

Point prevalence survey of antibiotic use in French hospitals in 2009

J. Robert^{1*}, Y. Péan², E. Varon³, J.-P. Bru⁴, J.-P. Bedos⁵, X. Bertrand⁶, A. Lepape⁷, J.-P. Stahl⁸ and R. Gauzit⁹ on behalf of the Société de pathologie infectieuse de langue française (SPILF), the Observatoire national de l'épidémiologie de la résistance bactérienne aux antibiotiques (ONERBA) and the Surveillance de la prescription des antibiotiques (SPA) Group†

¹Bacteriology-Hygiene, Université Pierre et Marie Curie, Pitié-Salpêtrière Hospital APHP, Paris, France; ²Microbiology, L'Institut Mutualiste Montsouris, Paris, France; ³Microbiology, Hôpital Européen Georges Pompidou, APHP, Paris, France; ⁴Infectious Diseases Department, CH de la Région d'Annecy, Pringy, France; ⁵Intensive Care Unit, CH Henri Mignot de Versailles, Le Chesnay, France; ⁶Hygiene, CHU de Besançon, Besançon, France; ⁷Intensive Care Unit, CHU Lyon-Sud, Pierre-Bénite, France; ⁸Infectious Diseases Department, CHU la Tronche, Grenoble, France; ⁹Intensive Care Unit, Hôtel-Dieu de Paris, APHP, Paris, France

*Corresponding author. Tel: +33-1-40-77-97-49; Fax: +33-1-45-82-75-77; E-mail: jerome.robert@psl.aphp.fr
†Members of the SPA Group are listed in the Acknowledgements section.

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Objectives: To evaluate the feasibility of a point prevalence survey for monitoring antibiotic use in a voluntary sample of French hospitals.

Methods: Demographic and medical data were collected for all inpatients. Additional characteristics regarding antimicrobial treatment, type of infection and microbiological results were collected only for patients receiving antimicrobials.

Results: Among 3964 patients in 38 hospitals, 343 (8.7%) received antimicrobial prophylaxis and 1276 (32.2%) antimicrobial therapy. The duration of surgical antimicrobial prophylaxis was >1 day in 41 out of 200 (21%) of the cases. Among patients with antimicrobial therapy, 959 (75.2%) received β -lactams (including 34.8% penicillins with β -lactam inhibitors, 22.1% third-generation cephalosporins and 7.8% carbapenems) and 301 (23.6%) received fluoroquinolones (50% orally). A total of 518 (40.6%) patients were treated with more than one drug and 345 (27.2%) were treated for >7 days. Patients treated for hospital-acquired infections (39.2%) were more likely to receive combinations (47.6% versus 34.4%, $P < 0.01$), carbapenems (14.4% versus 2.6%, $P < 0.01$), glycopeptides (14.4% versus 3.7%, $P < 0.01$) and antifungals (17% versus 5.3%, $P < 0.01$) for a longer duration (7.8 versus 6 days, $P < 0.01$). Fifty-six patients (4.4%) were treated for >7 days and did not have any microbiological sample drawn. The time allocated for the survey represented 18.3–25.0 h for 100 patients.

Conclusions: The data provide directions for further interventions, such as better use of diagnostic tools, decreasing the treatment duration and the use of combinations. In addition, the survey shows that, although cumbersome, it is feasible to improve the representativeness of national data in European surveys.

Keywords: antifungals, antibiotic usage, surveillance, prophylaxis, treatment

Introduction

Antibiotic resistance is increasingly prevalent in the hospital and community settings throughout the world. It is a major threat to patients, as it results in increased morbidity and mortality.¹ Moreover, very few new antibiotics have become available within the last three decades to interfere with such an alarming trend. Therefore, there is an urgent need to preserve the currently available drugs. The misuse of antibiotics, e.g. excessive and inappropriate antibiotic use, has been shown to be a major cause of the emergence of antibiotic-resistant bacteria.^{2–4}

Hence, reducing unnecessary antibiotic use is a public health priority and has been recently taken into account by the European Union Council.⁵

The central tenet in policies for the improvement of antimicrobial use tends to be the development of guidelines aimed at helping prescribers. However, it is likely that it will be necessary to develop multifaceted programmes to integrate prudent antibiotic use in the day-to-day behaviour of healthcare professionals. Antibiotic consumption surveys or assessment of the quality of antibiotic use with feedback to prescribers are components of such programmes.

The evaluation of antibiotic use can be done at the population level (macroeconomics) or at the patient level. Population-level surveys are numerous and often multicentric.^{6–9} Such studies are of interest to increase the awareness of the quantity of drug used and the delivered message is usually to prescribe less. Because it has been demonstrated that the level of bacterial resistance is related to the amount of antibiotic use, this message is necessary.^{3,4,10} In contrast, patient-based surveys are scarce,^{11,12} and the European Centre for Disease Prevention and Control (ECDC) has recently developed protocols to guide point prevalence studies (http://ecdc.europa.eu/en/activities/surveillance/HAI/about_HAI-Net/Pages/PPS.aspx?MasterPage=1). Such studies seek to evaluate the appropriateness, i.e. 'quality', of antibiotic use.

The aim of this nationwide point prevalence survey was to evaluate antibiotic use at the patient level. The study was designed to be a first step toward a larger survey including a higher proportion of French hospitals. It is therefore designed to be used for benchmarking and to increase the representativeness and external validity of data in international surveys. We targeted the European Antibiotic Awareness Day, which takes place each year on 18 November and is a European initiative coordinated by the ECDC, as the day for this first French point prevalence survey.

Methods

Study design

French hospitals ($n=420$) collaborating with the French observatory of epidemiology of bacterial resistance to antibiotics (ONERBA; www.onerba.org) were asked to participate, on a voluntary basis, in a 1 day prevalence survey (18 November 2009) by e-mailing the standardized study questionnaire. The questionnaire was partially adapted from European Surveillance of Antimicrobial Consumption (ESAC)¹¹ and French Health Agency questionnaires,¹³ and was administered by local physicians or pharmacists.

Data collection

Hospitals had the choice to include data from a single ward through to data for all inpatients present in the hospital on the day of the survey. No further direction on the selection of wards, if any, was given in the protocol. As opposed to formerly proposed questionnaires,^{11,13} we collected data for all inpatients, including those without antimicrobials, regarding basic demographic data, the presence of medical devices (bladder catheter, central venous catheter or endotracheal intubation), immunosuppression and prior surgery in the last month or in the last year in the case of prosthesis. In addition, risk factors for infection or colonization with multidrug-resistant (MDR) bacteria were systematically collected: prior antimicrobial treatment, previous hospital admission during the last 3 months, previously known carriage of MDR bacteria, late-onset hospital-acquired infections (HAIs) (i.e. >5 days after admission), admission from a long-term care facility (>3 months of hospitalization) and an outbreak of MDR bacteria within the ward or hospital.

Antimicrobials were grouped according to the Anatomical Therapeutic Chemical (ATC) classification (www.whocc.no/atc_ddd_index).

Medical or surgical antimicrobial prophylaxis was recorded as well as prophylaxis duration.

For inpatients receiving at least one dose of antimicrobial on the day of the survey, additional data were collected regarding antimicrobial therapy, including treatment duration from treatment start to the day of

survey. Site(s) of infection(s), community or nosocomial onset, device-related infection and microbiological results available on the date of survey were collected for the two most important infections, as considered by the physician in charge. Methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci, extended-spectrum β -lactamase-producing Enterobacteriaceae (ESBL-E), imipenem-resistant Enterobacteriaceae, and ceftazidime- and imipenem-resistant *Pseudomonas aeruginosa* or *Acinetobacter baumannii* were considered as MDR bacteria.

Statistical analysis

Continuous variables are expressed as the median and range, and were compared by using the Kruskal–Wallis test. Categorical variables are expressed as proportions and the χ^2 test or Fisher's exact test was used, as appropriate, for comparisons. Statistical significance was defined as $P<0.05$.

Results

Hospitals and patients

A total of 38 hospitals (18 teaching and 20 non-teaching hospitals), located in 11 of the 22 administrative regions of metropolitan France, participated in the survey. The number of wards included by hospitals varied from a single ward to all wards and from 15 to 393 patients, accounting for a total of 3964 patients. The patients' characteristics are summarized in Table 1. Most of the patients were hospitalized in medicine and surgery (39.5% and 29.5%, respectively). A total of 1276 (32.2%) patients received antimicrobial therapy, 343 (8.7%) received only antimicrobial prophylaxis (143 had medical and 200 surgical antimicrobial prophylaxis, respectively) and 2345 (59.1%) did not have any antimicrobial treatment on the date of survey. In univariate analysis, patients with antimicrobial therapy were more likely to be hospitalized in intensive care units (ICUs), and to have a longer stay in hospital before the survey (9 versus 5 days, $P<0.01$), indwelling devices, immunosuppression and previous history of antimicrobial treatment (Table 1). There was no difference regarding the median age of the patients in both groups.

Antimicrobial prophylaxis

Among the 143 patients with medical prophylaxis, 11 (7.7%) received two drugs. The most frequently used antibiotics were co-trimoxazole ($n=62$, 43.4%) and penicillin ($n=23$, 16.1%).

Among the 200 patients with surgical prophylaxis, 175 (87.5%) received a single drug, 16 (8%) two drugs and the number of drugs was unknown for the 9 (4.5%) remaining patients. The most frequently used antibiotics were first-generation ($n=86$, 43%) or second-generation ($n=52$, 26%) cephalosporins and penicillins combined with β -lactam inhibitors ($n=20$, 10%). Of interest, 41 (21%) of the patients received surgical prophylaxis for >1 day and 68% of the latter originated from 3 of the 27 hospitals reporting patients with surgical prophylaxis.

Drug use overview

Among the 1276 patients with antimicrobial treatment, 75.2% received β -lactams. Compared with medicine, the proportion of β -lactams was higher in ICUs (84.8%, $P<0.01$) and

Table 1. Characteristics of the patients included in the survey

Variable	Antimicrobial therapy				P value (univariate analysis)
	no (n=2688)		yes (n=1276)		
	n	%	n	%	
Wards					
medicine	997	37.1	567	44.4	<0.01
oncology/haematology	218	8.1	149	11.7	<0.01
surgery	951	35.3	219	17.2	<0.01
ICU	200	7.5	289	22.6	<0.01
others (rehabilitation/long-term care)	322	12.0	52	4.1	<0.01
Male sex	1377	53.1	514	41.6	<0.01
Immunosuppression	680	25.3	434	34.0	<0.01
Invasive procedures					
central venous catheter	367	13.6	440	34.5	<0.01
bladder catheter	382	14.2	412	32.3	<0.01
endotracheal intubation	137	5.1	205	16.1	<0.01
surgery in the previous 30 days	524	19.5	290	22.7	0.02
prosthetic devices in the year	109	4.1	49	3.8	0.80
Antibiotics in the previous 3 months	693	25.8	603	47.3	<0.01
Long-term care facilities	179	6.7	88	6.9	0.79
Hospitalization in the last 3 months	789	29.4	534	41.9	<0.01
Prior carriage of MDR bacteria	74	2.8	99	7.8	<0.01
Late-onset infection (>5 days after admission)	69	2.6	214	16.8	<0.01

onco-haematology (79.2%, $P=0.07$; Table 2). The proportion of antipseudomonal penicillins with β -lactam inhibitors was significantly higher than the median in haematology (33.3%, $P=0.01$), and lower in medicine (6.0%, $P=0.01$) and surgery (11.0%, $P=0.01$), while the proportion of carbapenems was higher than the median in ICUs (18.7%, $P<0.01$) and onco-haematology (13.4%, $P=0.01$). Overall, 50.2% of patients prescribed fluoroquinolones received them orally, and this proportion was highest in medicine (60.8%) and surgery (70.3%), and lowest in haematology (32.1%) and ICUs (13.3%, $P<0.01$). Among all ICU patients, the median proportions (25th and 75th percentiles) of patients treated with antipseudomonal penicillins+inhibitors, carbapenems and fluoroquinolones were 9.1% (5.6%–17.8%), 8.3% (0%–12.5%) and 11.1% (6.3%–16.7%), respectively. The respective figures for haematology wards were 12.5% (5.6%–20.0%), 7.1% (0%–9.1%) and 10.0% (0%–18.2%). The median use of antifungals in the latter wards was 12.5% (5.9% and 16.0%, respectively).

The overall proportion of patients treated with more than one drug was 40.6% (Table 2). Combinations including β -lactams, fluoroquinolones or aminoglycosides represented 88.4%, 36.5% and 18.7% of all combinations, respectively.

The median duration of antimicrobial therapy at the day of survey was 4 days (IQR: 2–8 days) and 27.2% of the patients were treated for >7 days. Patients treated with carbapenems were more likely to receive antimicrobials for >7 days (45.7%) than other patients (25.2%, $P<0.01$). Among patients with aminoglycosides, 21.4% were treated for >3 days. Of interest, patients treated with more than one drug ($n=507$) were more

likely to be treated for >7 days (31.8%) than patients treated with one drug (23.3%, $P<0.01$).

HAI versus community-acquired infections (CAIs)

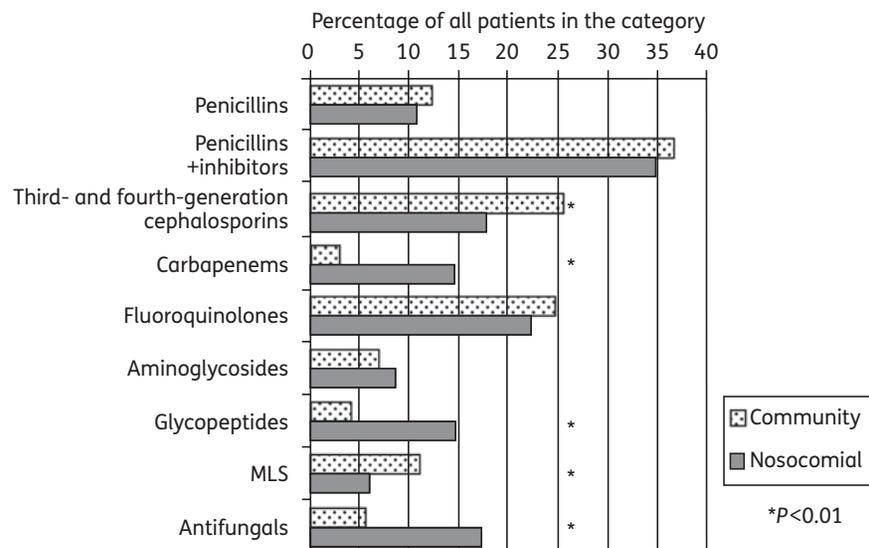
Overall, 50.5% of the patients were treated for CAI and 39.2% for HAI. The origin of infection was not reported for the remaining 10.3% of patients. The proportion of patients treated for CAI was highest in medical wards (71.3%), and lowest in ICUs (30.8%), rehabilitation and long-term care wards (8.5%) and onco-haematology (37.6%). Compared with patients with CAI, patients with HAI were more likely to receive two or more drugs (47.6% versus 34.4%, $P<0.01$), carbapenems (14.4% versus 2.6%, $P<0.01$), glycopeptides (14.4% versus 3.7%, $P<0.01$) and antifungals (17.0% versus 5.3%, $P<0.01$), and receive them for a longer duration (mean, 7.8 versus 6.0 days, $P<0.01$) (Figure 1). The proportion of patients with >7 days of treatment at the date of survey was 20.9% for patients treated for CAI and 32.4% for HAI ($P<0.01$). Among all 345 patients treated for >7 days, 16.0% had endocarditis or osteo-articular infections among those with CAI and 3.2% among those with HAI. Other patients treated for >7 days had mainly pneumonia ($n=108$, 31.3%), digestive tract ($n=36$, 10.4%) or urinary tract infections ($n=34$, 9.9%) and, overall, 45 (13.0%) had MDR bacteria. Patients with HAI were not significantly more likely to receive aminoglycosides (8.4% versus 6.8%, $P=0.37$) or fluoroquinolones (21.8% versus 24.3%, $P=0.32$). In contrast, patients with CAI were more likely than those with HAI to receive third- and fourth-generation cephalosporins (25.3% versus 17.6%,

Table 2. Number and proportion of patients receiving each type of antimicrobial among all patients receiving antimicrobial treatment by type of ward (patients may receive more than one antimicrobial)

Antimicrobials (ATC code)	Medicine (n=567)		Oncology (n=32)		Haematology (n=117)		Surgery (n=219)		Intensive care (n=289)		Rehabilitation and long-term care (n=47)		Total (n=1276)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Penicillins (J01CA, CE)	69	12.3	1	3.1	1	0.9	13	5.9	24	8.3	3	6.4	111	8.7
Penicillins A+inhibitors (J01CR01, 02)	143	25.2	9	28.1	17	14.5	62	28.3	42	14.5	12	25.5	286	22.4
Antipseudomonal penicillins+inhibitors (J01CR03, 05)	34	6.0	2	6.3	39	33.3	24	11.0	61	21.1	0	0	161	12.6
Penicillins M (J01CF)	15	2.7	1	3.1	1	0.9	7	3.2	11	3.8	0	0	37	2.9
Third- and fourth-generation cephalosporins (J01DD, DE)	138	24.4	5	15.6	23	19.6	41	18.7	58	20.1	16	34.0	282	22.1
Carbapenems (J01DH)	17	3.0	0	0	20	17.1	8	3.7	54	18.7	0	0	99	7.8
Fluoroquinolones (J01MA)	133	23.5	8	25.0	28	23.9	66	30.1	61	21.1	4	8.5	301	23.6
Aminoglycosides (J01GB)	41	7.2	0	0	10	8.6	21	9.6	27	9.3	1	2.1	101	7.9
Glycopeptides (J01XA)	22	3.9	5	15.6	35	29.9	17	7.8	34	11.8	1	2.1	114	8.9
MLS (J01FA, FF, FG)	61	10.8	5	15.6	8	6.8	4	1.8	23	8.0	5	10.6	106	8.3
Co-trimoxazole (J01EE01)	17	3.0	0	0	1	0.9	5	2.3	8	2.8	1	2.1	32	2.5
Imidazole derivatives (J01XD)	35	6.2	1	3.2	5	4.3	19	8.7	10	3.5	4	8.5	74	5.8
Other antibiotics	21	3.7	3	9.4	2	1.7	11	5.0	14	4.8	0	0	51	3.9
Antifungals (J02A)	36	6.4	7	21.9	34	29.1	16	7.3	39	13.5	1	2.1	133	10.4
Treated with ≥ 2 drugs	188	33.2	12	37.5	79	67.5	85	38.8	149	51.6	3	6.4	518	40.6

MLS, macrolides, lincosamides and streptogramins.

The ward of hospitalization was not reported for five patients.

**Figure 1.** Distribution of antimicrobial use by place of acquisition of infection. MLS, macrolides, lincosamides and streptogramins.

$P < 0.01$) and macrolides, lincosamides and streptogramins (11.0% versus 5.6%, $P < 0.01$). Patients with HAI were slightly more likely to receive intravenous fluoroquinolones than the other patients (55.1% versus 44.7%), although the difference was not statistically significant ($P = 0.10$). Patients treated for CAI and receiving combination regimens were mainly treated for lower respiratory tract infections (37.8%) and osteo-articular or diabetic foot infections (14%).

Microbiology

Among the 1276 patients receiving antimicrobial treatment, 972 (76.2%) had at least one clinical sample sent to the microbiology laboratory. At the time of the survey, 20 out of the 1276 (1.6%) had only microscopy results available, 17 (1.3%) a positive result for a pneumococcal or legionella urinary antigen test, 628 (49.2%) a microbiological culture result and 545 (42.7%) at least one antimicrobial susceptibility test result. In rehabilitation and long-term care units, 48.9% of the patients receiving antimicrobials did not have any sample drawn. This proportion was 30.6% in surgery, 28.0% in medicine, 21.5% in onco-haematology and 7.6% in ICUs ($P < 0.01$). Patients with HAI were more likely than those with CAI to have at least one clinical sample drawn (78.6% versus 65.4%, $P < 0.01$), even in ICUs (88.9% versus 79.8%, $P = 0.04$). The number of antimicrobials in the treatment regimen was not statistically different according to the availability of a culture result, whatever the community or nosocomial origin of the infection. Of note, 56 out of the 345 patients (16.2%) treated with antimicrobials for > 7 days did not have any microbiological sample drawn on the day of the survey.

Among the 1194 isolates, the most frequent were as follows: Enterobacteriaceae ($n = 319$), including 40 (12.5%) ESBL-E; *S. aureus* ($n = 101$), including 25 (24.8%) MRSA; and *P. aeruginosa* ($n = 93$), including 18 (19.4%) resistant to ceftazidime or carbapenem. Patients with MDR bacteria were more likely to receive more than one drug (59.3%) as compared with others (39.3%, $P < 0.01$) and for a longer duration of time (median, 9 versus 4 days, $P < 0.01$). Among the 114 patients receiving glycopeptides, 39 (34.2%) did not have any positive culture available, 19 (16.7%) had febrile neutropenia, 15 (13.2%) coagulase-negative staphylococci infections and 10 (8.8%) MRSA infections. Patients with ESBL-E were more likely to receive carbapenems (65.0%) than those without ESBL-E (8.7%, $P < 0.01$). Among all risk factors for infection with MDR bacteria, only late-onset infection [odds ratio (OR) 2.6, 95% confidence interval (CI) 1.2–4.6], previous hospitalization (OR 2.3, 95% CI 1.1–3.5) and previous carriage of MDR bacteria (OR 8.2, 95% CI 7.5–26.9) were significantly associated with an MDR infection among patients with antimicrobial treatment after multivariate logistic regression analysis. Among the 49 patients infected with *Candida* species, 28 received fluconazole, 7 voriconazole, 6 caspofungin, 1 amphotericin B and 7 did not receive any antifungal on the day of the survey. Among the 13 patients treated for aspergillosis, 1 received fluconazole, 8 voriconazole, 1 the combination of voriconazole and amphotericin B, and 3 did not receive any antifungal on the day of the survey. Of interest, 82 patients who received antifungals did not have any positive clinical sample displaying fungi on the day of survey.

Time required for data collection

The study involved three to five physicians or pharmacists in each hospital. Because none of the participating hospitals had electronic medical records or comprehensive electronic prescribing, data had to be collected in the ward. The time allocated to data collection was estimated in the range of 6–10 min for each patient and the time spent on data input was estimated to be 5 min (double entry), resulting in a total amount of 729–993 h for the creation of the database for the 3964 included patients or an average of 18.3–25.0 h for 100 patients.

Discussion

We conducted the first large-scale study of antimicrobial use at the patient level in French hospitals. It brings insight into antimicrobial prescribing in a country that has one of the highest rates of antibiotic use in Western Europe. The duration of surgical prophylaxis and antimicrobial therapy appeared to be longer than recommended in a high proportion of the cases (21.0% and 27.2%, respectively). It revealed also that combination therapy is widely used outside ICUs and this questions the appropriateness of the treatment. Finally, our study demonstrated that it is possible to collect data on antibiotic use on a large scale in French hospitals, although it is time consuming.

Overall, and as reported in most countries, β -lactams are the most commonly used antibiotics in the hospital setting. However, the frequency of use of third-generation cephalosporins was surprisingly high in CAI, although previously reported.^{8,11} The proportion of patients receiving quinolones is rather high and among the highest reported. It is almost double that observed in the 2009 ESAC survey.¹¹ These findings should enable more-focused surveys to be conducted in order to better understand the differences observed between countries. Lastly, carbapenems accounted for almost 8% of all prescribed drugs. This proportion is likely to increase in the near future, and trends in carbapenem use should be closely monitored because of the CTX-M-producing *Escherichia coli* pandemic and the emergence of carbapenemase-producing strains.

In the present study, the proportion of patients receiving surgical prophylaxis for > 1 day remains too high (21%) and not in accordance with current guidelines.¹⁴ However, this proportion is far lower than that reported in the 2008 and 2009 ESAC surveys,¹¹ and was observed in a minority of participating hospitals. Comprehensive education programmes for physicians in targeted hospitals should be implemented, because such programmes have been proven efficient in decreasing the misuse of antibiotic prophylaxis.¹⁵

Up to one-third of patients treated for HAI and almost one-quarter of those treated for CAI received antimicrobials for > 1 week at the day of survey. These proportions may be overestimated, because the likelihood to be included in point prevalence studies increases with treatment duration. However, in the present study, a minority of patients had infections that required a long duration of antibiotic treatment, such as endocarditis or osteo-articular infections. A majority had pneumonia or digestive tract infections, despite the fact that shorter durations of treatment have been shown to be as efficient as longer ones.^{16,17} The electronic monitoring of prescriptions with reminders or stop orders is urgently needed in French hospitals,

to better monitor antibiotic treatment. Of note, because in point prevalence surveys treatment duration is recorded on the day of survey in place of overall treatment duration, it is likely that the median and the maximum treatment durations are underestimated.

In the present survey, a high proportion (40%) of patients received more than one antimicrobial, and, surprisingly, one-third of patients hospitalized outside ICUs and onco-haematology units received combination regimens. The use of combination regimens outside ICUs is questionable, especially for β -lactam and aminoglycoside combinations, as these combinations have not shown any advantages over β -lactam monotherapies in a recent meta-analysis.¹⁸ However, some data suggest that among severely ill patients, combination regimens may decrease mortality in pneumococcal bacteraemia¹⁹ and in septic shock,²⁰ but obviously such patients are managed in ICUs. Lastly, one out of five patients treated with aminoglycoside combinations received aminoglycosides for >3 days, contrary to current guidelines.¹⁸ Therefore, it would be of interest to further analyse the use of combination regimens in French hospitals, in order to decrease antibiotic use.

The present survey has some weaknesses. First, participation was voluntary and, consequently, the representativeness of the participating hospitals at the national level may be questioned. In addition, the 38 participants represent 1.4% of all healthcare institutions in France. However, it should be noted that the 2009 ESAC survey conducted on the same topic included only 3 hospitals from France among a total of 172 hospitals throughout Europe.¹¹ Second, some hospitals participating in the survey did not include all inpatients, but only patients from selected wards. Therefore, antibiotic use does not represent the overall hospital use, but ward use and benchmarking should be done at the ward level.

Lastly, it has been shown that repeated point prevalence surveys may be of interest to evaluate the appropriateness of antimicrobial therapy.²¹ Although we advocate such studies, it should be borne in mind that they are difficult to conduct, because the data collection is cumbersome in the absence of electronic patient files. In the present study, we estimated that the data collection and validation necessitated 19–26 h, i.e. ~3 days of a full-time equivalent, for each hospital site. When the time needed for the survey implementation and data analysis is added, a minimum of 1 week of a full-time equivalent will be necessary for each site. Therefore, it seems obvious that, in the era of personnel shortage, such surveys cannot be conducted every single year.

In conclusion, the present survey demonstrates that a study of antibiotic use at the patient level can be performed on a large scale in a single country, although it may be cumbersome to conduct. It represents a first step to establish a network that may be used for participation in international surveillance. In addition, it provides insight into antibiotic use in French hospitals and underlines directions for quality improvement. However, the appropriateness of antimicrobial therapy should be evaluated on the basis of numerous factors, such as diagnostic accuracy, microbiological results, posology, de-escalation at 48–72 h, evaluation of pharmacokinetic and pharmacodynamic parameters, and total duration of treatment.^{22,23} Although simplified scores have been proposed,²¹ such detailed studies would be even more time-consuming than the current study, and their

feasibility relies on the development of electronic prescribing and reporting systems.

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