Cost of bacteraemia caused by methicillin-resistant vs. methicillin-susceptible *Staphylococcus aureus* in Spain: a retrospective cohort study

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Abstract

The aim of this study was to determine the impact on healthcare resource utilization and associated costs of bacteraemia due to methicillin-resistant *Staphylococcus aureus* (MRSA) vs. methicillin-susceptible *S. aureus* (MSSA) strains in Spain. An observational, retrospective, cohort multicentre study was conducted during 2005. The target population comprised Spanish patients with *S. aureus* bacteraemia (five and ten cases per hospital for resistant and susceptible strains, respectively). The resources used were obtained from the hospital patient records. The unit costs were obtained from the participating hospitals and from Spanish databases; the costs of a bacteraemic episode were estimated from resource utilization results and expressed in euros (€). Univariate sensitivity analyses were performed. The clinical records of 366 valid patients with *S. aureus* bacteraemia (121 MRSA and 245 MSSA) from 27 Spanish hospitals were reviewed. Resource use per bacteraemic episode was higher for MRSA cases than for MSSA cases, with longer antibiotic treatment (3.1 additional days) and greater length of hospital stay (LOS) (2.2 additional days), more diagnostic tests, and higher rates of admission to the intensive-care unit (ICU) (7.6%). As a consequence, a higher cost per episode was incurred, with an additional €1205 in episodes of MRSA infections (1.12-fold increase). The main drivers of the cost difference were the higher rates of ICU admission and hospital re-admission and increased LOS. The analysis confirmed that there were additional costs due to resistant strains, ranging from €293 to €5188. Overall, MRSA was associated with higher costs in bacteraemic patients, and this was attributable mainly to the greater rate of ICU admissions and increased LOS.

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Introduction

Bacterial resistance is increasing both in outpatient clinics and in hospitals, and has become the subject of much research. The impact of infections caused by resistant bacteria is reflected by higher mortality, increased length of hospital stay (LOS), and increased healthcare costs [1]. In addition, this increased resistance reduces the therapeutic options available for the treatment of infections involving these microorganisms.

One of the microorganisms whose incidence has recently increased dramatically in Spanish hospitals is methicillin-resistant *Staphylococcus aureus* (MRSA). At present, both in Spain and in many countries around the world, more than 25% of *S. aureus* isolates are resistant to methicillin (although low prevalences of these strains are also found in some European regions, including The Netherlands and Scandinavian countries) [2–5].

MRSA strains are resistant to currently available β-lactam agents and frequently also to other families of antibiotics, with the notable exception of most of the so-called community-acquired MRSA strains; but these strains, as compared with sensitive strains, also cause infections, increasing the LOS and healthcare costs [6–8].

Bacteraemia is a complex clinical syndrome that is constantly changing and causes high and increasing morbidity and mortality [9]; bacteraemias caused by MRSA are rapidly becoming a serious problem in Spanish hospitals [10].

This study was aimed at the calculation of the impact of MRSA vs. methicillin-susceptible *S. aureus* (MSSA) bacteraemia on healthcare resources and associated costs in Spain.

Materials and Methods

The present study was a Spanish multicentre, retrospective, observational cohort study of the use of healthcare resources and the associated costs in the treatment of bacteraemia caused by MRSA and MSSA.

The inclusion criteria were as follows: (i) either sex; (ii) age 18 years or over; (iii) bacteraemia caused by *S. aureus* (resistant or sensitive to methicillin); and (iv) strains isolated between 1 January and 31 December 2005. Pregnant patients and cases of bacteraemia resulting from a previous stay in hospital were excluded.

Hospitals with an interest in the investigation from throughout Spain were able to participate in the study. All participating centres were required to have the study protocol approved by their respective ethics committees.

The microbiology department of each participating hospital selected five MRSA and ten MSSA cases by systematic sampling [11] in the following way. A skipping factor, $k = n/5$, was calculated, with n being the number of MRSA bacteraemias in the hospital during the study time period. The first case was selected through a random number provided in a centralized way, and the following cases were selected by applying k repeatedly until all MRSA bacteraemia cases were selected. MSSA cases were selected similarly. *S. aureus* was identified in every participating centre with conventional methods, usually automated identification–susceptibility systems [12].

To find notable economic differences ($\geq$ €300) in the overall cost per patient between patients with MRSA and those with MSSA, for a standard deviation of €600, a bilateral α-risk of 0.05, and a β-risk of 0.10, 94 patients with MRSA and 188 patients with MSSA were needed.

The study was performed from the perspective of the National Health Service; therefore, only the use of healthcare resources was recorded. The costs of bacteraemia were expressed as direct healthcare costs.

Use of resources was documented by reviewing the clinical records of all the patients who met the inclusion criteria. The following data were retrieved from the clinical history for each episode of bacteraemia: (i) patient demographic and clinical characteristics; (ii) antibiotic therapy; (iii) complementary tests; (iv) rates of hospitalization, admission to the intensive-care unit (ICU), re-admission to the ward, and LOS; (v) rates of outpatient clinics; and (vi) resources consumed during the reconstitution of the vials of antibiotics and their intravenous infusion.

The mean costs of an episode of bacteraemia caused by resistant or sensitive strains of the microorganisms studied were calculated. The cost of the antimicrobial treatments was estimated by using the recommended retail price and the rates of use per episode of bacteraemia, and taking two possible treatments into account: (i) empirical antibiotics (those administered before the results of the microbiological study were known); and (ii) targeted antibiotics (those started or continued on the day when the results of the antibiogram of the cultured microorganisms became available). The costs of the other resources per episode of bacteraemia were calculated by using their rates of use and the unit costs obtained from the hospitals that participated in the study, and from a database of Spanish healthcare costs in the sensitivity analysis. All costs are presented in euros (€) as of October 2006.

The cost per episode of bacteraemia was calculated on the basis of the following tests: (i) general analysis; (ii) monitoring of vancomycin and/or aminoglycoside levels; (iii) diagnostic imaging studies; (iv) microbiological tests; and (v) other tests, such as electrocardiogram, bronchoscopy, laparoscopy, and lumbar puncture.

In the analysis of base-case costs, the average values of the resources used and of the unit costs obtained from the study were applied. The sensitivity analysis involves modifying the values of the variables with respect to which there is uncertainty in verifying to what extent the results of the base case are affected.

In order to verify the robustness of this analysis, several unifactorial simple sensitivity analyses were performed in the following scenarios: (i) use of unit costs from a database of healthcare costs in Spain; (ii) lower and upper limits of the 95% CI of the use of healthcare resources; (iii) minimum and maximum values of the unit costs of the resources obtained in the study; and (iv) minimum and maximum values of the resources and unit costs taken together.

Qualitative and quantitative descriptive analyses were performed for all variables. The qualitative variables were analysed using absolute frequencies and percentages, whereas the quantitative variables were analysed using the mean, 95% CI for the mean, median, standard deviation, minimum, and maximum. All demographic data and histories were analysed to examine any difference between the groups, using the Student *t*-test for independent measures in the case of continuous data distributed normally, or the Mann–Whitney *U*-test if the parametric requirements were not met. A chi-squared test (or Fisher exact test, where necessary) was used to compare the categorical variables between the treatment groups. The Kolmogorov–Smirnov test was used to compare the normality of the distribution of the continuous variables, whereas the Levene test was used to analyse the homogeneity of the variances. All analyses were performed using the statistical program SPSS 13.0.

Results

Of 530 initially recruited patients, we reviewed the clinical histories of 366 valid patients (patients from whom at least the following data had been collected: admission date, discharge date (or death), and number of complementary tests performed) with *S. aureus* bacteraemia (121 MRSA and 245 MSSA); 27 hospitals from throughout Spain participated in the study.

Older patients had more isolates of resistant strains of *S. aureus*. A large percentage of MRSA strains were from patients with nosocomial bacteraemia. No differences in Charlson's comorbidity index were observed among patients with *S. aureus* bacteraemia, although there was a greater incidence of cerebrovascular disease, dementia, hemiplegia and diabetes mellitus with end-organ damage in the group with MRSA bacteraemia, and of metastatic solid tumours in the group with MSSA bacteraemia (Table 1).

Table 2 summarizes the results obtained with respect to the antibiotics used in the bacteraemic episode. The proportions of patients with MRSA or with MSSA infections treated with antibiotics at the time of blood culture were 46.8% and 25.0%, respectively (p <0.001). Antimicrobial empirical therapy was administered in 90.2% of patients of each type. Differences in total duration of antibiotic therapy were not statistically significant.

The most frequently used (over 5%) empirical antibiotics in patients with resistant and susceptible strains were as follows: vancomycin (16.4% and 15.7%, respectively), amoxycillin–clavulanic acid (16.4% and 16.0%), ciprofloxacin (9.4% and 4.4%), piperacillin–tazobactam (8.2% and 5.2%), imipenem (7.5% and 5.0%), and levofloxacin (6.3% and 6.7%). The most frequently used targeted antibiotics in MRSA and MSSA bacteraemia were as follows: vancomycin (26.1% and 9.7%, respectively), teicoplanin (12.8% and 5.0%), linezolid (8.0% and 2.4%), amoxycillin–clavulanic acid (6.6% and 9.5%), and imipenem (5.8% and 3.7%).

As shown in Table 3, the number of complementary tests was greater in patients with resistant microorganisms than in the MSSA-infected patients. As compared with the latter, patients with MRSA infection had an increased LOS (2.2 additional days), a higher rate of admission to the ICU (7.6% more), and a lower rate of re-admission to hospital because of ineffective therapy (0.7% less) (Table 3).

No differences were observed in the number of external consultations or in the resources used for antibiotic preparation and administration. Average costs were estimated per episode of bacteraemia. Twenty-one per cent of patients

TABLE 1. Demographic and clinical characteristics of patients with bacteraemia included in the study

	MRSA *N* = 121	MSSA *N* = 245	p-value
Demographic characteristics			
Age (years), mean (SD)	67.9 (14.51)	62.8 (17.33)	0.003
Sex: women (%)	38.0	31.8	NS
Clinical characteristics			
Community-acquired/nosocomial (%)	19.2/80.8	45.9/54.1	<0.0001
Severity: with/without sepsis/septic shock (%)	63.6/36.4	51.0/49.0	0.023
Source of infection (%)			
Central venous catheter	30.4	22.7	–
Skin and soft tissue	20.7	14.9	–
Lower respiratory tract	16.3	10.8	–
Peripheral catheter	12.0	15.5	–
Underlying condition (McCabe and Jackson)			
Not life-threatening (%)	41.7	55.0	NS
Life-threatening (long-term) (%)	45.8	35.5	–
Life-threatening (short-term) (%)	12.5	9.5	–
Charlson comorbidity index, mean (SD)	3.63 (2.61)	3.24 (2.53)	NS
Myocardial infarction (%)	12.4	11.4	NS
Congestive heart failure (%)	25.6	21.2	NS
Peripheral vascular disease (%)	22.3	16.7	NS
Cerebrovascular disease (%)	16.5	7.8	0.01
Dementia (%)	10.7	4.5	0.023
Chronic pulmonary disease (%)	22.3	15.1	NS
Connective tissue disease (%)	1.7	2.0	NS
Chronic ulcer (%)	5.0	6.5	NS
Liver disease (mild–moderate) (%)	2.5	4.5	NS
Diabetes mellitus (%)	21.5	18.4	NS
Hemiplegia (%)	9.1	2.9	0.009
Renal disease (moderate–severe) (%)	23.1	21.6	NS
Diabetes mellitus with end-organ damage (%)	14.0	6.9	0.027
Malignant solid tumour (%)	14.9	14.3	NS
Leukaemia (%)	1.7	1.2	NS
Malignant lymphoma (%)	1.7	1.6	NS
Chronic liver disease (%)	8.3	6.1	NS
Metastatic solid tumour (%)	5.8	12.7	0.043
Other comorbidity factors			
Intravenous drug use (%)	0.8	6.9	0.001
Use of other drugs (%)	1.7	3.7	NS
Alcoholism (%)	10.7	7.3	NS
Neutropenia (%)	1.7	1.2	NS
Immunosuppressants (%)	2.5	4.5	NS
Corticosteroids (%)	14.0	7.3	0.04
Surgery or trauma (%)	24.0	8.2	<0.05
Hepatic insufficiency (%)	3.3	3.3	NS
Invasive procedures (%)	23.1	22.0	NS
Mechanical ventilation (%)	9.9	4.5	0.04
Total parenteral nutrition (%)	12.4	4.5	0.006
No. of hospital admissions, mean (SD)[a]	2.26 (1.65)	2.00 (1.46)	NS
Previous infection (%)	7.4	3.7	NS
Chemotherapy (%)	5.8	6.1	NS
Central/peripheral catheter (%)	75.2	64.9	0.04
Episode of bacteraemia			
Type: primary/secondary (%)	29.8/70.2	27.5/72.5	NS
Clinical repercussion: yes/no (%)	81.8/18.2	73.0/27.0	NS
Type of sepsis[b] (%)	–	–	0.01
Sepsis	58.3	62.9	–
Severe sepsis	22.9	13.5	–
Septic shock	2.1	10.7	–
Multi-organ failure	16.7	12.9	–
Deaths[c] (%)	39.7	25.3	0.005
Related to the infection	61.7	56.2	NS
Related to the underlying condition	29.8	34.4	NS
Other causes	8.5	9.4	NS

SD, standard deviation; NS, non-significant difference (p >0.05); MRSA, methicillin-resistant *Staphylococcus aureus* ; MSSA, methicillin-susceptible *S. aureus*.
[a]During the previous 12 months.
[b]Sepsis: the systematic response to infection, manifested by two or more of the following conditions as a result of infection: (i) temperature >38°C or <36°C; (ii) heart rate >90 beats/min; (iii) respiratory rate >20 breaths/min or P_{aCO_2} <32 mmHg; and white blood cell count >12 000/μL, <4000/μL, or >10% immature (band) forms.
[c]In-hospital mortality.
Severe sepsis: sepsis associated with organ dysfunction, hypoperfusion, or hypotension. Hypoperfusion and perfusion abnormalities may include, but are not limited to, lactic acidosis, oliguria, and acute mental alteration.
Septic shock: sepsis induced with hypotension despite adequate fluid resuscitation along with the presence of perfusion abnormalities that may include, but are not limited to, lactic acidosis, oliguria, or acute alteration in mental status. Patients who are receiving inotropic or vasopressor agents may not be hypotensive at the time when perfusion abnormalities are measured.
Multi-organ failure: presence of altered organ function in an acutely ill patient such that homeostasis cannot be maintained without intervention.

TABLE 2. Antibiotic treatment during the bacteraemic episodes

	MRSA	MSSA	p-value
Antibiotic treatment at the time of the blood culture			
Patients treated (%)	46.8	25	<0.001
Empirical antibiotic treatment[a]			
Patients treated (%)	90.2	90.2	NS
Duration of treatment (days), mean (SD)	3.45 (1.81)	3.17 (1.62)	NS
Evaluation of empirical treatment (%)			
Appropriate[b]	79	82.7	NS
Inappropriate	21	17.3	NS
Modification or suspension of empirical treatment (%)	61	61.1	NS
Because of antibiogram results	73.8	76.9	NS
Because of microbiological findings not being covered	14.8	9.1	NS
Because of poor clinical response	13.1	13.2	0.04
Because of adverse effects	6.6	0.8	NS
Because of other causes	9.8	13.2	NS
Targeted antibiotic treatment[c]			
Patients treated (%)	86.8	84.5	NS
Duration of treatment (days), mean (SD)	19.07 (22.63)	16.03 (13.35)	NS
No. of antibiotics, mean (SD)	2.17 (1.13)	2.00 (1.29)	
Total duration of antibiotic treatment			
Days, mean (SD)	20.99 (22.03)	17.82 (13.24)	NS

SD, standard deviation; NS, non-significant statistical difference (p >0.05); MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *S. aureus*.
[a]Empirical treatment is defined as that administered before the results of the antibiogram are known.
[b]Treatment with an empirical antibiotic was considered to be 'appropriate' if at least one of the antimicrobial agents administered showed proven *in vitro* activity against the microorganism and had been administered at the correct dose and by the correct route for a sufficient period of time.
[c]Targeted treatment is defined as that started or continued on the day when results of the antibiogram of the cultured microorganism became available.

were hospitalized in infectious diseases units and 36% in the internal medicine department.

The results of the analysis of costs for the base case are shown in Table 4. The greater consumption of resources observed in cases of bacteraemia caused by MRSA generated a greater cost per episode than for the MSSA cases. The main determinants of the difference in costs were the greater risk of admission to the ICU and the increased LOS for patients with bacteraemia due to MRSA. The average costs per episode of bacteraemia were €11044.59 and €9839.25, with and without staphylococcal resistance to methicillin, respectively (a difference of €1205.34; 1.12-fold greater cost for MRSA episodes) (Table 4). The costs of complementary tests were higher in cases of bacteraemia caused by MSSA than in that caused by MRSA (Table 4), as patients infected with MSSA received more aminoglycosides (2.4 vs. 1.3, respectively) and underwent more laparoscopies (1.2 vs. 0, respectively) (Table 3).

The sensitivity analyses confirmed the robustness of the base case, with incremental costs due to resistant strains ranging from €293 to €5188 for MRSA, according to the setting (Table 4). The use of unit costs obtained from

TABLE 3. Complementary tests, hospitalization, admission to the intensive-care unit (ICU), and re-admissions per bacteraemic episode (values of the number of tests or days expressed as mean (95% CI); patients expressed as percentages)

Item	MRSA	MSSA
No. of complementary tests		
General analyses		
Biochemistry	9.5 (7.1–11.9)	7.2 (6.1–8.3)
Complete blood count	8.7 (6.5–10.9)	6.7 (5.5–7.7)
Urine sediment	2.0 (1.7–2.3)	1.9 (1.5–2.3)
Arterial blood gas	8.5 (3.4–13.6)	5.9 (4.0–7.8)
Coagulation tests	4.9 (3.7–6.1)	4.7 (3.8–5.6)
Antibiotic monitoring		
Vancomycin	2.9 (1.8–4.0)	2.6 (0.3–4.9)
Aminoglycosides	1.3 (0.6–2.0)	2.4 (1.6–3.2)
Imaging tests		
X-ray	4.9 (3.3–6.5)	3.8 (3.0–4.6)
Ultrasound	1.4 (1.0–1.8)	1.2 (1.1–1.3)
Computed tomography	1.5 (1.3–1.7)	1.5 (1.3–1.7)
Magnetic resonance imaging	1.2 (0.9–1.5)	1.4 (1.1–1.7)
Transoesophageal echocardiogram	1.0 (1.0–1.0)	1.4 (1.2–1.8)
Transthoracic echocardiogram	1.1 (0.9–1.3)	1.2 (1.1–1.3)
Microbiological tests		
Blood cultures	3.1 (2.7–3.5)	3.0 (2.7–3.3)
Urine cultures	1.6 (1.3–1.9)	1.4 (1.3–1.5)
Other cultures	5.0 (3.7–6.3)	3.7 (2.9–4.5)
Other tests		
Electrocardiogram	2.6 (1.5–3.7)	2.4 (1.9–2.9)
Bronchoscopy	1.5 (0.7–2.3)	1.0 (1.0–1.0)
Laparoscopy	0 (0–0)	1.2 (0.8–1.6)
Lumbar puncture	1.8 (0.6–3.0)	1.2 (1.0–1.4)
Hospitalization		
Days in the ward	24.88 (19.9–29.9)	22.66 (18.8–26.5)
Admission to the ICU		
Percentage of patients admitted	28.7	21.1
Days in the ICU	18.70 (10.9–26.5)	14.88 (10.1–19.7)
Re-admission to the ward		
Percentage of patients re-admitted	5.2	5.9
Days in the ward[a]	18.0 (15.1–20.9)	13.9 (11.8–16.1)

MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *S. aureus*.
[a]Re-admission is estimated to be 50% of the duration of the initial admission.

Spanish databases instead of the costs provided by the participating hospitals slightly increased the cost differences between cases caused by resistant and sensitive strains (Table 4).

Discussion

The current study shows that MRSA bacteraemias generate additional costs per episode, as compared with those generated by MSSA bacteraemias. The total cost of an MRSA bacteraemia episode was 1.12-fold higher than that of an episode caused by sensitive strains (€11044 and €9839, respectively), with the MRSA-associated cost increase being mainly due to the greater rate of admissions to the ICU and increased LOS.

The costs of *S. aureus* bacteraemias are higher (although within the range) than those of Diagnosis Related Group (DRG) 416 (septicaemia in patients aged over 17 years),

TABLE 4. Cost analysis of treatment for methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-susceptible *S. aureus* (MSSA) bacteraemias; costs per bacteraemia episode (€, October 2006)

	MRSA	MSSA	Difference
Base case[a]			
Empirical antibiotic	51.05	36.69	14.36
Targeted antibiotic	285.12	128.55	156.57
Complementary tests	1820.50	2572.44	−751.94
Hospitalization/ICU	8703.86	6917.51	1786.35
Consultations and intravenous administration	184.06	184.06	0
Total	11 044.59	9839.25	1205.34
Sensitivity analysis			
Unit costs as per database	12 540.80	10 775.30	1765.50
Minimum use of resources	7880.71	6189.06	1961.65
Maximum use of resources	14 518.47	15 489.20	−970.73
Maximum use of resources[b]	14 518.47	9330.34	5188.13
Minimum values of unit costs	4028.21	3426.26	601.95
Maximum values of unit costs	19 706.04	19 386.58	319.46
Minimum values of resources and costs	3080.24	2787.24	293
Maximum values of resources and costs	25 207.20	22 360.06	2847.14

ICU, intensive-care unit.
[a]Base case: mean values of the use of resources and of the unit costs obtained from the retrospective study.
[b]Laparoscopy test was excluded.

which in Spain are €5710 (between €2742 and €9811). The costs of DRG 416 are similar to data available for catheter-related bacteraemia, according to the Spanish healthcare database. Nevertheless, DRG 416 includes all types of sepsis, regardless of whether the causative microorganism is resistant to antimicrobials. In fact, the maximum costs of DRG 416 are similar to those incurred for bacteraemia caused by MSSA strains, i.e. €9839.

The costs of complementary tests were greater in cases of bacteraemia caused by MSSA than in those caused by MRSA, as patients infected with the sensitive strain received more aminoglycosides. Among the latter, there were more intravenous drug users, and the greater use of aminoglycosides might be related to the presence of endocarditis.

No Spanish study evaluating the cost of bacteraemia due to *S. aureus* has been identified. In 1988, a study was published concerning the cost of catheter-related bacteraemia in 22 patients [13]; the cost was calculated to be €4152 per episode (updated to 2006), which is lower than the cost per MRSA bacteraemic episode (€9839).

The cost of resistance in MRSA has been evaluated in studies carried out in other countries. One study examined the impact of methicillin resistance on LOS and the costs in patients with MRSA bacteraemia [14]. When deaths were excluded, resistance to methicillin was associated with a significant increase in the mean LOS after acquisition of infection and with an increase in costs ($26 424 in the MRSA group as compared with $19 212 in the methicillin-sensitive group; p 0.008). Methicillin resistance was an independent predictor of an increase in LOS (1.3-fold; p 0.016) and in costs (1.4-fold; p 0.017). Another prospective and comparative study in patients on haemodialysis and with MRSA bacteraemia as compared with MSSA bacteraemia also found an increase in LOS and hospital costs [15]. A study published in the USA in 2000 [16] calculated the mean cost of a patient with MRSA infection to be $23 000, whereas, if the strain was sensitive, the cost fell to $19 500. These costs were greater than the average observed in the current study (€11 044 and €9839, respectively). In the US study [18], the presence of resistant strains led to a 2.7-day longer LOS than that attributable to sensitive strains, and was associated with higher mortality (34% vs. 24%, respectively). In our study, LOS increased by 2.2 days, and higher mortality was also observed (39.7% vs. 25.3%; p 0.005) in the group with MRSA bacteraemia.

In the study of Abramson *et al.* [7], median attributable hospital stay associated with MSSA bacteraemia was 4 days, much less than the 12 days recorded for MRSA (p 0.023). Moreover, MRSA infection led to a three-fold increase in direct costs relative to MSSA infection. Most of the differential cost was due to the notable impact of MRSA infection on LOS. Other recent studies have confirmed that patients with MRSA infection have increased LOS [17,18] and generate greater sanitary costs [20]. It is also interesting to point out that Dutch/Belgian studies have shown that, from an economic perspective, the search and destroy policy is the best alternative for maintaining an endemic MRSA level at <1% and is a cost-effective policy at an MRSA prevalence of ≤8% [19,20].

The main limitation of our study is its retrospective design, which explains the lack of some data in the clinical histories in a small number of patients. This led us to carry out the analyses only in patients with available data for each variable. Regarding the comparability of study patients, it must be taken into account than MRSA-infected patients were older, with a higher incidence of nosocomial bacteraemia. An important strength of the study was that the results obtained were those observed in clinical practice. Another strength was the robustness of the results of the sensitivity analyses performed, which were based mainly on the limits of the 95% CI of the average values obtained.

Given the high incidence of infections caused by MRSA, quantifying their health and economic impact is important for clinicians, hospital financial managers, and policy-makers. Taking measures to minimize the spread of MRSA within the hospital is essential; so this information is necessary to justify resource allocation for the development of strategies to fight against antibiotic resistance and to prevent the spread of

resistant organisms within the healthcare environment. Antimicrobial management programmes should be directed at ensuring the most appropriate use of antimicrobials rather than focusing simply on limiting choices.

Transparency Declaration

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Appendix: Cost of Resistance Study Group

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