Using the clinical information system and self-supervision to rationalize the need for antibiotic stewardship: An interventional study in a 2000-bed university hospital

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Short communicationUsing the clinical information system and self-supervision to rationalise the need for antibiotic stewardship: an interventional study in a 2000-bed University Hospital.

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Abstract

Objectives: To describe electronic medical records (EMR) and computerised physician order entry system (CPOE) usefulness to support and assess antimicrobial stewardship programs (ASP).

Methods: In our hospital, Infectious diseases specialists (IDS) supervise antimicrobial prescription when solicited by physicians in charge of patients. From January to October 2015, we calculated treatment days of antibiotic prescriptions, supervised or unsupervised by IDS (SAP or UAP respectively) in all wards, except intensive care units. Embedding recommendations on carbapenem indications as a checklist into CPOE, we implemented in 2017 a self-administered ASP. We reviewed EMR to determine global compliance with carbapenem prescription guidelines (combining introduction of therapy and 72-hour assessment) before and after implementation of self-administered ASP in departments with low rate of SAP of these antibiotics.

Results: Among 16,090 prescriptions extracted, 19.9% were SAP. We identified three patterns of antibiotic prescriptions. The first pattern (amoxicillin-clavulanate, ceftriaxone) is characterised by high rate of UAP in every department, the second (cloxacillin, rifampin) by high rate of SAP in every department and the third (broad-spectrum beta-lactams) by heterogeneous distribution of SAP/UAP among departments. We reviewed carbapenem prescriptions in 5 departments with low SAP of carbapenems during 6 months, 94 before and 107 after implementation of self-administered ASP. Global compliance with guidelines significantly increased from 22% to 37% (risk difference, 15% [CI, 2.3 - 28.5%]; P=0.02).

Conclusion: Clinical information system may help rationalise antibiotic stewardship in a context of scarce medical resources. Mapping of antibiotic prescription and self-supervision are efficient, complementaryl and easy to implement tools.

Keywords

Antimicrobial stewardship, Information systems, Electronic medical records, computerised physician order entry system, carbapenems

Abbreviations

ASP: antimicrobial stewardship program
CPOE: computerised order entry system
EMR: electronic medical record
IDS: infectious diseases specialist

55 SAP: supervised antibiotic prescription

56 UAP: unsupervised antibiotic prescription

1 Introduction

The global increase in prevalence of bacterial resistance is a major concern [1, 2]. Amongst different approaches to fight bacterial resistance, reducing unnecessary prescription of antibiotics is one of the most challenging [3]. Pollack *et al.* recommended tracking and reporting antibiotic use as a core element of antimicrobial stewardship program (ASP) [4]. Comprehensive ASP has proved efficient in reducing costs, length of hospital stay and complications of antibiotic therapy. However, it may be time-consuming and difficult to implement, it may be difficult to assess the human resources needed for implementation [5-8]. In some countries, like in France, persuasion and collaboration are preferred to coercive approaches [9]. Data comparing the effectiveness and relevance of the various programs are lacking and do not allow for a strategy to be defined [10].

The use of information technology support may be associated with a better control of antibiotic consumption [11]. In 2012, we implemented an innovative ASP program supported by the electronic medical record (EMR) in the University hospital of Montpellier, France, a 2000-bed tertiary hospital [12]. Such a clinical information system generates huge quantity of data but, little has been published on data analytics with the purpose to evaluate infectious diseases specialists' (IDS) collaborations with other physicians and design data-driven ASP. We took this opportunity to assess whether data analytics could guide our ASP strategy.

We report here a step-by-step study using EMR and the computerised physician order entry (CPOE) system to 1) analyse antibiotic prescribing behaviour at the hospital level, 2) detect potential misuse and deduce areas for potential improvement, 3) implement and evaluate data-driven brief and short interventions to improve antibiotic prescriptions, especially for carbapenems.

2 Materials and methods

2.1 Implementation of ASP program

The program was elaborated by the IDS department in collaboration with pharmacists, microbiologists and the Information technology department. Each prescriber using CPOE system to prescribe antibiotics had to fill a specific electronic form. A notification reminded 1) that multidrug resistance is associated with misuse of antibiotics, and 2) the 24/7 availability of tele-expertise from an IDS. After solicitation by the physicians in charge of the patient, IDS have an access to medical chart and data. All advice for antibiotic therapy management were available in real time in patients' EMR [12].

2.2 Mapping of antibiotic prescription

The first step was the analysis of prescription behaviours and of physicians' collaborations with IDS. We built an algorithm to identify, among all antibiotic prescriptions, those filled in connection with the documented opinion of an IDS through tele-expertise. To map antibiotic prescriptions, we collected all inpatient electronic antimicrobial order entries prescribed through CPOE from May 1st to October 31st 2015. We excluded intensive care, Emergency and Bone marrow transplantation units, which did not use the CPOE system, and paediatric units. Prescriptions cancelled before drug administration were excluded.

For each prescription, we extracted the number of days of antibiotic treatment administered and we examined whether the antibiotic therapy had been guided or not by an IDS notified opinion. For each department, we distinguished between the treatment days of supervised antibiotic prescriptions (SAP) or unsupervised antibiotic prescriptions (UAP) by an IDS.

2.3 Intervention

The second step was to build and evaluate a self-administered ASP.Prescription of carbapenems was chosen to assess the effectiveness of self-supervision of antibiotic prescription through the CPOE. In January 2017, we implemented the recommendations on carbapenem indications directly into the CPOE in the form of a checklist to be filled-in by the prescriber. Prior to this implementation, recommendations (see Supplementary Figure 1) were available in the hospital guidelines, implemented in December 2015, which necessitated a voluntarily consultation by the prescriber. For imipenem, meropenem and ertapenem prescriptions, a mandatory pop-up with a short and interactive reminder of the recommendations appeared. Before validating the prescription, prescribers had to tick the following conditional information: 1) for empiric therapy, risks factors for multidrug-resistant (MDR) Gram-negative infections and severity of the disease (i.e. neutropenia, sepsis or septic shock) 2) for targeted therapy, indication (i.e. MDR *Pseudomonas aeruginosa* or extended-spectrum beta-lactamase-producing Enterobacteriaceae infection) and site of infection. The system explicitly informed whether prescriptions conformed to the guidelines, but not coercively as off-label prescriptions were allowed. Provision of administrator email in the pop-up allowed users' feedback.

2.4 Target audience, pre and post-intervention evaluation

Using the results of the mapping, we targeted departments with the same patterns: 1) high level administration days of carbapenems and 2) high proportion of carbapenem UAP. We conducted a retrospective audit of carbapenem prescriptions in the selected departments from May to October 2015 (pre-intervention evaluation) and from February to July 2017 (post-intervention evaluation).

Inclusion of several infectious events with carbapenem prescription for the same patient was possible.

All data were extracted from EMR and CPOE system. Benjamin Viala reviewed each EMR and determined compliance of prescriptions with local guidelines (see Supplementary Figure 1), French guidelines for the management of urinary tract infections [13] and recommendations of the Fourth European Conference on Infections in Leukaemia (ECIL-4) for neutropenic patients [14]. We also evaluated 72-hour antibiotic therapy assessment and appropriate adjustment according to national guidelines (i.e. discontinuation of carbapenem except for empiric prescription for neutropenic patients with history of MDR Gram-negative bacteria infection or colonization; targeted prescriptions without carbapenem-sparing alternative or alternative contraindicated) [15]. We calculated risk difference with 2-sided 95% confidence interval (CI) and we used a bilateral Chi-squared test for comparison of proportions.

The institution's anti-infective drug commission considered that this study was part of the analysis of current care practices, which did not require the approval of an ethics committee.

3 Results

3.1 Mapping antibiotic prescriptions

From May 1st to October 31st 2015, 20,479 hospital stays were recorded. At least one prescription of antibiotic therapy was recorded during 6,145 stays (30%). We analysed 16,090 lines of prescriptions corresponding to 83,085 days of therapy (DOT). Antibiotic consumptions in major departments are summarised in Supplementary Table 1. Proportions of supervised prescriptions per department were very heterogeneous, ranging from 0.9% to 64.2% with an average of 19.9%.

Figure 1 represents visually the share of each antibiotic in the overall volume in the hospital during the period, with the proportion of SAP/UAP. Supplementary Table 2 provides detailed figures. The three antibiotics more frequently used were third-generation cephalosporins (15.4%), amoxicillin-clavulanic acid (13.3%) and piperacillin-tazobactam (10.6%). The IDS team was widely involved in prescriptions of tigecycline, ceftaroline, cloxacillin, daptomycin and rifampicin but not in amoxicillin-clavulanic acid.

Figure 2 shows how each department is positioned for the prescription of given antibiotics, based on the rate of SAP and the weight of this prescription in proportion to the hospital. By mapping each department’s SAP proportions in proportion of hospital DOT, we were able to identify different patterns of prescription.

The first pattern, characterised by a high rate of UAP in every department, is exemplified by amoxicillin-clavulanate and ceftriaxone, which are evenly distributed over the majority of departments. Only 2 departments had a prescription proportion of amoxicillin-clavulanate >10% of the total DOT (internal medicine: 19.6% and ENT/maxillofacial surgery: 17.8%).

A second pattern was characterised by antibiotics with a high rate of SAP in all departments. The main examples of this pattern were cloxacillin and rifampicin. The only exception was the pneumology department, in which rifampicin prescriptions represented 14% of all rifampicin prescription and were mainly UAP.

The third pattern was characterised by a heterogeneous distribution and concerned broad-spectrum molecules such as piperacillin-tazobactam or carbapenems. Five departments prescribed 55.4% of the carbapenem hospital consumption with low rates of SAP. Regarding piperacillin-tazobactam, four departments concentrated 54.3% of the total consumption, with 8.1% of their prescriptions (53/656) having a duration of more than fourteen days, corresponding to 1,526 DOT (17.2% of all piperacillin-tazobactam DOT).

3.2 Audits of carbapenem use

In the five targeted departments, we assessed conformity with guidelines of 94 carbapenem pre-intervention and 107 post-intervention prescriptions (see Supplementary Figure 2). In the post-intervention evaluation, the checklist was filled for 79% of carbapenem prescriptions. The majority of patients who received carbapenems had been hospitalised and had received broad-spectrum antibiotic therapy in the three previous months (Supplementary Table 3). More than half of the carbapenem prescriptions followed another antibiotic therapy. Other characteristics of infections are summarised in Supplementary Table 3. Enterobacteriaceae represented the majority of isolated pathogens (see Supplementary Table 4).

Carbapenem prescription compliance with local guidelines and with ECIL-4 guidelines for antibiotic therapy increased from 36% to 47% after intervention (risk difference, 11% [2-sided 95% CI, -3 to 24.1%]) but this increase was not statistically significant (P=0.13). Appropriate adjustment of carbapenem prescriptions in the three days following initial prescription also tended to increase from 49% before intervention to 62% after intervention (risk difference, 12% [2-sided 95% CI, -2.1 to 26.7%]; P=0.10). When combining the two indicators, compliance with antibiotic therapy introduction and 72-hour assessment, compliance significantly increased from 22% to 37% (risk difference, 15% [2-sided 95% CI, 2.3 to 28.5%]; P=0.02). About 40% of inappropriate empirical prescriptions were escalation therapy, a situation initially not addressed in our local guidelines. We

thus subsequently modified our guidelines to add a new indication for carbapenems in case of failure of a broad-spectrum antibiotic therapy with third-generation cephalosporin or piperacillin-tazobactam, preferably after advice of an IDS. Results are summarised in table 1. Evolution of pre and post intervention compliance with guidelines for antibiotic therapy introduction was heterogeneous among targeted departments. Compliance for 72-hour reassessment increased in all departments (see Supplementary Figure 3).

4 Discussion

We used data from the clinical information system to further evaluate prescribing behaviours according to each class of antibiotics and interactions between prescribers and IDS. This mapping allowed a focused intervention using self-supervision, which was targeted on wards with a high rate of carbapenem prescriptions without advice of IDS. We showed that this intervention was feasible using very few resources and led to improvement of conformity of prescription to guidelines. Results also allowed us to make real-time modifications of our local recommendations.

Our method allowed us to highlight patterns of interaction between physicians and IDS for antimicrobial prescription. For pattern I, characterised by high volume of prescription and low proportion of supervision rather equally distributed in all departments, relevant interventions may be implementation of guidelines applicable to all departments. Audits and specific IDS interventions may be limited to a few exceptions easily identifiable. For example, we identified two departments with high consumption of amoxicillin-clavulanate. This is easily explained by the type of clinical activity, i.e. treatment of community acquired respiratory infections (internal medicine) and prophylaxis and treatment of oro-facial infections (ENT/maxillofacial surgery). Audits targeting these indications would help check validity of prescriptions. For pattern II, with a high level of stewarded prescriptions, there is no need for an intervention. The exception of rifampicin, mainly UAP in pneumology department is explained by treatment of tuberculosis. For pattern III, characterised by a high heterogeneity between departments and concerning mostly broad-spectrum antibiotics, a relevant strategy would be to target ASP to departments with high rate of unsupervised prescriptions.

The intervention we designed specifically for carbapenem antimicrobial stewardship had several benefits. The implementation of interactive reminder in CPOE was comprehensive, consumed minimal human resources and was at very low costs.

Data provided by the prescriber by filling up the checklist facilitate audits. It captures the prescriber intention and the misfits between the guidelines and the clinical situations. For example, we

revealed that escalation therapy situation to carbapenems (40% of carbapenem prescriptions considered inappropriate) were not taken into account in our guidelines so these were changed.

To our knowledge, this is the first study assessing the weight of IDS advice for antibiotics in almost all departments of a hospital. Volumes and rates of patients receiving antibiotics are consistent with results of previous studies [16]. As suggested by Forrest *et al.* our model demonstrates that EMR can serve as a tool for implementation and analyse of ASP and allows a better elaboration of antibiotic control policies [17]. Moreover, to our knowledge, this is the first study assessing the implementation of a CPOE-embedded survey as a self-stewardship strategy. Some studies included some self-stewardship strategies as CPOE-embedded guidelines, but most of "IDS-free" ASP involved computerised decision support system, with inconstant efficacy [17-19]. Our self-stewardship strategy has numerous benefits: 1) fast and easy implementation with large distribution; 2) minimal human resources consumption; 3) very low costs; 4) can be easily changed, for example to implement new indications or to address another antibiotic; 5) data provided by the survey facilitate audits; 6) it allows users' feedback (survey's administrator email is provided) in order to improve both survey and local guidelines. Moreover, our strategy led to a global improvement of quality of prescriptions in a context marked by poor adherence to guidelines.

Our study has further limitations. First, we tried to build a comprehensive global picture of antimicrobial prescription but we were not exhaustive. We did not include intensive care, emergency, and bone marrow transplantation units, which are high antibiotic consumers. Paediatrics units were excluded because most IDS advices were informal. Further work will be required to determine if completeness is relevant and modifies necessary interventions. Second, due to the low number of prescriptions, we were not able to identify effects of our intervention on antimicrobial resistance or on patients' outcome. Third, our main result of the evaluation before and after the targeted intervention reached statistical significance only when combining introduction of therapy and 72-hours assessment, but this is probably due to the small sample size and the short periods of evaluation. We were unable to estimate the number of carbapenem prescriptions avoided directly as a result of our intervention. The before-after design cannot establish definitive causality between our intervention and prescription improvement. Finally, we were not able to provide data on the effects of our intervention on antimicrobial resistance or on patients' outcome. However, improving antibiotic prescriptions proved to be efficient in many other studies [5-7, 20]. However, we believe that our paper is a proof of concept that data analysis can target most relevant problems in antimicrobial prescription in a large tertiary hospital, help design actions and evaluate

their impact. Our approach also enables to quantify the weight of an action in relation to the overall volume of prescriptions.

Beyond the results of the audit of our targeted intervention, our main contribution to the studies on antimicrobial stewardship is to propose a reproducible method to rationalise the conduct of ASPs. This first step allows us to consider many research perspectives and to guide software publishers on how information systems could fight against antimicrobial resistance.

5 Conclusion

We developed an original way to rationalise antibiotic stewardship by using a clinical information system, combining mapping of prescription according to their supervision by an IDS followed by an audit and self-supervision through a CPOE embedded checklist. We believe that this easy to implement and non-coercive approach is adapted to settings characterised by a high autonomy of prescribers, like the French healthcare system [9]. Use of the clinical information system may be particularly useful in large hospitals where a direct intervention of an IDS on all antibiotic prescriptions is hardly feasible.

6 Acknowledgments

Some of these data were presented at the 27th ECCMID 2017 in Vienna, Austria, 22-25 April 2017 (P1157) and at the 28th ECCMID 2018 in Madrid, Spain, 21–24 April 2018 (P0876).

Declarations

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Competing Interests: None

Ethical Approval: Not required

Contribution

Conception and design of the study D. Morquin, V. Le Moing

Acquisition analysis and interpretation of data: B. Viala, A. Redor, M. Villiet, MN Didelot

Drafting the article: B. Viala, A. Redor, D. Morquin

Revising the article: V. Le Moing, A. Makinson, J. Reynes

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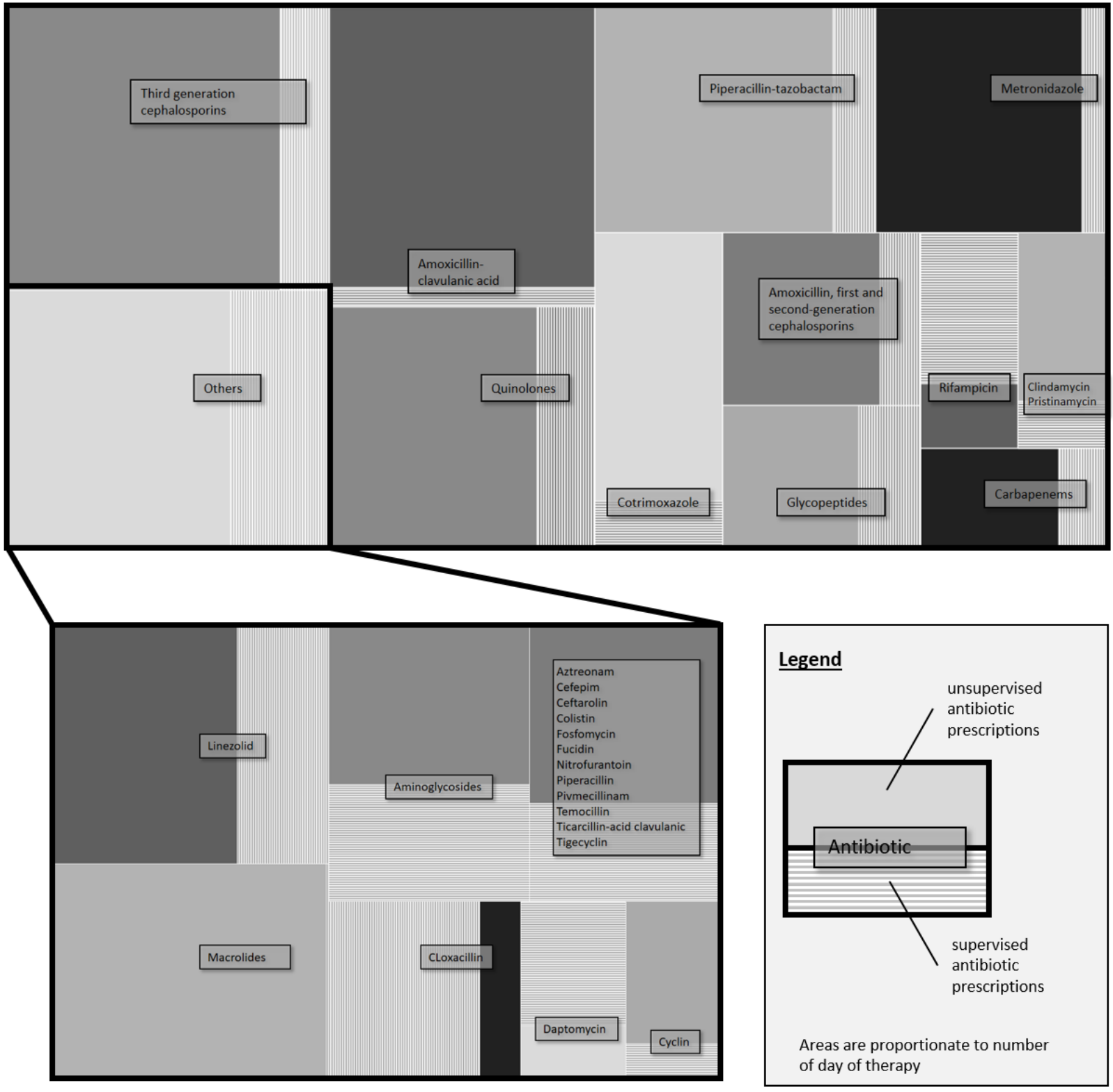
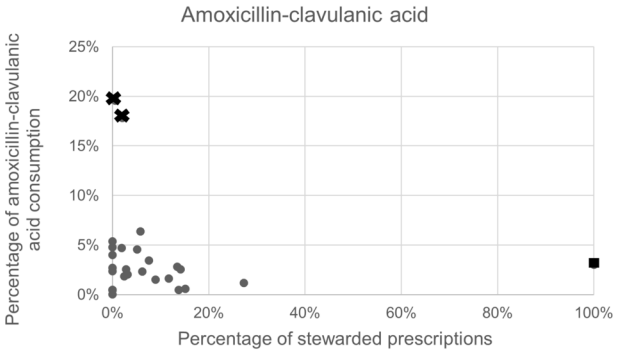
Figure legends

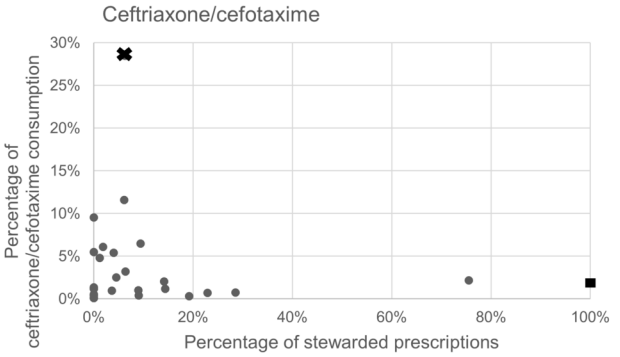
Figure 1: Representation of the supervised/unsupervised days of therapy for each antibiotic

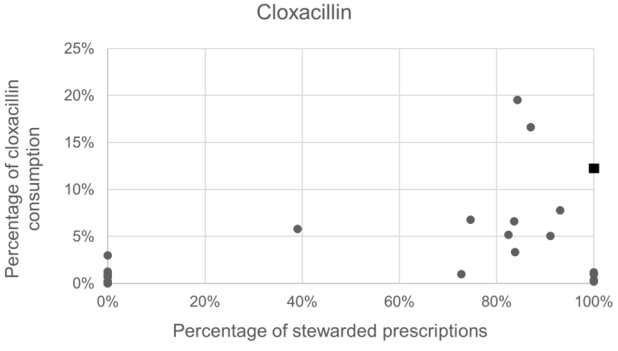
Figure 2: Patterns of prescriptions by mapping departments' antibiotic use with the proportion of stewarded prescription.

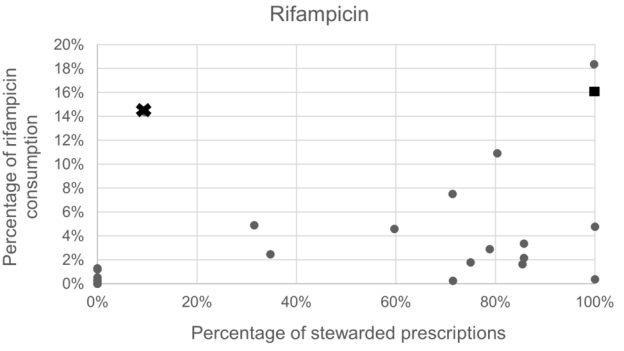
Each dot represents a unit. The presence of crosses reflects an important volume of non-IDS stewarded antibiotic consumption. The square systematically on the right represents infectious diseases department.

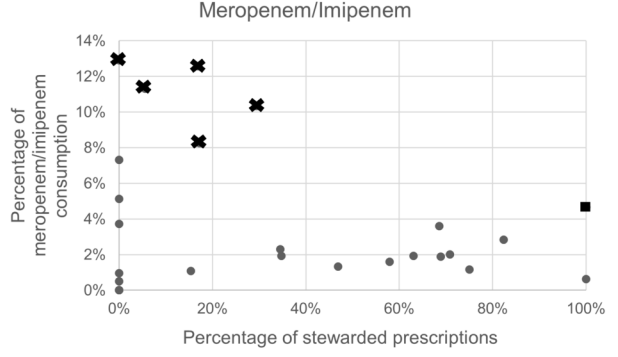

Third generation cephalosporins
Amoxicillin-clavulanic acid
Piperacillin-tazobactam
Metronidazole
Others
Quinolones
Amoxicillin, first and second-generation cephalosporins
Rifampicin
Clindamycin Pristinamycin
Cotrimoxazole
Glycopeptides
Carbapenems
Linezolid
Aminoglycosides
Aztreonam
Cefepim
Ceftarolin
Colistin
Fosfomycin
Fucidin
Nitrofurantoin
Piperacillin
Pivmecillinam
Temocillin
Ticarcillin-acid clavulanic
Tigecyclin
Macrolides
CLoxacillin
Daptomycin
Cyclin
Legend
unsupervised antibiotic prescriptions
Antibiotic
supervised antibiotic prescriptions
Areas are proportionate to number of day of therapy


Amoxicillin-clavulanic acid
Percentage of amoxicillin-clavulanic acid consumption
25%
20%
15%
10%
5%
0%
0%
20%
40%
60%
80%
100%
Percentage of stewarded prescriptions


Ceftriaxone/cefotaxime
Percentage of ceftriaxone/cefotaxime consumption
30%
25%
20%
15%
10%
5%
0%
0%
20%
40%
60%
80%
100%
Percentage of stewarded prescriptions


Cloxacillin
Percentage of cloxacillin consumption
25%
20%
15%
10%
5%
0%
0%
20%
40%
60%
80%
100%
Percentage of stewarded prescriptions


Rifampicin
Percentage of rifampicin consumption
20%
18%
16%
14%
12%
10%
8%
6%
4%
2%
0%
0%
20%
40%
60%
80%
100%
Percentage of stewarded prescriptions


Meropenem/Imipenem
Percentage of meropenem/imipenem consumption
14%
12%
10%
8%
6%
4%
2%
0%
0%
20%
40%
60%
80%
100%
Percentage of stewarded prescriptions

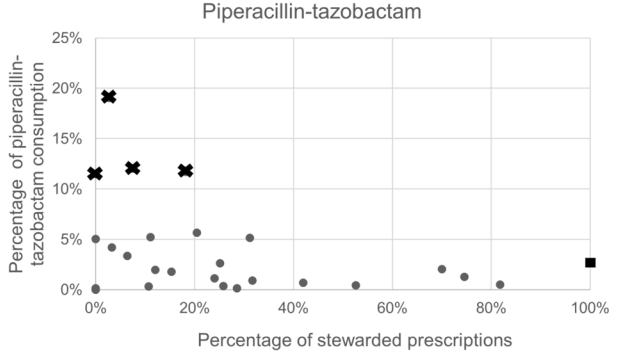

Piperacillin-tazobactam
Percentage of piperacillin-tazobactam consumption
25%
20%
15%
10%
5%
0%
0%
20%
40%
60%
80%
100%
Percentage of stewarded prescriptions

Table 1: Audits of the use of carbapenems, main results

	Pre-intervention group— no./Total no. (%)	**Post-intervention group—no./Total no. (%)**	**Risk Difference, % (2-Sided 95% CI)**	**P Value**
Compliance with guidelines for initial prescription	34/94 (36)	50/107 (47)	11 (-3 to 24.1)	0.13
Empirical prescription	24/78 (31)	34/81 (42)	11 (-3.6 to 26.1)	0.14
Targeted therapy	10/16 (63)	16/26 (62)	-1 (-3.1 to 29.2)	0.95
72-hour antibiotic therapy assessment	55/87 (63)	68/94 (72)	9 (-4.5 to 22.7)	0.19
Correct antibiotic therapy adjustment	43/87 (49)	58/94 (62)	12 (-2.1 to 26.7)	0.1
Both compliance with antibiotic therapy introduction and 72-hour assessment	19/87 (22)	35/94 (37)	15 (2.3 to 28.5)	**0.02**

CI: confidence interval