylaxis—were used, each of which consisted of two main types of indication. The former category comprised therapeutic antimicrobial prescribing for both community-acquired and health-care-associated infections (infections that become symptomatic 48 h after hospital admission). The latter category included antimicrobial prescribing for both surgical and medical prophylaxis. For patients receiving surgical prophylaxis, administration had to be checked in the previous 24 h to encode the duration of prophylaxis as either one dose, one day (ie, multiple doses given in one day), or more than one day.

Additional indicators of antimicrobial-prescribing quality were documentation of the diagnosis in the patient's notes at the start of treatment, the choice of antibiotic being compliant with local guidelines, and documentation of a stop or review date for the antimicrobial in the notes. Additionally, empirical or targeted treatment (ie, based on microbiology data from a relevant clinical specimen, such as blood or sputum, excluding screening tests) was recorded. When treatment choice was made on the basis of available microbiology data, we recorded whether it targeted one of nine multidrug-resistant organisms (appendix). Finally, we recorded whether biomarker data (eg, C-reactive protein, procalcitonin, any other biomarker) were used to support prescribing decisions.

Antimicrobials included antibiotics for systemic use, antimycotics and antifungals for systemic use, drugs to treat tuberculosis, oral antibiotics prescribed as intestinal anti-infectives (eg, oral vancomycin), nitroimidazole derivatives, neuraminidase inhibitors, and antimalarials. All antimicrobials were automatically classified online according to the standardised and internationally recognised WHO anatomical therapeutic chemical classification system (2014 version).[20] No discussion or personal judgment on the appropriateness of antibiotic prescribing was allowed during the survey.

All data were inputted into the freely available Global-PPS program, an internet-based application for anonymised data entry, validation, and reporting. A helpdesk and several supplementary documents, such as a frequently asked questions list, were freely available to support the participants. The British Society for Antimicrobial Chemotherapy also developed an e-learning course. Data validation included several built-in checks with error and warning messages that had to be managed by the user to generate a real-time feedback report. As a check on the completeness of data, participants had to record whether the whole hospital was surveyed. The software was also designed to prevent missing and erroneous data entry, such as inconsistencies between the indication and the diagnosis (eg, an antibiotic given for prophylactic use but prescribed for sepsis), extremely high total daily doses, and double entry of the same drug (appendix). Additionally, all hospitals with an overall antibiotic prescription prevalence higher than 70% were individually contacted to confirm the prevalence. All data were completely anonymised within the database and safeguarded at the University of Antwerp (Antwerp, Belgium). However, all data remained the property of the hospital.

For the **e-learning course** see http://www.futurelearn.com/courses/point-prevalence-surveys

See **Online** for appendix

Data analysis

We focus on prescribing of antibiotics for systemic use, which we report as the number of treated patients, the number of therapies, and the number of prescriptions. Therapy was defined as one treatment (ie, receiving at least one antibiotic) per diagnosis. A prescription was defined as the use of one substance by one route of administration. Antimicrobial prescribing rates were expressed as a percentage of patients on antimicrobials, or as a percentage of all antibiotic or antimicrobial prescriptions (proportional use). Means and ranges were aggregated at UN regional level,[18] by ward type and indication. We ranked the number of antibiotics accounting for 90% and 75% of drug use. Antibiotic resistance patterns were expressed as the proportion of patients receiving at least one antibiotic targeting at least one resistant micro-organism of all patients for whom an antimicrobial result (ie, targeted treatment) was available.

Role of the funding source

The study funder had no role in the study design or data collection, analysis, or interpretation. IC, M-FG, and MM are employees of the funder, and had roles in the writing of the report. The corresponding author had access to all study data and had final responsibility for the decision to submit for publication.

	Countries (n)	Hospitals (n)	Medical wards		Surgical wards		Intensive-care units		Haematology oncology wards		Pneumology wards		Transplant (bone marrow or solid transplants)		Total	
			Admitted (n)	Anti-microbial use (%)	Admitted (n)	Anti-microbial use (%)	Admitted (n)	Anti-microbial use (%)	Admitted (n)	Antimicrobial use (%)	Admitted (n)	Anti-microbial use (%)	Admitted (n)	Anti-microbial use (%)	Admitted (n)	Antimicrobial use (%, country range)
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)
East and south 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)
West and 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)
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)
North 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)

A version of this table containing numerical data for all percentages is in the appendix. Empty cells mean that no cases or too few cases (ie, fewer than 10 admitted or treated inpatients) were recorded (these cases are included in the totals).
*Includes south, east, and southeast Asia.

Table 1: **Antimicrobial use in adult hospital inpatients, by UN region, 2015**

Results

335 hospitals in 53 countries (including eight lower-middle-income and 17 upper-middle-income countries) were included in the Global-PPS (appendix). 18 hospitals had successfully participated in the pilot study. For this analysis, we excluded data from 32 hospitals: 22 paediatric hospitals (4091 patients), three hospitals that did not provide data for adult wards, and seven with denominator issues with ward-level data. Thus, 303 hospitals were eligible for inclusion in the final analysis.

The adult 2015 Global-PPS dataset included 45 primary care hospitals (5805 patients [6·7%]), 129 secondary care hospitals (31790 patients [36·6%]), 107 tertiary care hospitals (44873 patients [51·7%]), and 22 infectious diseases or specialised hospitals (4308 patients [5·0%]; appendix). The number of beds in participating hospitals ranged from 16 to 2387 beds (median 266 [IQR 131–459]). We collected data for 86776 patients admitted to 3315 adult wards. Overall, 15564 (52·1%) of the 29861 patients treated on adult wards were male (ranging from 44·8% in North America to 58·5% in eastern Europe).

41213 antimicrobial prescriptions were issued. Antibacterials for systemic use accounted for 36792 (89·3%) prescriptions, antimycotics and antifungals for systemic use for 1724 (4·2%) prescriptions, drugs to treat tuberculosis for 1053 (2·6%) prescriptions, nitroimidazole derivatives for 835 (2·0%) prescriptions, antibiotics prescribed as intestinal anti-infectives for 692 (1·7%) prescriptions, and neuraminidase inhibitors for 117 (0·3%) prescriptions. Antimicrobial use varied between continents (from 27·4% in eastern Europe to 50·0% in Africa) and by ward type (from 29·0% in medical wards to 77·0% in transplant wards; table 1).

36792 antibacterials for systemic use were used in patients admitted to adult wards on the day of the survey, including 139 different agents (appendix). 31 antibacterials accounted for 90% of drug use in east and south Asia, compared with 15 in Africa and 13 in eastern Europe. The combination of penicillins with a β-lactamase inhibitor was the most commonly prescribed class, mainly amoxicillin with β-lactamase inhibitors (11·4%) and piperacillin with β-lactamase inhibitors (7·7%) (appendix). The second and third most commonly prescribed antibiotics were third-generation cephalosporins (mainly ceftriaxone) and fluoroquinolones (mainly ciprofloxacin and levofloxacin; appendix).

The top five indications for antibiotic prescription—pneumonia or lower respiratory tract infections, skin and soft tissue infections, intra-abdominal infections, lower urinary tract infections, and upper urinary tract infections—accounted for 13703 (45·9%) treated patients (table 2). Pneumonia was overall the most common indication, accounting for 5722 (19·2%) of treated patients worldwide (table 2). Overall, 16781 (45·6%) antibiotics were prescribed for community-acquired infections (table 3). Targeted prescribing was more

	Eastern Europe (n=646)	Northern Europe (n=2791)	Southern Europe (n=5452)	Western Europe (n=8414)	Africa (n=870)	East and south Asia* (n=5402)	West and central Asia (n=1626)	Oceania (n=967)	Latin America (n=1554)	North America (n=2139)	Total (n=29 861)
Pneumonia or lower respiratory tract infection	15·2%	28·2%	14·3%	23·3%	10·3%	16·2%	14·8%	19·0%	16·5%	21·1%	19·2%
Skin and soft tissue infections†	13·5%	9·1%	6·7%	8·0%	16·2%	8·2%	7·9%	15·6%	12·5%	11·6%	9·0%
Intra-abdominal infections‡	1·2%	8·3%	5·6%	7·1%	3·8%	7·8%	5·2%	9·1%	10·2%	7·4%	7·0%
Lower urinary tract infections (cystitis)	0·5%	6·7%	4·3%	8·1%	2·4%	3·5%	4·6%	8·5%	5·5%	11·2%	6·0%
Upper urinary tract infections§	4·6%	5·9%	4·3%	4·9%	1·4%	4·5%	5·3%	3·6%	6·0%	4·3%	4·7%
Prophylaxis for bone and joint infections¶	7·6%	2·4%	6·3%	4·7%	6·6%	4·4%	3·1%	6·1%	4·1%	3·5%	4·7%
Upper respiratory tract infection (acute bronchitis or chronic exacerbations)	5·6%	3·5%	4·5%	7·3%	0·7%	1·1%	5·2%	3·0%	1·8%	2·9%	4·2%
Prophylaxis for gastrointestinal infections‖	6·3%	1·8%	8·1%	2·4%	2·8%	4·3%	8·2%	1·7%	5·3%	1·7%	4·2%
General prophylaxis	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%
Prophylaxis for obstetric or gynaecological infections (surgery)	3·9%	2·5%	4·4%	0·9%	9·8%	4·4%	3·8%	1·3%	2·9%	2·6%	3·0%
Bone or joint infections**	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%
Prophylaxis for urinary tract infections (surgery or recurrent infections)	5·3%	2·0%	3·4%	2·8%	1·7%	1·5%	4·5%	2·6%	2·8%	1·3%	2·6%
Gastrointestinal infections	4·8%	1·5%	2·3%	2·3%	2·4%	2·3%	4·4%	1·4%	1·7%	2·9%	2·4%

Patients recorded with more than one diagnosis were counted by number of diagnoses. Patients not treated with antibiotics for systemic use, but who were treated with other antimicrobials (eg, antimalarials) were not included. A version of this table containing numerical data for all percentages is in the appendix. *Includes south, east, and southeast Asia. †Includes cellulitis, wound infections (including surgical site infections), deep soft tissue infections not involving bone (eg, infected pressure or diabetic ulcers, abscesses). ‡Includes intra-abdominal sepsis and hepatobiliary and intra-abdominal abscesses. §Includes catheter-related urinary tract infections and pyelonephritis. ¶Includes prophylaxis for skin and soft-tissue infections, and for plastic or orthopaedic surgery. ‖Includes prophylaxis for surgery of the gastrointestinal tract, liver, or biliary tree, and prophylaxis in patients with neutropenia or hepatic failure. **Includes septic arthritis (including prosthetic joints) and osteomyelitis. ††Includes sepsis syndrome or septic shock with no clear anatomical site.

Table 2: **Most common reasons to treat adult inpatients with at least one antibiotic for systemic use, 2015**

	Total antibiotic prescriptions	Therapeutic use				Prophylactic use	
		Community-acquired infection	Community-acquired infection (targeted prescribing)	Health-care-associated infection	Health-care-associated infection (targeted prescribing)	Medical	Surgical
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 and south Asia*	6781	36·9%	22·2%	27·7%	31·7%	9·8%	21·3%
West and 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%
North America	2752	52·2%	22·8%	26·1%	31·2%	5·1%	8·6%
Total	36 792	45·6%	20·9%	25·2%	36·9%	7·4%	17·8%

Data are n or %. Overall, 486 antibiotic prescriptions were recorded for another indication, and 1009 had an unknown indication; these antibiotics are not listed in the table. A version of this table containing numerical data for all percentages is in the appendix. *Includes south, east, and southeast Asia.

Table 3: **Antibiotic use by indication and type of treatment (ie, targeted *vs* empirical) for adult inpatients in 2015, by region**

common for health-care-associated infections (36·9%) than for community-acquired infection (20·9%; table 3).

Overall 7278 (8·4%) of 86 776 adult inpatients were treated with antibacterials for systemic use for at least one health-care-associated infection. 66 (2·8%) of patients in eastern Europe, 1064 (7·5%) in southern Europe, 2322 (7·7%) in western Europe, 321 (8·7%) in western and central Asia, 714 (8·8%) in northern Europe, 225 (8·9%) in Oceania, 533 (9·6%) in North America, 1457 (10·1%) in east and south Asia, and 489 (11·9%) in

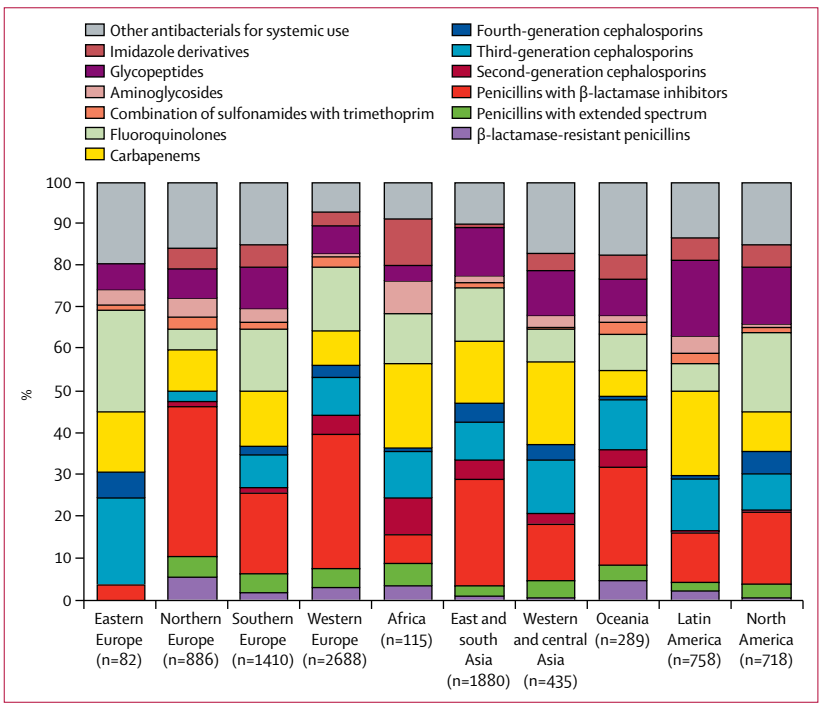

Figure 1: **Proportion of prescribed antibiotics for systemic use for health-care-associated infections among adult inpatients, 2015 (n=9261)**
East and south Asia includes south, east, and southeast Asia.

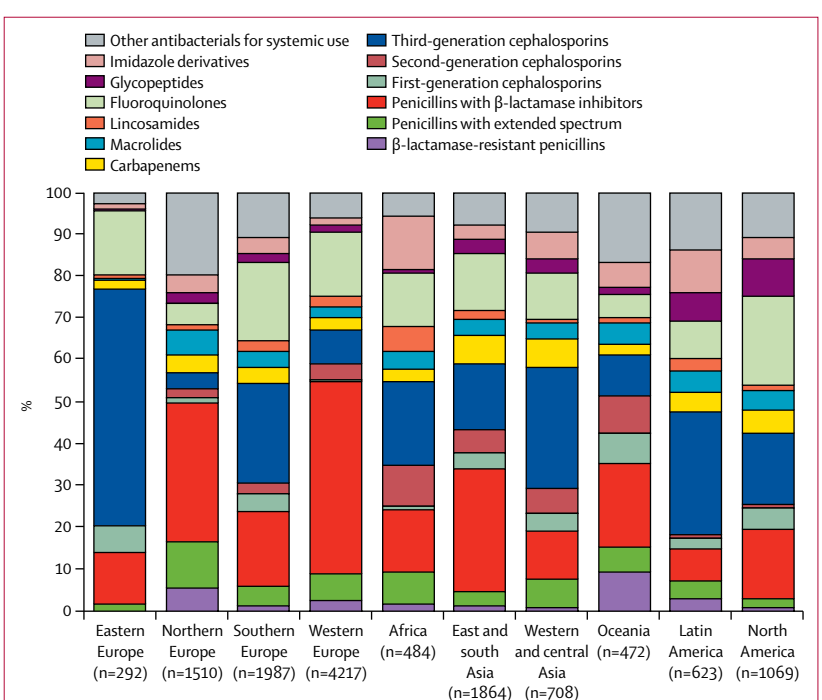

Figure 2: **Proportion of prescribed antibiotics for systemic use for community-acquired infections among adult inpatients, 2015 (n=13 226)**
East and south Asia includes south, east, and southeast Asia.

Latin America were treated with such antibacterials. The most frequently reported indications (appendix) were non-intervention-related or other health-care-associated infections (3667 [4·2%] patients), followed by post-operative surgical site infections (1382 [1·6%] patients).

The most prescribed antibiotics for health-care associated infections were penicillins with a β-lactamase inhibitor (24·8%), of which piperacillin with a β-lactamase inhibitor accounted for 14·6% and amoxicillin and a β-lactamase inhibitor for 8·9% (figure 1). Fluoroquinolones were the second most prescribed (12·8%), followed by carbapenems (mainly meropenem; 12·2%) and glycopeptides (mainly vancomycin; figure 1). The most commonly prescribed antibiotics for community-acquired infections were penicillins with a β-lactamase inhibitor (29·2%), of which amoxicillin with a β-lactamase inhibitor accounted for 16·3% and piperacillin with a β-lactamase inhibitor accounted for 7·7% (figure 2). Third-generation cephalosporins were the second most commonly prescribed (mainly ceftriaxone; 15·5%) antibiotics for community-acquired infections, followed by fluoroquinolones (14·0%; figure 2).

7546 (26·3%) adult patients receiving antibiotics, ranging from 419 (15·6%) in northern Europe to 282 (43·9%) in eastern Europe, were given at least one antibiotic for prophylaxis. The overall mean prevalence for surgical prophylaxis was 17·8% (table 3). Cefazolin was the most commonly prescribed antibiotic for surgical prophylaxis (accounting for 1801 [27·5%] of the 6538 prescriptions), with the highest prescribing rates noted in Oceania (prescribed to 100 [64·5%] of the 155 patients who were prescribed surgical prophylaxis), North America (148 [62·4%] of 237 patients), and western Europe (655 [57·7%] of 1136 patients). Ceftriaxone was the most commonly prescribed antibiotic for surgical prophylaxis in eastern Europe (49 [39·5%] of 124 patients), southern Europe (559 [28·0%] of 1995 patients), and Africa (78 [27·7%] of 282 patients). Prolonged surgical prophylaxis (ie, >1 day) was very common in all regions (range 40·6% in Oceania to 86·3% in eastern Europe; appendix). Overall, mean prevalence of medical prophylaxis was 7·4% (2717 of the 36729 antibiotics prescribed; table 3). Many different antibiotics were used for medical prophylaxis, but sulfamethoxazole–trimethoprim was the most commonly prescribed worldwide, and accounted for 63·4% (59 of 93 patients) of all medical prophylactic prescribing in Oceania and 56·0% (371 of 663 patients) in east and south Asia. Ceftriaxone was the most commonly prescribed in eastern Europe (91 [54·2%] of 168 patients), southern Europe (95 [16·9%] of 561 patients), and west and central Asia (27 [16·9%] of 160 patients).

The stop or review date for antibiotic treatment was poorly documented overall (38·3% of antimicrobial prescriptions; table 4). Of 29 891 treated patients, 5926 (19·8%) received at least one targeted antibacterial treatment for systemic use, and 1769 (5·9%) received a treatment targeting at least one multidrug-resistant

	Antimicrobial prescriptions	Antibiotic prescriptions	Targeted treatment*	Targeted treatment (resistant organisms)*	Reason recorded†	Stop or review date recorded†	Parenteral administration‡	Guidelines available§	Compliant to local guidelines¶	No guidelines available‖
Eastern Europe (n=653)	747	708	51 (7·8%)	42 (6·4%)	64·3%	50·5%	87·6%	79·8%	85·7%	19·2%
Northern Europe (n=2783)	3880	3536	396 (14·2%)	80 (2·9%)	81·4%	51·6%	62·2%	90·0%	83·4%	6·5%
Southern Europe (n=5534)	7674	6837	838 (15·1%)	292 (5·3%)	69·5%	29·1%	80·0%	60·5%	70·8%	29·6%
Western Europe (n=8458)	10612	9485	2204 (26·1%)	469 (5·5%)	80·5%	40·3%	64·0%	81·0%	78·7%	10·1%
Africa (n=899)	1502	1213	131 (14·6%)	25 (2·8%)	70·4%	36·6%	62·7%	49·5%	67·9%	26·7%
East and south Asia** (n=5363)	7607	6781	938 (17·5%)	287 (5·4%)	74·6%	43·5%	71·8%	76·4%	81·5%	21·4%
West and central Asia (n=1612)	2252	2084	236 (14·6%)	153 (9·5%)	72·8%	19·8%	85·2%	53·4%	66·3%	40·5%
Oceania (n=932)	1411	1226	218 (23·4%)	63 (6·8%)	85·1%	27·0%	60·5%	87·4%	73·2%	11·7%
Latin America (n=1518)	2403	2170	403 (26·5%)	231 (15·2%)	81·4%	40·3%	84·4%	76·5%	64·1%	19·9%
North America (n=2139)	3125	2752	511 (23·9%)	127 (5·9%)	84·9%	39·6%	73·1%	77·3%	85·8%	18·5%
Total (n=29 891)	41 213	36 792	5926 (19·8%)	1769 (5·9%)	76·9%	38·3%	71·4%	74·3%	77·4%	19·2%

Data are n or %. A version of this table containing numerical data for all percentages is in the appendix. *Patients receiving at least one antibiotic for systemic therapeutic use only (ie, health-care-associated or community-acquired infection). †Includes all antimicrobials; the total number of antimicrobial prescriptions was used to calculate percentages. ‡Patients who received at least one parenteral antibiotic for systemic use. §Antibiotic prescriptions for which guidelines were available to guide antibiotic choice (not route, dose, or duration), which was calculated as all antibiotic prescription for which a local guideline was available/all antibiotic prescription. ¶The number of antibiotic prescriptions for which guidelines were available was used as the denominator to calculate percentages. ||The total number of antibiotic prescriptions was used as the denominator to calculate percentages. **Includes south, east, and southeast Asia.

Table 4: **Overview of antimicrobial and antibiotic quality indicators for adult inpatients by region, year 2015**

organism (table 4). Overall, 58·3% of these patients received antibiotics targeting Gram-negative bacteria, with the highest proportional numbers noted in eastern Europe (appendix). Only in North America did a higher proportion of patients receive targeted treatment against Gram-positive bacteria than against Gram-negative bacteria. Table 5 shows the prevalence of patients receiving targeted treatment against resistant bacteria.

Discussion

We showed the feasibility of doing the Global-PPS, which focused on antibiotic prescribing and resistance, with a simple and affordable method on an international scale. Many hospitals assessed antibiotic prescribing patterns and collected information about antibiotic resistance in their hospital for the first time. These data are essential for development of antimicrobial stewardship programmes. Other point prevalence surveys have been done successfully in high-income countries in the European Union and the USA,[21,22] but our simple Global-PPS tool also allowed for the participation of many hospitals in low-income and middle-income countries.

We identified substantial differences in the prevalence of antibiotic prescribing between and within regions or countries, with the highest prevalence in Africa (50·0%; country range 27·8–74·7) and the lowest in eastern Europe (27·4%; 23·7–27·8). The overall prevalence for Europe (31·9%; 23·7–62·0) was similar to the weighted prevalence of previous point prevalence surveys in Europe in 2011–12 (32·6%; range 21·4 [France]–54·7 [Greece]),[21] but lower than that in a survey done in 183 US hospitals in 2011 (49·9% [95% CI 49·0–50·9).[22] Combinations of penicillins with a β-lactamase inhibitor were the most frequently prescribed antibiotic class in this survey, largely because of high prescribing rates in northern and western Europe (and particularly in Belgian hospitals; appendix). Third-generation cephalosporins, mainly ceftriaxone, were the next most commonly prescribed, with a high frequency of prescription in Asia, Latin America, and southern and eastern Europe for both community-acquired and health-care-associated infections. The frequent use of ceftriaxone in these regions suggests that at least a proportion of this prescribing could be inappropriate.

Fluoroquinolones were the third most commonly prescribed antibiotics, because of frequent use of levofloxacin in hospitals in North America and east and south Asia (mainly for pneumonia in both cases) and of ciprofloxacin in western Europe (mainly for cystitis) and elsewhere in Europe (for various indications). Striking differences in levofloxacin use were noted in the Americas (12·8% in North America *vs* 1·2% in Latin America) and Asia (7·4% in east and south Asia *vs* 0·9% in west and central Asia; appendix). Differences in cost of, or access to, fluoroquinolones could preclude their use in some countries. These differences in prescribing patterns could also be due to marketing strategies or differing antibiotic regulations. A remarkably high frequency of vancomycin use was noted in North American and Latin American hospitals (appendix). This high vancomycin use can be explained by the high prevalence of meticillin-resistant *Staphylococcus aureus* (MRSA) infection reported in Latin American hospitals,[23] which is in line with the high proportion of patients who received

	MRSA	MRCoNS	VRE	ESBL	Third-generation cephalosporin-resistant Enterobacteriaceae*	Carbapenem-resistant Enterobacteriaceae	ESBL-producing non-fermenting Gram-negative bacilli	Carbapenem-resistant non-fermenting Gram-negative bacilli	Other multidrug-resistant organisms
Eastern Europe (n=53)	7·5%	1·9%	..	37·7%	5·7%	..	15·1%	20·8%	3·8%
Northern Europe (n=435)	5·3%	0·7%	1·6%	6·0%	0·9%	0·2%	0·2%	1·8%	2·3%
Southern Europe (n=1021)	5·0%	2·2%%	2·9%	8·4%	1·5%	2·1%	2·8%	3·6%	4·9%
Western Europe (n=2472)	3·4%	1·8%	0·2%	7·1%	3·0%	0·4%	0·5%	0·6%	2·8%
Africa (n=170)	1·2%	0·6%	..	5·3%	0·6%	..	1·8%	2·4%	2·9%
East and south Asia (n=1070)†	6·2%	2·8%	0·9%	6·5%	3·6%	2·1%	1·7%	3·6%	2·4%
West and central Asia (n=266)	9·8%	1·1%	0·8%	13·9%	3·8%	3·0%	6·8%	7·5%	15·0%
Oceania (n=227)	4·8%	1·8%	1·8%	6·6%	2·6%	0·4%	11·5%	1·8%	0·9%
Latin America (n=450)	10·4%	4·9%	1·3%	19·1%	4·4%	4·0%	2·4%	1·1%	4·4%
North America (n=586)	7·8%	2·0%	1·4%	4·3%	2·9%	..	1·4%	5·1%	3·1%
Total (n=6750)	5·3%	2·1%	1·1%	8·1%	2·8%	1·2%	2·0%	2·6%	3·6%

Targeted treatment is treatment based on microbiological results—ie, any culture or sensitivity result from a relevant clinical specimen (eg, blood, sputum), excluding screening specimens, or any other microbiology result (eg, *Legionella* urinary antigen). Patients could be counted more than once depending on the number of targeted antibiotics administered for more than one resistant microorganism. A version of this table containing numerical data for all percentages is in the appendix. MRSA=meticillin-resistant *Staphylococcus aureus*. MRCoNS=meticillin-resistant coagulase-negative staphylococci. VRE=vancomycin-resistant enterococci. ESBL=Extended-spectrum β-lactamases. *Non-ESBL producing, or ESBL status unknown. †Includes south, east, and southeast Asia.

Table 5: **Prevalence of resistant organisms in adult inpatients who received targeted antibiotics in 2015, by region**

targeted treatment against MRSA infections in our survey (table 5). Carbapenems (mainly meropenem) were widely prescribed in Latin America and Asia, probably because of the high frequency of infections caused by extended-spectrum β-lactamase-producing Gram-negative bacteria (table 4), which has been reported in previous surveillance studies.[24–26]

The most frequent indication for antibiotic therapy worldwide was pneumonia, followed by urinary tract infections. More in-depth analyses are needed to establish the proportion of health-care-associated urinary tract infections caused by extended-spectrum β-lactamase-producing organisms. We noted a high proportion of prophylaxis for a range of indications, but unusually high prophylactic prescribing for gastrointestinal infections in west and central Asia. Further research is warranted to explain the reasons for this pattern.

To identify inappropriate antibiotic prescribing, we investigated five indicators of quality, which could easily be used to set benchmarks for quality improvement of antibiotic use in hospitals.[11] Documentation of the reason for prescription ensures communication of diagnosis and treatment among clinicians and other health-care providers, and allows for recording of prescription stop or review dates and other interventions such as de-escalation. In northern and western Europe, the Americas, and Oceania, findings for this indicator were similar to those in the 2009 European Surveillance of Antimicrobial Consumption point prevalence survey among European adults (80%).[9] Frequency of documentation of the reason for the prescription was less common in hospitals in eastern (64%) and southern (70%) Europe, Africa (70%), and Asia (73%; table 3).

The second indicator, formal review of the appropriateness of an antimicrobial administered within 48 h of the initial order (post-prescription review),[27] 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 can reduce selection pressure, and prevent adverse effects such as drug-related toxicity and damage to the normal intestinal bacterial flora leading to *Clostridium difficile* infection. A stop or review date was recorded for less than a third of antimicrobials prescribed in southern Europe, west and central Asia, and Oceania (table 3). This review process should be targeted as a key intervention, and the effects of such intervention should be measured with repeated point prevalence surveys.[11]

Parenteral administration, the third quality indicator, was most common in west and central Asia, Latin America, and eastern and southern Europe, where it accounted for more than 80% of patients on antibiotics. Broad-spectrum antibiotics are commonly administered in these regions (such as third-generation cephalosporins), and broad-spectrum oral antibiotics are scarce. The switch from intravenous to oral antibiotics has many advantages, including reductions in catheter-related complications, health-care costs, and duration of hospital stays, and is recognised as a key metric for stewardship processes in hospitals.[27,28] However, to what extent different administration routes affect antimicrobial resistance is not known.[29]

The fourth quality indicator referred to the existence of, and adherence to, antibiotic treatment guidelines. In west and central Asia, local guidelines were not available

for 40·5% of antibiotic prescriptions, especially for medical prophylaxis in the absence of a clear diagnosis (tables 2, 3). In one African country, 11% of patients were treated with antibiotics for an unknown diagnosis, contrary to guidelines for low-income and middle-income countries that state "an appropriate treatment must be preceded by diagnoses that ensures the correct clinical path".[30] Correct diagnosis and treatment planning necessitate the existence of a clinical microbiology laboratory and antimicrobial stewardship involvement—eg, daily laboratory rounds.[31] Guideline compliance referred only to the choice of drug for therapeutic or prophylactic use. Overall mean compliance to guidelines was 77·4%, but compliance was less than 70% in Latin America, west and central Asia, and Africa. Next to developing and updating local treatment guidelines, adherence to guidelines could improve clinical outcomes—eg, mortality, treatment duration, and length of hospital stay.[32] A systematic review and meta-analysis[6] showed that guideline-adherent empirical therapy was associated with a significant relative risk reduction for mortality of 35%. The reason for poor compliance with guidelines is uncertain and probably multifactorial. Local resistance patterns, clinical uncertainty, and fear of treatment failure could all have roles. Our data will enable further detailed investigation at a country and hospital level.

The fifth quality indicator concerned prolonged surgical prophylaxis, which was common in our survey (particularly in southern [85%] and eastern [86·3%] Europe) and in previous studies done in Europe.[21] Antibiotic prophylaxis for more than 24 h for most surgical indications does not prevent development of postoperative infections compared with surgical prophylaxis for 24 h or less, but increases the risk of antimicrobial resistance and side-effects.[33] In the absence of preoperative infection or severe complications, prolonged postoperative antibiotic prophylaxis is unnecessary.[34]

The strengths of our study include the uniformity of data collection, the simplicity of the protocol and data collection templates, data completeness and validation via the internet-based tool, and the opportunity for real-time educational feedback of results to participating centres (including comparisons with national and regional results).[10] Although we had to rely on 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 survey with help from the online supporting materials (eg, frequently asked questions), helpdesk support, and the e-learning course. The simple protocol and tool for data entry and feedback allowed for inclusion of hospitals from lower-middle-income (n=8) and upper-middle-income countries (n=17; appendix).

The study, which was done on a voluntary basis with few resources (in terms of finance, IT, and workforce), provided a good utility value for the required time commitment. It also encouraged clinical prescriber buy-in, particularly because the data accrued were 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 worldwide awareness about antibiotic use and resistance, but also helps participants to set targets to improve antibiotic prescribing, thereby driving improved prescribing behaviour.[11]

The limitations of this study are inherent to the epidemiological methods of our cross-sectional survey, in which the main purpose was to describe prescribing patterns in hospitals.[14] The overall rates provided are averages. We did not control for patient case mix, disease incidence, prevalence of different types of infections, variations in resistance levels, institutional factors, or differences in climates and seasons, among other factors, all of which can influence antibiotic use patterns. Thus, we urge caution in interpretation of the reported prevalences. Although we noted substantial differences in the prevalence of antibiotic prescribing between and within regions or countries, our data are not representative for most of these countries and regions. For instance, northern Europe was mainly presented by the UK, and data for western Europe included most Belgian hospitals because of coordination by the Belgian Antibiotic Policy Coordination Committee at federal level.[36] Western European results might therefore be biased by typical Belgian prescribing practices (eg, the high use of amoxicillin with a β-lactamase inhibitor). We hope that in future surveys, countries could participate with a representative number of hospitals, which would allow more meaningful analysis at country and regional level.

The Global-PPS was repeated in 2017, with increased participation. We focused again on low-income and middle-income countries because our survey tool is the only means available for measurement of antibiotic prescribing in hospitals in these countries, which often have the highest prevalence of antibiotic prescribing and resistance. We aim to do repeated point prevalence surveys at hospital or ward level (yearly or quarterly) to measure the effect of antimicrobial stewardship interventions. Governments can use the Global-PPS tool to support the antimicrobial stewardship framework as part of their WHO National Action Plan. In some countries (eg, Belgium, the Philippines, Saudi Arabia), the Global-PPS was endorsed by their ministries of health, which invited hospitals to participate in the 2017 edition. The UN Interagency Coordination Group on Antimicrobial Resistance could use the Global-PPS tool to map international antimicrobial prescribing and resistance in hospitals and to build a sustainable hospital surveillance framework, with a focus on low-income and middle-income countries. The Global-PPS could complement WHO's Global Antimicrobial Resistance

For an **assessment of the time commitment in the Global-PPS** see http://www.global-pps.com/documents

Surveillance System (GLASS).[3] Ultimately, we aim to develop appropriate benchmarking standards, including quantifiable quality targets, but recognise the substantial pitfalls associated with use of these quantitative data for benchmarking.[37] We are also developing an educational framework and training programme for health-care professionals working on hospital antimicrobial stewardship in low-income and middle-income countries.

Contributors

AV, PZ, VJ, DN, and HG conceived and designed this work. AV managed, analysed, and interpreted the data, which were also interpreted by PZ and HG. AV drafted the Article, which was critically revised by all authors for important intellectual content. All authors approved the final version.

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IC, M-FG, and MM are employees of bioMérieux, the study funder. All other authors declare no competing interests.

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