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Novel scores relevant to antimicrobial resistance and hospital-acquired infections developed with data from a multi-hospital consortium in the Parisian region of France

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SUMMARY

Purpose: Indicators for comparing and understanding differences in antimicrobial resistance (AMR) and healthcare-associated infections (HAIs) for benchmarking are essential to identify priorities for hospitals.

Methods: This study measured the incidence of hospital-acquired or resistant Gram-negative bacilli bloodstream infections (GNB-BSIs) in a large public healthcare consortium in the Parisian region of France.

Results: Within each hospital, there was a strong positive correlation between the incidence of GNB-BSIs due to resistant GNB and the incidence of hospital-acquired GNB-BSIs. Two scores measuring AMR and HAI rates by combining different GNB-BSI incidence rates were developed as indicators. These scores were highly variable within the hospital consortium. On multi-variate analysis, AMR and HAI scores were significantly associated with the proportion of surgical beds, staff absenteeism and the consumption of alcohol-based hand rub, with the latter two characteristics being amenable to interventions.

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Carbapenem use was also linked to AMR, but this may be because carbapenems are the preferred drug for treating resistant infections.

Conclusion: These results shed light on the incidence of HAIs and AMR in the study hospitals, and suggest possibilities for targeted interventions at healthcare facility level.

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Introduction

Antimicrobial resistance (AMR) and healthcare-associated infections (HAIs) are reaching alarming levels worldwide. Hospitals combine a fragile population with a large number of invasive procedures, immunosuppressive therapies and high rates of antimicrobial drug consumption with respect to the size of the population – factors known to promote both AMR and HAIs [1]. In hospitals, HAIs increase mortality and morbidity, lengthen hospital stays and increase costs. Furthermore, the frequency of AMR is increasing in bacteria, making it crucial to prevent HAIs to combat the further spread of resistance. The monitoring and comparison of AMR and HAIs are crucial to improving understanding and control of these two phenomena. Surveillance is generally performed at national, and sometimes regional, level [2–5]. Worldwide comparative studies of AMR between countries are based on scores derived exclusively from antibiotic consumption [6], the evaluation of antibiotic stewardship programmes [7] or, partially, AMR rates [3]. In this last case, most of the other components of the score relate to AMR surveillance systems or laboratory networks. In order to compare HAIs, the hospital-acquired condition scores are mainly based on measurements of quality, such as patients' health insurance claims [8].

The incidence of AMR and HAIs varies considerably between hospitals in France [4,5], but surveillance data are presented without considering the factors that might explain this high degree of heterogeneity.

Monitoring the incidence of bloodstream infections (BSIs) is of particular relevance when studying HAIs due to the severity of these infections and their impact on patient morbidity and mortality [9]. Analyses focusing on BSIs appear to be pertinent for comparisons between hospitals. First, local practices and standard operating procedures for blood cultures are likely to be similar throughout the country, whereas multi-drug-resistant organism screening may vary considerably, depending on local policy. In addition, BSIs can be monitored in a bacteriology laboratory alone, because they are defined primarily on the basis of positive results for microbiological samples, with the exclusion of positive results for species generally considered to be contaminants [10]. Finally, Gram-negative bacteria (GNB) are among the principal pathogens responsible for BSIs in healthcare settings [11], and are increasingly developing resistance to most of the antibiotics available. Indicators measuring GNB-BSI levels are therefore suitable markers for use in evaluation of the burden of HAIs and AMR in hospital settings.

The primary objective of this study was to develop composite measurements of HAIs and AMR for GNB-BSIs, used as indicators for comparing and benchmarking the hospitals of Assistance Publique-Hôpitaux de Paris (APHP), the largest hospital group in France (38 hospitals, 20,000 beds). This

consortium of teaching hospitals covers the city of Paris and its suburbs (12 million inhabitants).

This study also explored differences in scores between hospitals. These differences can probably be explained, in part, by differences in the characteristics of the inpatients (case mix), but several factors relating to practices (e.g. hand hygiene), and the structural and organizational choices of each hospital could also have an impact on scores assessing HAIs and AMR [12]. The identification of the factors associated with HAIs and AMR would therefore be relevant to drive targeted interventions.

Methods

This study included a subset of 28 hospitals (approximately 14,000 beds, corresponding to 70% of the capacity of APHP) from the 38 hospitals in the APHP network: 18 acute care hospitals and 10 rehabilitation/long-term care hospitals with bacteriology laboratories using the same laboratory information system, making it possible to perform standardized data extraction and analysis. This study was performed on data for 2019 alone because the coronavirus disease 2019 (COVID-19) pandemic greatly affected the organization of the hospitals, with an impact on AMR [13]. A blood culture (BC) set was defined as the combination of one aerobic and one anaerobic culture of blood samples drawn through the same puncture. A BC set was considered positive if microbial growth was observed in at least one of the two bottles. A clinically significant episode of GNB-BSI was defined as a BC set positive for *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter cloacae*, *Pseudomonas aeruginosa* or *Acinetobacter baumannii*. BSIs due to *Staphylococcus aureus* and enterococci were also evaluated to calculate the incidence of BSIs due to methicillin-resistant *S. aureus* (MRSA) and vancomycin-resistant enterococci (VRE). If several BC sets were positive for the same micro-organism for a given patient, only the first BSI episode was considered. Infections detected in blood sampled for culture >48 h after admission were considered to be hospital-acquired [10]. All the laboratories involved in this study participate in the national 'COFRAC' accreditation process, and use the EUCAST European quality standards for drug susceptibility testing [14]. Data were extracted anonymously in accordance with the regulations in force in France. All patients admitted to APHP hospitals are informed, on admission, about the potential use of their data for research purposes.

Several administrative or organizational characteristics were recorded for each hospital. The structure of each hospital was assessed based on the total number of open beds. The percentages of beds in intensive care units (ICUs), surgical wards, medical wards, haematology, long-term care wards and single rooms were recorded. Annual expenses for nurses or

nursing assistants on temporary contracts were standardized by dividing the total amount (in Euros) spent annually by the total number of healthcare workers in the facility. The annual rate of healthcare worker absenteeism was determined as the total number of unplanned absences divided by the total number of staff workdays during the year. The indicators of antibiotic use at hospital level used were defined daily doses per 1000 patient-days, as calculated by the central APHP pharmacy according to the World Health Organization's definitions [15] for antibiotics widely used to treat serious bacterial infections: extended-spectrum cephalosporins (ESC), fluoroquinolones (FQ) and carbapenems. Two variables were used for the indirect measurement of infection control and prevention at each hospital. First, alcohol-based hand rub (AHR) consumption was recorded; this indicator of hand hygiene is used by the Ministry of Health and is readily available for each French hospital. This indicator is calculated as a percentage, as follows: (actual volume of AHR delivered to the hospital/theoretical minimum volume to be used, defined according to the type of activity and the minimum number of frictions recommended for each of these activities per patient-day) x 100 [16]. Second, staffing levels for healthcare workers in both the infection control team (ICT) and the antimicrobial stewardship team (AST) were evaluated by calculating the difference between the number of full-time-equivalent members of each team and the number of team members requested in relation to hospital size, as defined by national rules [17,18].

The burden of HAIs and AMR was assessed at each healthcare facility by determining the annual incidence or incidence density rates of GNB-BSIs, and constructing two global composite scores for each facility. For the AMR score, the incidence of various combinations of BSIs per 100 admissions or per 1000 patient-days caused by GNB with predefined resistance patterns (Enterobacterales resistant to extended-spectrum cephalosporins, carbapenems and/or FQ) and naturally resistant Gram-negative species (*A. baumannii* and *P. aeruginosa*) was determined. These last two species were considered because they are intrinsically resistant to numerous antibiotics (e.g. aminopenicillin- β -lactamase inhibitor combinations, first- and second-generation cephalosporins, cefotaxime/ceftriaxone, ertapenem, trimethoprim, tetracyclines and first-generation quinolones). The HAI score was calculated from the incidence rates of GNB-BSIs caused by the same species as for the AMR score, but isolated from blood cultures drawn >48 h after admission, regardless of their pattern of resistance.

Statistical analysis

Correlations between incidence density rates for resistance patterns of concern per 1000 patient-days were assessed by calculating Spearman's rank correlation coefficient. For the purposes of exploration, a preliminary principal component analysis (PCA) was performed to identify the correlations existing between the incidence rates of GNB-BSIs due to the various species, patterns of resistance and nosocomial infections, and to select the two scores to be used for subsequent analyses. If the incidence density rate of a pattern was equal to zero in more than half of the participating hospitals, it was not included in the PCA because it was not considered to be discriminant, and would be expected to account for only a small proportion of the variance in the PCA.

The groups of acute care hospitals and long-term care hospitals were compared in univariate analysis. Multi-variate linear regression analyses were then performed with each of the two scores as the dependent variable, and with the inclusion, in the various models, of independent variables significant on univariate analysis and variables considered relevant *a priori*. If two variables were considered to be co-linear, they were not included simultaneously in the same model. Two procedures were tested for robustness to the imbalance between the number of variables and the number of hospitals evaluated. The first was a backward selection based on minimization of Akaike information criterion to find the subset of variables yielding the model with the best performance and the lowest prediction error. The validity of this model was assessed in Durbin–Watson, Breusch–Pagan and Shapiro–Wilk normality tests. The second procedure involved confirming the results of the stepwise approach in a sensitivity analysis with Lasso (least absolute shrinkage and selection operator) regression. This second approach is a more conservative method for the selection of variables in cases of imbalance between the number of observations (i.e. number of hospitals) and the number of variables [19]. Data were analysed using R v4.0.5 (R Foundation for Statistical Computing, Vienna, Austria).

Results

In line with national reports [20], only infrequent BSI events or no BSI events at all were reported for Enterobacterales resistant to carbapenems or VRE in several hospitals of the consortium. Therefore, these indicators were not considered in subsequent analyses. The first axis of the PCA accounted for 76.4% of the variance (Figure 1). All incidence rates projected well on to the circle and were very close to each other, indicating a high degree of correlation. Indeed, within each hospital, strong positive correlations were observed between the total incidence density rates per 1000 patient-days for BSIs due to *K. pneumoniae* non-susceptible to ESC and/or FQ, *E. coli* non-susceptible to ESC and/or FQ, and *E. cloacae* non-susceptible to ESC and/or FQ. Positive correlations were also observed between the total incidence density rates for hospital-acquired BSIs due to *K. pneumoniae*, *E. coli*, *E. cloacae* and *P. aeruginosa* together with *A. baumannii* (Figure 1). Interestingly, HAIs and AMR were found to be related phenomena in the hospitals. Two incidence rates were slightly further from the others in the PCA: incidence per 100 admissions of BSIs due to *K. pneumoniae* non-susceptible to ESC, and incidence per 1000 patient-days of BSIs due to MRSA. The first of these indicators is based on the incidence per 100 hospital admissions, which is not relevant at long-term care hospitals, which have very small numbers of admissions. This may account for the distance of this incidence from the other points. The second indicator, the MRSA incidence density rate, was slightly removed from the GNB-BSI incidence density rates, probably due to their different reservoirs. As such, the decision was made to exclude these two indicators from subsequent analyses. The two scores retained combined incidence rates for the same group of bacteria species (GNB). The first of the scores retained was an AMR score adding rates per 1000 patient-days for *E. coli* non-susceptible to ESC + *K. pneumoniae* non-susceptible to ESC + *E. cloacae* non-susceptible to ESC + *P. aeruginosa* + *A. baumannii*. The second score retained was an HAI score adding rates for

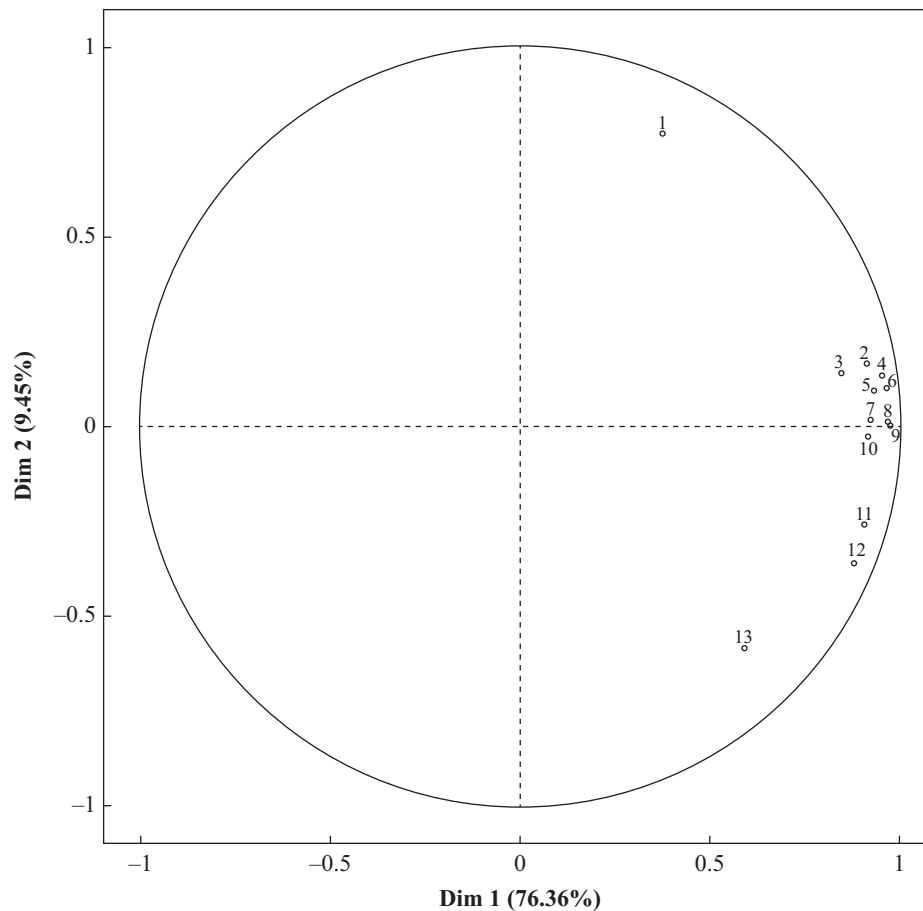


Figure 1. Principal component analysis of different micro-organisms (resistant or hospital acquired) isolated from bloodstream infections. Variances of each axis (Dim1 and Dim2) are provided. ¹*Klebsiella pneumoniae* non-susceptible to extended-spectrum cephalosporins per 100 admissions. ²*K. pneumoniae* non-susceptible to fluoroquinolones per 1000 patient-days. ³Hospital-acquired *Acinetobacter baumannii* plus *Pseudomonas aeruginosa* per 1000 patient-days. ⁴Hospital-acquired *K. pneumoniae* per 1000 patient-days. ⁵*K. pneumoniae* non-susceptible to extended-spectrum cephalosporins per 1000 patient-days. ⁶*Enterobacter cloacae* non-susceptible to fluoroquinolones per 1000 patient-days. ⁷*A. baumannii* plus *P. aeruginosa* per 1000 patient-days. ⁸Hospital-acquired *E. cloacae* per 1000 patient-days. ⁹Hospital-acquired *Escherichia coli* per 1000 patient-days. ¹⁰*E. cloacae* non-susceptible to extended-spectrum cephalosporins per 1000 patient-days. ¹¹*E. coli* non-susceptible to fluoroquinolones per 1000 patient-days. ¹²*E. coli* non-susceptible to extended-spectrum cephalosporins per 1000 patient-days. ¹³Meticillin-resistant *Staphylococcus aureus* per 1000 patient-days.

hospital-acquired BSI per 1000 patient-days for the following species: *E. coli* + *K. pneumoniae* + *E. cloacae* + *P. aeruginosa* + *A. baumannii*.

The distributions of the two scores differed considerably between hospitals (Figure 2). Most long-term care hospitals had low incidence rates for resistant and/or hospital-acquired GNB-BSIs. Scores were heterogeneous for the acute care hospitals, with a six-fold difference between the lowest and highest incidence of resistant and/or hospital-acquired GNB-BSIs. There is a need to understand the reasons for this heterogeneity, given the similarity of the hospitals participating in this study, which were all teaching hospitals, in the same region and with the same institutional policies.

The comparison of acute care and long-term care hospitals in a univariate analysis (Table I) revealed significant differences between these two groups of hospitals in terms of various variables of interest for antibiotic consumption and AHR use. They also differed significantly in terms of

administrative (percentages of ICU and surgical care beds) and organizational (staffing levels in the ICT and AST) factors. Therefore, separate analyses were performed for these two groups of hospitals.

In univariate analysis, the percentages of surgical and haematology beds ($P < 0.01$), and antibiotic use (carbapenems, $P < 0.001$) were associated with the two scores in acute care hospitals. In long-term care hospitals, the use of any of the antibiotics considered (carbapenems, FQ and third-generation cephalosporins, $P < 0.05$) was associated with the two scores.

For acute care hospitals, the stepwise multi-variate analysis identified several factors significantly associated with the HAI score, with a final multiple R^2 of 0.91 (Table II). A higher HAI score was linked to a higher percentage of surgical care beds ($P < 0.001$), a higher level of carbapenem consumption ($P < 0.001$), and a higher rate of absenteeism among healthcare workers ($P = 0.017$). A lower HAI score was associated with a high level of AHR consumption ($P = 0.012$). Lasso regression

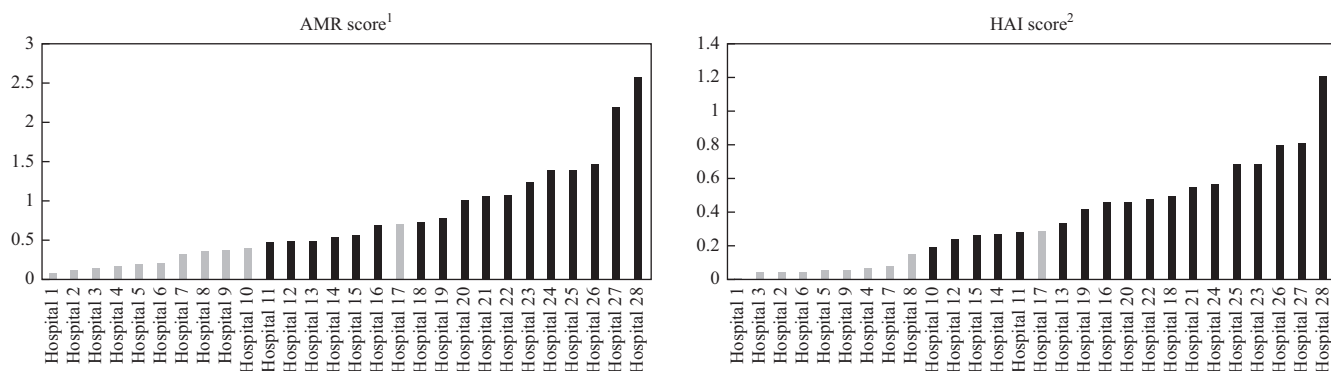


Figure 2. Distribution of the two scores of Gram-negative bacilli bloodstream infections among the cohort of 28 hospitals. Incidence is expressed per 1000 patient-days. AMR, antimicrobial resistance; HAI, hospital-acquired infection. ¹(*Escherichia coli* non-susceptible to extended-spectrum cephalosporins (ESC) + *Klebsiella pneumoniae* non-susceptible to ESC + *Enterobacter cloacae* non-susceptible to ESC + *Pseudomonas aeruginosa* + *Acinetobacter baumannii*) per 1000 patient-days. ²(Hospital-acquired *E. coli* + hospital-acquired *K. pneumoniae* + hospital-acquired *E. cloacae* + hospital-acquired *P. aeruginosa* + hospital-acquired *A. baumannii*) per 1000 patient-days.

analysis gave similar results, except that carbapenem use was not significantly associated with HAI score (Table II).

Similarly, the stepwise multi-variate analysis identified several factors significantly associated with AMR score in acute care hospitals, with a final multiple R^2 of 0.93 (Table II). A higher AMR score was linked to a higher percentage of surgical care beds ($P=0.003$), a higher level of carbapenem consumption ($P<0.001$), and a higher rate of absenteeism among healthcare workers ($P=0.007$). A lower

AMR score was associated with high levels of AHR consumption ($P=0.007$). Expenditure on temporary healthcare workers was not significantly linked to AMR score ($P=0.08$). The Lasso regression analysis gave similar results, except that absenteeism rate was not significantly associated with AMR ($P=0.07$) (Table II).

Multi-variate analysis was not performed for long-term care hospitals due to the small number of hospitals ($N=10$) in this category.

Table I

Comparison between acute care hospitals and long-term care hospitals

	Total N=28	Acute care N=18	Long-term care N=10	P-value
Number of beds	445.70 (355.78–671.75)	458.77 (357.34–782.36)	430 (367.06–458.52)	0.159
Percentage of intensive care beds (%)	9.95 (0–14.58)	12.72 (10.21–18.1)	0 (0–0)	<0.001
Percentage of surgical beds (%)	15.73 (0–20.61)	19.88 (16.41–22.31)	0 (0–0)	<0.001
Percentage of haematology beds (%)	0 (0–1.24)	0 (0–3.37)	0 (0–0)	0.081
Percentage of individual rooms (%)	45.05 (39.04–53.22)	42.92 (39.16–48.03)	50.84 (40.76–54.45)	0.419
ESC (DDD)	39.63 (14.20–47.39)	46.08 (40.56–58.40)	11.67 (10.19–14.20)	<0.001
Carbapenems (DDD)	8.8 (1.1–13.2)	12.05 (8.5–15.4)	0.9 (0.8–1.1)	<0.001
Fluoroquinolones (DDD)	30.47 (9.38–47.29)	40.33 (32.14–50.82)	8.36 (5.11–9.38)	<0.001
Alcohol-based hand rub consumption indicator (%)	55.59 (47.5–62.28)	57.94 (52.86–67.89)	44.39 (40.17–53.35)	0.006
Staffing level of antimicrobial stewardship team ^a	0.15 (-0.1–0.6)	0.5 (0.13–0.93)	-0.1 (-0.18–0)	<0.001
Staffing level of infection control team ^a	0.51 (0.03–0.77)	0.67 (0.42–0.83)	0.11 (-0.0–0.45)	0.029
Rate of absenteeism (%)	8.50 (7.70–9.91)	7.85 (7.43–8.52)	10.26 (9.30–10.77)	<0.001
Expenses for temporary healthcare workers (Euros per number of present healthcare workers)	724.7 (419.88–1016.75)	646.95 (441.20–865.88)	1007.85 (253.5–1764.83)	0.182
AMR score ^b	0.29 (0.08–0.51)	0.48 (0.30–0.66)	0.06 (0.05–0.08)	<0.001
HAI score ^c	0.55 (0.35–1.06)	0.89 (0.55–1.34)	0.20 (0.16–0.35)	<0.001

DDD, defined daily dose; ESC, extended-spectrum cephalosporins; AMR, antimicrobial resistance; HAI, hospital-acquired infection. Values are presented as median (interquartile range).

^a Number of full-time-equivalent members minus the number of requested members defined by national rules.

^b (*Escherichia coli* non-susceptible to ESC + *Klebsiella pneumoniae* non-susceptible to ESC + *Enterobacter cloacae* non-susceptible to ESC + *Pseudomonas aeruginosa* + *Acinetobacter baumannii*) per 1000 patient-days.

^c (Hospital-acquired *E. coli* + hospital-acquired *K. pneumoniae* + hospital-acquired *E. cloacae* + hospital-acquired *P. aeruginosa* + hospital-acquired *A. baumannii*) per 1000 patient-days.

Table II
Multi-variate analysis of the AMR and HAI scores in acute care hospitals

	HAI score				AMR score			
	Stepwise model		Lasso model		Stepwise model		Lasso model	
	Coefficient	Pr(> t)	Estimate	Pr(> z)	Coefficient	Pr(> t)	Estimate	Pr(> z)
Percentage of surgical beds (%)	0.049087	9.38e-05	0.04763	0.00837	0.015084	0.00124	0.011865	0.028747
Carbapenems (DDD)	0.039352	7.86e-05		NS	0.018803	1.47e-05	0.030675	0.043369
Alcohol-based hand rub consumption indicator (%)	-0.022856	0.0119	-0.03580	0.02345	-0.007744	0.02507	-0.014286	0.002694
Staffing level of the antimicrobial stewardship team ^a		NS		NS	0.075317	0.04297	0.145988	0.000729
Rate of absenteeism (%)	0.160376	0.0165	0.21479	0.06506	0.056451	0.02798	0.063037	0.071705

HAI, hospital-acquired infection; DDD, defined daily dose; NS, non-significant.

^a Number of full-time-equivalent members minus the number of requested members defined by national rules.

Discussion

Indicators for monitoring AMR and HAIs and improving understanding of these phenomena are essential to identify priority areas for curbing these threats in hospitals. At patient level, antibiotic exposure, indwelling devices, hospitalization in an ICU and case mix are among the factors identified as associated with AMR [21,22]. However, these characteristics are not easily and constantly available for hospital benchmarking; as a result, hospital comparisons are often limited to bed capacity [23,24] or antibiotic use [25]. From an institutional perspective, the present results highlight differences in AMR and HAIs within the hospital consortium, and identify administrative and organizational factors associated with a higher incidence of BSIs caused by drug-resistant organisms or HAIs.

This study was focused on GNB to ensure greater homogeneity in terms of AMR epidemiology and relationships with antibiotic use. Furthermore, MRSA and VRE are no longer of major importance in France [2], and are not, therefore, currently a matter of priority. Two different scores were developed for assessing AMR and HAIs in BSIs, with the aim of developing more comprehensive indicators. Strong correlations were found between the incidence rates for AMR to the various drugs tested in BSIs and the hospital-acquired BSI incidence rates included in the scores (Figure 1). The present results confirm the correlations between resistance patterns reported in a previous study conducted at European level [26], and highlight the positive relationship between AMR and HAIs within facilities.

Several factors were found to be linked to the two indicators in acute care hospitals. The association between AMR or HAIs and the number of surgical beds is not straightforward. It may be a proxy for patient case mix, but it is surprising that similar factors, such as the proportion of ICU beds, were not linked to AMR. Antimicrobial prophylaxis for surgery, accounting for up to one-third of the antimicrobial agents used in a point prevalence survey [27], may be a risk factor for AMR, as reported previously at patient level [28]. Surgery itself may increase the risk of BSI following surgical site infection, as surgical devices create a micro-environment similar to that of burns, facilitating the growth of bacterial species [29]. Moreover, both scores were significantly linked to the level of AHR use, highlighting the key role of hand hygiene in preventing HAIs and the transmission of multi-drug-resistant bacteria. This result is consistent with those from many international studies

[12,30,31], reinforcing the need to continue promoting hand hygiene.

The two indicators considered were also associated with staff absenteeism rates. The ratio of nurses and nursing assistants to patients is crucial to ensure the quality of care. Staff turnover and understaffing have been matters of considerable concern for years, particularly in the wake of the COVID-19 pandemic. Absenteeism is partially compensated by overtime, and by the employment of temporary staff who are likely to be less well informed about the institution standard of care as concerns hand hygiene, for example. Staffing rates for nurses have been reported to affect patient outcomes (length of stay, re-admission, mortality) [32] and primary BSI rates [33]. Periods of understaffing have also been associated with higher rates of cross-transmission for multi-drug-resistant bacteria [34]. Healthcare worker absenteeism was significantly correlated with both scores in the stepwise model in the present study, but not in the second analysis based on a more conservative statistical model ($P=0.07$ for both scores). This discrepancy may be explained by the small number of hospitals in this study ($N=18$); the results require confirmation in a larger group of hospitals.

Unsurprisingly, carbapenem use was also linked to the two scores in the stepwise model. Carbapenem is probably used in response to a high frequency of resistance to ESC in Enterobacterales [35], which is frequently encountered in HAIs, and may therefore be an effect rather than a cause of AMR [36]. This conclusion is supported by the fact that the AMR score does not specifically consider resistance to carbapenems. In an era in which carbapenem resistance is on the increase in GNB, this finding highlights the importance of policies controlling the cross-transmission of extended-spectrum beta-lactamase-producing bacteria, and aiming to spare carbapenems through the use of alternative antibiotic regimens [36]. Interestingly, carbapenem use was not associated with HAI score in the Lasso model, probably because the use of antibiotics is less strongly related to the incidence of HAIs than the use of AHR.

Of note, it was not possible to demonstrate a relationship between the size of the ICT and the two scores. Most healthcare facilities in the consortium comply with national recommendations. ICT staffing ratios were therefore fairly similar between hospitals, and were not discriminant for comparisons. Finally, AST staffing levels remained associated with AMR score but not with HAI score. The number of infections and the use of

antibiotics varied between hospitals, possibly due to differences in the types of activities and numbers of hospital beds between hospitals in the consortium. The policy is to support the staffing of ASTs to promote good practice, particularly in hospitals treating large numbers of infections and with high levels of antibiotic use, potentially accounting for the positive correlation of this factor with the AMR score for resistant GNB-BSIs. The lack of association of HAI score with the staffing level of ASTs is not surprising, as the mission of these teams is the promotion of correct antibiotic use rather than the prevention of HAIs [37].

This study has several limitations. First, the results are derived from data limited to 2019, but similar results were obtained for the variables associated with AMR score in 2020 (data not shown). The COVID-19 pandemic may have triggered changes in hospital organization and hygiene practices. As such, the authors intend to apply this model to more recent data from the hospital consortium. However, confirmation of the validity of the scores is required in a larger, external cohort of hospitals. Second, it was not possible to consider all the variables known to affect the risk of AMR or HAIs at patient level. New information technologies may make it possible to combine patient-level data, including case mix, and hospital-level data.

In conclusion, two scores were developed that take into account many indicators of HAIs or AMR in GNB-BSIs. These scores varied considerably between hospitals. Following multi-variable analyses, characteristics of interest linked to a higher AMR or HAI score were identified, and these should be considered for adjustment during benchmarking. The proportion of surgical beds in the facility emerged as a variable of interest for adjustment before comparisons, and carbapenem use should be considered to be a consequence of high AMR. The rate of staff absenteeism and the level of hand hygiene, evaluated indirectly on the basis of AHR consumption, were independently associated with higher scores and should be targeted as priorities for prevention. Hence, and as stressed by the World Health Organization, adequate nurse staffing and hand hygiene should be considered matters of priority and should be improved to curb AMR and HAIs.

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Author contributions

RA: conceptualization, methodology, investigation, writing – original draft, writing – review and editing. BG: methodology. SF: investigation. CM: methodology and investigation. DT: data collection. VS: data collection. VJ: investigation. JR: supervision, writing – review and editing. CBVH: data collection.

Conflict of interest statement

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References

- [1] Prestinaci F, Pezzotti P, Pantosti A. Antimicrobial resistance: a global multifaceted phenomenon. *Pathog Glob Health* 2015;109:309–18.
- [2] European Centre for Disease Control and Prevention. Antimicrobial resistance in the EU/EEA (EARS-Net): annual epidemiological report for 2021. Stockholm: ECDC; 2022. Available at: https://www.ecdc.europa.eu/sites/default/files/documents/AER-EARS-Net-2021_2022-final.pdf.
- [3] Zhou N, Cheng Z, Zhang X, Lv C, Guo C, Liu H, et al. Global antimicrobial resistance: a system-wide comprehensive investigation using the Global One Health Index. *Infect Dis Poverty* 2022;11:92.
- [4] Santé Publique France. Surveillance de la consommation d'antibiotiques et des résistances bactériennes en établissement de santé. Mission Spares. Résultats 2021. Saint-Maurice: Santé Publique France; 2021. Available at: <https://www.santepubliquefrance.fr/import/surveillance-de-la-consommation-d-antibiotiques-et-des-resistances-bacteriennes-en-etablissement-de-sante.-mission-spares.-resultats-2021>.
- [5] Surveillance et Prévention des Infections Associées aux Dispositifs Invasifs (SPIADI). Rapport national de surveillance des infections associées aux dispositifs invasifs. Résultats de la surveillance menée en 2021. Tours: SPIADI; 2021. Available at: <https://www.spiadi.fr/> [last accessed August 2023].
- [6] Browne AJ, Chipeta MG, Haines-Woodhouse G, Kumaran EPA, Hamadani BHK, Zarea S, et al. Global antibiotic consumption and usage in humans, 2000e18: a spatial modelling study. *Lancet Planet Health* 2021;5:e893–904.
- [7] Dumartin C, Rogues A-M, Amadeo B, Pefau M, Venier A-G, Parneix P, et al. Antibiotic stewardship programmes: legal framework and structure and process indicator in Southwestern French hospitals, 2005–2008. *J Hosp Infect* 2011;77:123–8.
- [8] Menendez ME, Ring D. Do hospital-acquired condition scores correlate with patients' perspectives of care? *Qual Manag Health Care* 2015;24:69–73.
- [9] Prowle JR, Echeverri JE, Ligabo EV, Sherry N, Taori GC, Crozier TM, et al. Acquired bloodstream infection in the intensive care unit: incidence and attributable mortality. *Crit Care* 2011;15:R100.

- [10] European Centre for Disease Prevention and Control. European surveillance of healthcare-associated infections in intensive care units: HAI Net ICU protocol, Version 1.02. Stockholm: ECDC; 2015. Available at: <https://www.ecdc.europa.eu/sites/default/files/media/en/publications/Publications/healthcare-associated-infections-HAI-ICU-protocol.pdf>.
- [11] Fluit AC, Jones ME, Schmitz F-J, Acar J, Gupta R, Verhoef J, et al. Antimicrobial susceptibility and frequency of occurrence of clinical blood isolates in Europe from the SENTRY Antimicrobial Surveillance Program, 1997 and 1998. *Clin Infect Dis* 2000;30:454–60.
- [12] Pittet D, Allegranzi B, Sax H, Dharan S, Pessoa-Silva CL, Donaldson L, et al. Evidence-based model for hand transmission during patient care and the role of improved practices. *Lancet Infect Dis* 2006;6:641–52.
- [13] Witt LS, Howard-Anderson JR, Jacob JT, Gottlieb LB. The impact of COVID-19 on multidrug-resistant organisms causing healthcare-associated infections: a narrative review. *JAC Antimicrob Resist* 2022;5:dla130.
- [14] European Committee on Antimicrobial Susceptibility Testing. Clinical breakpoints – breakpoints and guidance. Växjö: EUCAST; 2023. Available at: https://www.eucast.org/clinical_breakpoints.
- [15] World Health Organization. Definition and general considerations. Geneva: WHO; 2018. Available at: https://www.whocc.no/ddd/definition_and_general_considera/.
- [16] Autorité de santé Haute. Fiche descriptive 2019. Thème infections associées aux Soins, ICSHA. Version 3. Saint Denis: HAS; 2019. Available at: https://www.has-sante.fr/upload/docs/application/pdf/2019-04/fiche_descriptive_icsha.3_2019.pdf.
- [17] Direction Générale de la Santé, République Française, circulaire DGS/DHOS/E2 N° 645 du 29 décembre 2000, relative à l'organisation de la lutte contre les infections nosocomiales dans les établissements de santé. Paris; 2000. Available at: <https://www.preventioninfection.fr/document/circulaire-dgs-dhos-e2-n-2000-645-du-29-decembre-2000-relative-a-lorganisation-de-la-lutte-contre-les-infections-nosocomiales-dans-les-etablissements-de-sante/> [last accessed August 2023].
- [18] Autorité de santé Haute. Fiche descriptive 2018. Thème infections associées aux Soins, ICATB.2. Saint Denis: HAS; 2018. Available at: https://www.has-sante.fr/upload/docs/application/pdf/2016-04/2016_has_fiche_descriptive_icatb_2.pdf.
- [19] Columbia University Irving Medical Center. Least absolute shrinkage and selection operator (LASSO). New York: Columbia University; 2014. Available at: <https://www.publichealth.columbia.edu/research/population-health-methods/least-absolute-shrinkage-and-selection-operator-lasso>.
- [20] Santé publique France. Surveillance de la consommation d'antibiotiques et des résistances bactériennes en établissement de santé: mission Spares. Résultats 2021. Saint Maurice: Santé publique France; 2021. Available at: <https://www.santepubliquefrance.fr/maladies-et-traumatismes/infections-associees-aux-soins-et-resistance-aux-antibiotiques/resistance-aux-antibiotiques/documents/rapport-synthese/surveillance-de-la-consommation-d-antibiotiques-et-des-resistances-bacteriennes-en-etablissement-de-sante-mission-sparres.-resultats-2021>.
- [21] Poku E, Cooper K, Cantrell A, Harnan S, Sin MA, Zanzudana A, et al. Systematic review of time lag between antibiotic use and rise of resistant pathogens among hospitalized adults in Europe. *JAC Antimicrob Resist* 2022;5:dla001.
- [22] Maki DG, Crnich CJ, Safdar N. Nosocomial infection in the intensive care unit. In: *Critical care medicine*. Maryland Heights, MO: Mosby; 2008. p. 1003–69.
- [23] Nelson EC, Wang C-H, Huang G, Kuo N-W. Institutional factors associated with the incidence rates of central line-associated bloodstream infection in California community hospitals. *PLoS One* 2022;17:e0274436.
- [24] Yu KC, Ye G, Edwards JR, Gupta V, Benin AL, Ai C, et al. Hospital-onset bacteremia and fungemia: an evaluation of predictors and feasibility of benchmarking comparing two risk-adjusted models among 267 hospitals. *Infect Control Hosp Epidemiol* 2022;43:1317–25.
- [25] European Centre for Disease Prevention and Control. Antimicrobial consumption in the EU/EEA (ESAC-Net), Annual Epidemiological Report for 2021. Stockholm: ECDC; 2021. Available at: https://www.ecdc.europa.eu/sites/default/files/documents/ESAC-Net_AER_2021_final-rev.pdf.
- [26] Jarlier V, Diaz Högberg L, Heuer OE, Campos J, Eckmanns T, Giske CG, et al. Strong correlation between the rates of intrinsically antibiotic-resistant species and the rates of acquired resistance in Gram-negative species causing bacteraemia, EU/EEA, 2016. *Eurosurveillance* 2019;24:1800538.
- [27] Santé Publique France. Principaux résultats de l'enquête nationale de prévalence 2022 des infections nosocomiales et des traitements anti-infectieux en établissement de santé. Saint Maurice: Santé Publique France; 2022. Available at: <https://www.santepubliquefrance.fr/import/principaux-resultats-de-l-enquete-nationale-de-prevalence-2022-des-infections-nosocomiales-et-des-traitements-anti-infectieux-en-etablissement-de-s>.
- [28] Menz BD, Charani E, Gordon DL, Leather AJ, Moonesinghe SR, Phillips CJ. Surgical antibiotic prophylaxis in an era of antibiotic resistance: common resistant bacteria and wider considerations for practice. *Infect Drug Resist* 2021;14:5235–52.
- [29] Clancy C, Dunne SS, Baban C, Tormey S, Merrigan A, O'Connell NH, et al. A hypothesis for association between electrical surgical incision techniques and surgical site infection. *J Hosp Infect* 2022;128:36–8.
- [30] World Health Organization. WHO guidelines on hand hygiene in health care. Geneva: WHO; 2009. Available at: https://apps.who.int/iris/bitstream/handle/10665/44102/9789241597906_eng.pdf;jsessionid=849762C65E851A297560B56D529CD6E1?sequence=1.
- [31] Fournier S, Brun-Buisson C, Jarlier V. Twenty years of antimicrobial resistance control programme in a regional multi hospital institution, with focus on emerging bacteria (VRE and CPE). *Antimicrob Resist Infect Control* 2012;1:9.
- [32] McHugh MD, Aiken LH, Sloane DM, Windsor C, Douglas C, Yates P. Effects of nurse-to-patient ratio legislation on nurse staffing and patient mortality, readmissions, and length of stay: a prospective study in a panel of hospitals. *Lancet* 2021;397:1905–13.
- [33] Robert J, Fridkin SK, Blumberg HM, Anderson B, White N, Ray SM, et al. The influence of the composition of the nursing staff on primary bloodstream infection rates in a surgical intensive care unit. *Infect Control Hosp Epidemiol* 2000;21:12–7.
- [34] Dancer SJ, Coyne M, Speekenbrink A, Samavedam S, Kennedy J, Wallace PGM. MRSA acquisition in an intensive care unit. *Am J Infect Control* 2006;34:10–7.
- [35] Gauzit R, Pean Y, Alfordari S, Bru J-P, Bedos J-P, Rabaud C, et al. Carbapenem use in French hospitals: a nationwide survey at the patient level. *Int J Antimicrob Agents* 2015;46:707–12.
- [36] Maillard A, Delory T, Bernier J, Villa A, Chaibi K, Escout L, et al. Effectiveness of third generation cephalosporins or piperacillin compared to cefepime or carbapenems for severe infections caused by wild-type AmpC β -lactamase-producing Enterobacterales: a multicenter retrospective propensity-weighted study. *Int J Antimicrob Agents* 2023:106809.
- [37] World Health Organization. Antimicrobial stewardship interventions: a practical guide. Geneva: WHO; 2021. Available at: <https://apps.who.int/iris/bitstream/handle/10665/340709/9789289054980-eng.pdf>.