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**Authors:** Tissot F, Calandra T, Prod'homme G, Taffe P, Zanetti G, Greub G, Senn L

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1 **Mandatory infectious diseases consultation for MRSA bacteremia is associated with**  
2 **reduced mortality.**

3 Tissot F, Calandra T, Prod'hom G, Taffe P, Zanetti G, Greub G, Senn L

4 **Lausanne University Hospital**

5

6 **Summary**

7 **Objectives :** Although infectious disease (ID) consultation has been associated with lower  
8 mortality in *Staphylococcus aureus* bloodstream infections, it is still not mandatory in many  
9 centers. This study aimed at assessing the impact of ID consultation on diagnostic and  
10 therapeutic management of methicillin-resistant *S. aureus* (MRSA) bacteremia.

11 **Methods :** Retrospective cohort study of all patients with MRSA bacteremia from 2001 to  
12 2010. ID consultations were obtained on request between 2001 and 2006 and became  
13 mandatory since 2007.

14 **Results :** 156 episodes of MRSA bacteremia were included, mostly from central venous  
15 catheter (32%) and skin and soft tissue (19%) infections. ID consultation coverage was 58%  
16 between 2001 and 2006 and 91% between 2007 and 2010. ID consultation was associated  
17 with more echocardiography (59% vs. 26%,  $p<0.01$ ), vancomycin trough level measurements  
18 (99% vs. 77%,  $p<0.01$ ), follow-up blood cultures (71% vs. 50%,  $p=0.05$ ), deep-seated  
19 infections (43% vs. 16%,  $p<0.01$ ), more frequent infection source control (83% vs. 57%,  
20  $p=0.03$ ), a longer duration of MRSA-active therapy (median and IQR: 17 days, 13-30, vs. 12,  
21 3-14,  $p<0.01$ ) and a 20% reduction in 7-day, 30-day and in-hospital mortality.

22 **Conclusions :** ID consultation was associated with a better management of patients with  
23 MRSA bacteremia and a reduced mortality.

24 **Key words:**

25 MRSA; bloodstream infection; infectious diseases consultation; outcome

26 **Introduction**

27 *Staphylococcus aureus* is a leading cause of both community-acquired and healthcare-  
28 associated bloodstream infections, with a reported mortality of 20-40% that has remained  
29 stable over the last decades [1-4]. Factors associated with mortality include comorbidities,  
30 severity of infection, community acquisition, inappropriate treatment, failure to identify a  
31 primary source of infection and to remove intravascular foci of infection [1, 2, 5-8]. Several  
32 studies have shown a higher mortality rate associated with methicillin-resistant *S. aureus*  
33 (MRSA) infection compared to methicillin-susceptible *S. aureus* (MSSA), although this issue  
34 remains controversial and could be related to confounding factors such as age, underlying  
35 conditions and inappropriate treatment rather than methicillin-resistance per se [3, 7-9].

36 Timely and effective management of *S. aureus* bloodstream infections is of utmost  
37 importance. Several publications have reported a significant impact of infectious diseases  
38 (ID) consultation in improving diagnostic work-up and outcome of *S. aureus* bacteremia [1,  
39 10-12]. Although some centers have reported an impact of mandatory consultation, , it is still  
40 not applied universally, with proportions of *S. aureus* bacteremia seen by ID specialists as  
41 low as 27-51% [5, 11-13]. Besides lack of randomized clinical trials, one potential obstacle to  
42 universal uptake is limited knowledge of which patients would particularly benefit from ID  
43 consultation. Specifically, published data on impact of ID consultation on MRSA bacteremia  
44 are scarce [14].

45 The aim of the present study was to assess the impact of ID consultation on the diagnostic  
46 workup, choice of antimicrobial treatment, source control and patient's outcome of methicillin-  
47 resistant *S. aureus* (MRSA) bacteremia.

48

49 **Methods**

50 **Study setting.** Our hospital is a 1000-bed tertiary-care center with 36000 admissions per  
51 year. The proportion of MRSA among clinical *S. aureus* isolates was 12% between 2001 and  
52 2008, and increased to 23% in 2010. The microbiology laboratory reports daily all positive  
53 blood cultures to the physician in charge and to ID physicians.

54 **Study design.** To assess the impact of ID consultation on the diagnostic workup, choice of  
55 antimicrobial treatment, source control and patient's outcome of MRSA bacteremia, we  
56 conducted a retrospective cohort study. All MRSA bacteremia that occurred in adult patients  
57 between January 2001 and December 2010 were identified through the microbiology  
58 laboratory database. Medical charts and written ID consultations were reviewed for  
59 demographic and clinical data including sex, age, underlying conditions, site of infection,  
60 antimicrobial therapy, source control and clinical outcome. Exclusion criteria were: age under  
61 18, transfer to another hospital or initiation of palliative care for end-of-life situations within  
62 72h of bacteremia onset or death before result of blood cultures. The study was approved by  
63 the institutional ethics committee; informed consent was not needed.

64 **Definitions.** MRSA bacteremia was defined as the occurrence of at least one positive blood  
65 culture for MRSA in the presence of concomitant signs of infection. Recurrence of MRSA  
66 bacteremia within the same patient was considered a distinct episode only if occurring more  
67 than 12 weeks after the initial episode and once antimicrobial therapy was completed [11].  
68 MRSA bloodstream infections were classified as healthcare-associated or community-  
69 associated infections according to CDC criteria (<http://www.cdc.gov>). Healthcare-associated  
70 bacteremia was further subclassified as hospital-onset or community-onset infection if it  
71 occurred more than 48h after admission or less than 48h after admission, respectively.

72 Except for skin and soft tissue, only microbiologically-documented primary sites of infection  
73 mentioned in the medical charts were considered. Deep-seated infections were defined as  
74 microbiologically or radiologically documented remote foci. Catheter-related bloodstream  
75 infection was defined as exit site infection and/or a catheter tip culture growing > 15 MRSA

76 cfu with concomitant bacteremia [15]. Modified Duke criteria were used to define infective  
77 endocarditis [16]. Severe infection was defined as bacteremia with severe sepsis or septic  
78 shock [17]. Antimicrobial treatment was considered empirical before the identification of  
79 MRSA in blood cultures and targeted thereafter. Antimicrobial therapy was considered  
80 appropriate when a parenteral anti-infectious agent with in vitro activity against MRSA was  
81 used. Appropriate duration of treatment was 14 days for uncomplicated bacteremia and at  
82 least 28 days for complicated bacteremia, using standard definitions [18].

83 **Impact of ID consultation.** Between 2001 and 2006, ID consultations were obtained on  
84 request. After 2006, a senior ID resident supervised young ID consultants and checked that a  
85 formal ID consultation was performed on a mandatory basis within the same day for all  
86 patients in whom blood cultures were positive for suspected or confirmed *S. aureus*. Follow-  
87 up consultations were performed systematically as long as infection was ongoing or until  
88 discharge. All initial and follow-up consultations resulted in written reports transmitted to  
89 physicians in charge the same day of the evaluation. ID advice for MRSA bacteremia  
90 included follow-up blood cultures after 48h of appropriate treatment and then until  
91 sterilization, transthoracic and/or transoesophageal echocardiography for suspected  
92 endocarditis or sustained bacteremia, use of vancomycin as first-line antimicrobial agent at  
93 an initial dose 15 mg/kg of body weight with adjustment to trough level targeting 15 mg/l,  
94 source control by eradication of infectious foci, such as removal of peripheral or central  
95 venous catheters (CVC), and whenever possible drainage of deep-seated sites. The  
96 following variables were compared between episodes managed with and without ID  
97 consultations: early (7-day), late (30-day) and in-hospital mortality; performance of follow-up  
98 blood cultures, echocardiography when indicated and diagnosis of deep-seated sites of  
99 infection; appropriateness of empirical and definitive treatment including duration of  
100 antimicrobial therapy and vancomycin trough level measurement; eradication of removable  
101 foci including removal of all catheters and surgical debridement/drainage.

102 **Statistical analysis.** Categorical variables were compared using Fisher's exact test.  
103 Continuous variables were compared using parametric Student's *t* test when normally

104 distributed and non-parametric Mann-Whitney *U* test otherwise. Potential predictors of 7-day  
105 and 30-day mortality were first assessed in univariate analysis and then included into a  
106 logistic regression analysis whenever their p-value was  $\leq 0.2$ . Kaplan-Meier (KM) and Cox  
107 survival analysis were performed to assess the impact of ID consultation on in-hospital  
108 mortality and comparison between groups was performed by the log-rank test for KM and  
109 Wald test for Cox. Two-sided statistical significance was set at  $p=0.05$ . Cox proportional  
110 hazards assumption was assessed by inspection of the log(-log(survival)) versus log of  
111 survival time graph for each regressor, as well as by formal diagnostic testing. Results of  
112 logistic regression analyses are presented as Odds Ratios (OR) and those of Cox analyses  
113 as Hazard Ratios (HR). Data were analyzed using Stata 12.1 (Stata Corporation, College  
114 Station, Texas, USA) and GraphPad Prism 5.0 (GraphPad Software, San Diego, California,  
115 USA).

## 116 **Results**

117 **Study population.** Of 176 identified episodes of MRSA bacteremia, 20 were excluded for  
118 the following reasons: age < 18 (n=2), transfer to another hospital (n=3), initiation of palliative  
119 care (n=3) within 72h of bacteremia, or death before result of blood cultures (n=12). Thus,  
120 156 episodes that occurred in 148 patients (six patients had two episodes and one patient  
121 had three) were analyzed. Only thirty (20%) patients did not receive ID consultation.  
122 Demographic and clinical characteristics of the 148 patients with or without ID consultation  
123 are shown in Table 1. The only significant differences between groups were older age and a  
124 higher proportion of nursing home residents in patients without ID consultation. All but three  
125 patients had at least one underlying condition associated with an increased risk for MRSA  
126 carriage and 57% had previously-documented MRSA colonization.

127 **MRSA bacteremia.** Annual incidence of MRSA bacteremia is shown in Figure 1. Our  
128 institution faced a large nosocomial MRSA outbreak in 2009-2010 and the incidence rate of  
129 MRSA bloodstream infections increased to 0.9 per 1000 admissions in 2010. One hundred  
130 fifty-one episodes (97%) were healthcare-associated infections (116 hospital-onset and 35

131 community-onset) and only five (3%) community-associated infections. Primary sites of  
132 infection were: CVC (50), skin (30), urinary tract (21), respiratory tract (21), surgical site (12),  
133 peripheral catheter (9) and abdomen (3). In 36 episodes (23%), no primary focus of infection  
134 was detected. Deep-seated sites of infection were diagnosed in 58 episodes (38%).  
135 Characteristics of MRSA bacteremia episodes with or without ID consultation are  
136 summarized in Table 2.

137 **ID consultations.** An ID consultation was performed in 124 episodes (80%). The proportion  
138 of MRSA bacteremia episodes managed with ID consultation rose from a median of 58% in  
139 2001-2006 to 91% in 2007-2010 ( $p<0.01$ ) (Figure 1). Between 2007 and 2010, seven  
140 patients were not seen by ID specialists despite mandatory ID consultation. Although the  
141 reason for not having a consultation was not known precisely, the only factor associated with  
142 not having a consultation was older age (median age 81 vs. 71 years,  $p=0.04$ ). Median time  
143 from blood culture sampling to initial consultation was 1 day (IQR 0-2). Median ID follow-up  
144 was 13 days (IQR: 6-27).

145 **Diagnostic work-up and identification of primary and deep-seated site of infection**  
146 (Table 2). Catheters and skin and soft tissue were identified as the most frequent primary  
147 foci. In the ID group, significantly more echocardiography (59% vs. 26%,  $p<0.01$ ) and more  
148 follow-up blood cultures (71% vs. 50%,  $p=0.05$ ) were performed. Deep-seated sites of  
149 infection were diagnosed 4 times more often in the ID consultation group than in the  
150 comparative group (39% vs. 12%,  $p<0.01$ ). All episodes with endocarditis, deep-seated  
151 osteoarticular sites (except one sternitis) or deep systemic emboli were managed with an ID  
152 consultation. Nine out of 13 cases of endocarditis had definite endocarditis with vegetations  
153 seen on echocardiography. One patient not seen by ID consultation was discharged after 2  
154 weeks of therapy for primary bacteremia without surveillance blood cultures or  
155 echocardiography and was re-admitted 3 weeks later with a diagnosis of mitral valve  
156 endocarditis.

157 **Management of MRSA bacteremia** (Table 3). Patients in the ID group were hospitalized for  
158 a significantly longer period overall and after bacteremia onset. Empirical antibiotic therapy

159 was given in 68% of patients with ID consultation vs. 65% in controls ( $p=0.53$ ). One third of  
160 patients received no antimicrobial treatment before positive blood culture results. Empirical  
161 therapy was appropriate in 49% vs. 30% respectively, although the difference did not reach  
162 statistical significance ( $p=0.14$ ). Targeted treatment was appropriate in all episodes of both  
163 groups. Vancomycin was used as first-line targeted therapy in 115 (94%) episodes managed  
164 with ID consultation vs. 32 (100%) in controls, daptomycin in 6 (5%) vs. 0, linezolid in 2 (2%)  
165 vs. 0 and teicoplanin in 1 (1%) vs. 0. Reasons for not using vancomycin were allergy to  
166 glycopeptides (4), intent to obtain a more bactericidal effect (3), linezolid use for MRSA  
167 pneumonia (1) and impossibility to obtain a venous access (1). Duration of antimicrobial  
168 therapy was significantly longer in ID consultation group. A higher proportion of patients were  
169 treated for more than 14 or 28 days in ID group (71% vs. 39%,  $p<0.01$ , 31% vs. 10%,  
170  $p=0.02$ , respectively). Among 78 evaluable episodes of uncomplicated bacteremia,  
171 appropriate duration of treatment ( $\geq 14$  days) was 51/59 (86%) in the ID consultation group  
172 vs. 11/19 (58%,  $p=0.02$ ) in controls. Among 37 evaluable episodes of complicated  
173 bacteremia, appropriate duration of treatment ( $\geq 28$  days) was 31/36 (86%) vs. 0/1 (0%),  
174 respectively. Vancomycin trough level was measured in 99% of patients receiving this drug  
175 for  $\geq 48$ h in episodes managed with ID consultation vs. 77% in others ( $p<0.01$ ). No significant  
176 difference was observed in trough levels between the two groups. Eradication of removable  
177 infectious foci was performed significantly more often in the ID consultation group (83% vs.  
178 57%,  $p=0.03$ ). However, interventions were not statistically different when compared  
179 individually.

180 **Patient's Outcome** (Table 3). Seven-day, 30-day and in-hospital mortality for all episodes  
181 were 8%, 24% and 34%, respectively. ID consultation was associated with a marked  
182 decrease in 7-day (5% vs. 22%, OR 0.18, 95% CI 0.06-0.59,  $p<0.01$ ), 30-day (20% vs. 40%,  
183 OR 0.38, 95% CI 0.16-0.90,  $p=0.03$ ) and in-hospital mortality (29% vs. 53%, HR 0.38, 95%  
184 CI 0.20-0.74,  $p<0.01$ ) (Table 3). The cumulative probability of death at 30 days was  
185 significantly higher in the non-ID group ( $p<0.01$  by the log-rank test) (Figure 2). No time  
186 period effect was found after investigating the interaction between ID consultation and the



187 indicator variables for the MRSA outbreak period and for the mandatory ID consultation  
188 period. Likewise, Cox's proportional assumption was not rejected by the variable ID  
189 consultation. In univariate analysis, factors significantly associated with higher early (7-day)  
190 and late (30-day) mortality were pneumonia, severe infection, absence of ID consultation and  
191 lack of source control (Figure 3). Inappropriate empirical antimicrobial therapy and lack of  
192 CVC removal were not associated with an increase in early or late mortality. Vancomycin  
193 trough level tended to be lower in patients who died within the first 7 days (median 9.3 mg/l,  
194 IQR 8.3-15.8 vs. 13.6, 10.6-16.1,  $p=0.24$ ), although the difference was not significant. In  
195 multivariate analysis, predictors of early and late mortality were: severity of infection (OR  
196 32.56, 95% CI 4.31-246.11,  $p<0.01$  and OR 4.31, 95% CI 1.68-11.07,  $p<0.01$ , respectively),  
197 pneumonia (OR 5.26, 95% CI 1.39-19.81,  $p=0.01$  and OR 3.02, 95% CI 1.40-6.51,  $p<0.01$ ),  
198 absence of ID consultation (OR 30.19, 95% CI 3.76-242.18,  $p<0.01$  and OR 3.74, 95% CI  
199 1.34-10.43,  $p=0.01$ ) and lack of source control (OR 10.03, 95% CI 1.39-19.81,  $p=0.01$  and  
200 OR 3.69, 95% CI 1.22-11.13,  $p=0.02$ ).

## 201 **Discussion**

202 In the present study, we found a major impact of ID consultation on management and  
203 outcome of MRSA bacteremia in hospitalized patients with a relative reduction of 30-day  
204 mortality from 40% to 20%, an effect that remained significant after adjustment for  
205 confounding factors in logistic regression analysis. ID consultation was also associated with  
206 more frequent identification of CVC infection and deep-seated sites of infection, as well as  
207 more frequent eradication of removable infectious foci.

208 In 1998, Fowler *et al.* showed that compliance to standard-of-care management of *S. aureus*  
209 bacteremia provided by ID specialist could improve diagnosis of metastatic complication,  
210 clinical cure and reduce relapses [10]. Since then, the usefulness of ID consultation in this  
211 setting has been confirmed by several studies, although early reports failed to demonstrate  
212 an impact on survival [1, 11, 19]. The last five years, some retrospective data have  
213 suggested that ID consultation could also have an impact on mortality, especially within the

214 first 28 days of bacteremia [5, 9, 12-14, 20]. However, some of these studies included  
215 patients dying before blood culture results or untreated because of palliative context, raising  
216 concerns about the existence of a survival bias favoring patients living long enough to be  
217 seen by ID specialists [9, 13, 14, 20]. These reports combined healthcare-associated and  
218 community-acquired *S. aureus* bacteremia, with various rates of methicillin-resistance  
219 (mainly MSSA), as well as various rates of ID consultation coverage (27-82%) depending on  
220 ID consultation policy (on request vs. mandatory), making comparisons difficult. The present  
221 study confirmed the major impact of mandatory ID consultation on mortality in patients with  
222 healthcare-associated MRSA bacteremia after exclusion of palliative patients and death  
223 before result of blood cultures.

224 The likelihood of appropriate empirical therapy was quite low in patients who did and did not  
225 receive ID consultation. This observation resulted probably from the fact that empirical  
226 MRSA-active therapy upon growth of Gram-positive cocci in blood cultures was not standard  
227 of care in our institution due to the low prevalence of MRSA between 2001 and 2008 (12%).  
228 Robinson *et al.* found that receiving an effective empirical therapy was the only variable  
229 associated with reduced mortality by multivariate analysis in patients managed with ID  
230 consultation [12]. Indeed, several studies have reported that inadequate empirical treatment  
231 or delayed therapy were strong predictors of fatal outcome and contributed to the higher  
232 mortality observed with MRSA compared to MSSA [8, 21, 22]. In this study, we found that ID  
233 consultation was associated with more frequent administration of appropriate empirical  
234 therapy but this variable was surprisingly not a predictor of survival at 7 or 30 days, not even  
235 in univariate analysis. In addition to the small sample size limiting the power to detect such a  
236 difference, this finding is also probably due to the very short time between blood culture  
237 sampling and start of appropriate definitive treatment (median 1 day, IQR 0-2), 73% of  
238 patients receiving appropriate therapy within 24 hours and 95% within 48 hours. Accordingly,  
239 Lodise *et al.* found that the time breakpoint after obtaining positive blood culture beyond  
240 which delayed appropriate treatment increased *S. aureus* bacteremia mortality was 45 hours  
241 [22]. Delayed treatment beyond was independently associated with a 1.7-fold increase in

242 mortality. Taken together with the present data, these findings might suggest that  
243 hemodynamically stable patients could tolerate the absence of appropriate treatment during  
244 the first 24 (to 45) hours, although our study was not adequately powered to address this  
245 question. However, an MRSA-active empirical therapy should be initiated as soon as  
246 possible in all situations.

247 In patients with MRSA bacteremia, ID consultations are associated with lower mortality  
248 probably thanks to a bundle of diagnostic and therapeutic measures that allow better clinical  
249 management and improve the outcome. A crucial aspect in management of *S. aureus*  
250 bacteremia is source control and some of the previous studies have reported that source  
251 control is more often associated with ID consultation [11, 13]. Our data confirm these findings  
252 and show that lack of source control is independently associated with increased mortality. In  
253 episodes managed without ID specialists, the most frequently reported primary source of  
254 infection was the urinary tract, an uncommon origin for *S. aureus* infection. It is possible that  
255 MRSA bacteriuria was misinterpreted as the primary source of infection while in fact it more  
256 probably reflected hematogenous renal seeding, a current finding in *S. aureus* bacteremia  
257 [23]. Conversely, CVC infection was the most frequent primary source and deep-seated sites  
258 were diagnosed more often in the ID consultation group. Accordingly, source control was  
259 achieved significantly more often in the latter group, although the difference was not  
260 statistically significant when comparing removal of CVC and surgical debridement  
261 individually, likely due to the small sample size. Although none of these factors influenced  
262 mortality in univariate analysis, source control was associated with reduced mortality in  
263 multivariate analysis for 7-day, 30-day and in-hospital mortality. Therefore, reduced mortality  
264 associated with ID consultation could have been related to a bundle of actions, such as early  
265 initiation of appropriate therapy, removal of infected CVC and surgical debridement.

266 The present study has several limitations. The low percentage of patients without ID  
267 consultation limited the power to detect differences in patients who did and did not receive ID  
268 consultation. The retrospective design of the study is another limitation. Yet, it seems unlikely  
269 that a prospective, randomized trial addressing the impact of ID consultation on mortality will

270 ever be conducted for ethical reasons given the increasing amount of data suggesting a  
271 better outcome in *S. aureus* bacteremia managed by ID specialists. However, data collection  
272 bias was limited by the fact that clinical and microbiological information was available for all  
273 patients and prospectively written ID consultations allowed an accurate assessment of  
274 infection management. Attributable mortality being difficult to assess retrospectively, crude  
275 mortality was chosen as the primary endpoint of the study, as in previous studies [1, 5, 12,  
276 20]. Overrepresentation of terminally-ill patients in episodes treated without ID specialists is a  
277 classical bias in retrospective analyses, but this limitation was minimized in the present study  
278 by excluding palliative patients. Moreover, patients seen by ID specialists tended to have a  
279 more severe infection at the time of diagnosis and were hospitalized for a longer period after  
280 diagnosis, making it unlikely that difference in mortality was simply due to imbalance in  
281 severity of infection. Finally, as the majority of bloodstream infections were healthcare-  
282 associated, these results might not be generalized to community-acquired MRSA infections.  
283 In conclusion, the present results indicate that early intervention of ID specialists is  
284 associated with a better management and lower mortality among patients with MRSA  
285 bacteremia. ID consultation was associated with more frequent identification of CVC  
286 infections and deep-seated foci, better antibiotic management with more frequent use of  
287 MRSA-active empirical treatment and longer duration of therapy, and more frequent infection  
288 source control. ID consultation should be mandatory for all cases of MRSA bacteremia.

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383



384 **Table 1. Characteristics of patients with MRSA bacteremia with or without infectious**  
 385 **diseases (ID) consultation.**

Characteristics	All n=148*	ID consultation n=118	No ID consultation n=30	p-value
Male sex	107 (72)	85 (72)	22 (73)	NS
Age, median years (IQR)	71 (59-78)	71 (59-77)	77 (59-83)	0.04
Known MRSA colonization	84 (57)	70 (59)	14 (47)	NS
Hospital stay within previous 12 months	100 (68)	80 (68)	20 (67)	NS
Underlying conditions				
Hemodialysis	10 (7)	9 (8)	1 (3)	NS
Diabetes	44 (30)	38 (32)	6 (20)	NS
Malignancy	31 (21)	25 (21)	6 (20)	NS
Peripheral arteriopathy	23 (15)	19 (16)	4 (13)	NS
Joint prosthesis	10 (7)	10 (8)	0 (0)	NS
Prosthetic valve	9 (6)	8 (7)	1 (3)	NS
Pacemaker	3 (2)	3 (2)	0 (0)	NS
Immunosuppression	19** (13)	16 (13)	3 (10)	NS
Nursing home resident	14 (9)	7 (6)	7 (27)	<0.01
Injection drug use	5 (3)	4 (3)	1 (3)	NS

386 Data are number of patients (%) unless indicated otherwise. IQR: interquartile range. NS: not significant.

387 \* six patients had 2 MRSA bacteremic episodes and one had 3: only the initial episode was considered.

388 \*\* HIV infection (6), solid organ transplant recipients (8), immunosuppressive therapy (4), neutropenia (3).

389

390 **Table 2. Characteristics of MRSA bacteremia episodes with or without infectious**  
 391 **disease (ID) consultation.**

Characteristics	ID consultation n=124	No ID consultation n=32	p-value
Acquisition of infection			
Healthcare-associated, hospital-onset	93 (75)	23 (72)	NS
Hospital stay from admission to bacteremia, median days (IQR)	16 (1-36)	9 (1-24)	NS
Healthcare-associated, community-onset	26 (21)	9 (28)	NS
Community-associated	5 (4)	0	NS
ICU stay at time of bacteremia	22 (18)	3 (9)	NS
ICU admission within 72h of bacteremia	20 (16)	2 (6)	NS
Severe sepsis / septic shock	32 (26)	5 (16)	NS
<b>Primary source of infection (≥ 1 possible)</b>			
Unknown	28 (23)	8 (25)	NS
Catheters	50 (40)	9 (28)	NS
peripheral	6 (5)	3 (9)	NS
central	44 (35)	6 (19)	0.09
Skin and soft tissue	22 (18)	7 (22)	NS
Lung	19 (15)	2 (6)	NS
Urinary tract	14 (11)	7 (22)	NS
Abdomen	2 (2)	1 (3)	NS
Surgical site	11 (9)	1 (3)	NS
<b>Diagnostic workup</b>			
Blood culture (sets): median number (IQR)	6 (4-9)	3.5 (2-7.5)	<0.01
Follow-up blood culture	84 (71)	14 (50)	0.04
Positive at 48-72h	33/84 (39)	4/14 (29)	NS
Time to clearance: median days (IQR)	4 (2-6)	3 (2-4)	NS
Echocardiography			
Any	73 (59)	8 (26)	< 0.01
Transoesophageal	19 (17)	1 (3)	0.08
<b>Deep-seated sites of infection (≥ 1 possible)</b>			
Any	53 (43)	5 (16)	<0.01
Cardiovascular	35 (28)	3 (9)	0.03
Endocarditis	13 (11)	0	0.07
Vascular prosthesis infection	13 (10)	1 (3)	NS
Septic thrombophlebitis	10 (8)	2 (6)	NS
Osteoarticular	24 (19)	1 (3)	0.03
Osteomyelitis	9 (7) <sup>*</sup>	0	NS
Septic arthritis	8 (6)	0	NS
Sternitis	7 (6)	1 (3)	NS
Deep systemic emboli	6 (5) <sup>**</sup>	0	NS
Deep-tissue abscess	6 (5) <sup>†</sup>	1 (3) <sup>†</sup>	NS

392 Data are numbers. (%) unless indicated otherwise. IQR: interquartile range. ICU: intensive care unit. NS: not  
 393 significant.

394 <sup>\*</sup> including 5 vertebral (3 of which associated with epidural abscess) and 3 foot osteomyelitis.

395 \*\* including 2 lung, 3 retinal, 2 cerebral and 2 splenic emboli.

396 † including 3 epidural, 2 retrosternal, 1 liver, 1 psoas abscesses.

397

398 **Table 3. Management and outcome of MRSA bacteremia episodes with or without**  
 399 **infectious diseases (ID) consultation.**

Characteristics	ID consultation n=124	No ID consultation n=32	p-value
<b>Length of hospital stay: median days (IQR)</b>			
From bacteremia onset to hospital discharge	27.5 (37-7)	22 (7-35)	0.02
Total length of stay	56 (26-88)	33 (14-58)	0.01
<b>Antimicrobial therapy</b>			
Empirical treatment (any)	85 (68)	20 (65)	NS
Targeted treatment (any)	124/124 (100)	32 (100)	NS
Appropriate treatment:			
Empirical	42/85 (49)	6/20 (30)	NS
Targeted	124/124 (100)	32 (100)	NS
Time to treatment <sup>‡</sup> : median days (IQR)	1 (0-2)	1 (1-2)	0.08
Duration of antimicrobial therapy:			
median days (IQR)	17 (13-30)	12 (3-14)	< 0.01
> 14 days	86 (71)	12 (39)	<0.01
> 28 days	37 (31)	3 (10)	0.02
Vancomycin level measurement <sup>**</sup>	110/111 (99)	21/28 (77)	<0.01
Vancomycin trough level <sup>†</sup> : median (IQR)	13.7 (10.5-16.7)	13.1 (8.6-15.5)	NS
First measurement	11.65 (8.1-15.4)	10.3 (7.1-13.5)	NS
Measurement after dosage adaptation	14.9 (10.5-21.1)	14.1 (7.8-20)	NS
<b>Eradication of removable infectious foci<sup>‡</sup></b>			
Any	70/84 (83)	8/14 (57)	0.03
Peripheral catheter removal	5/5 (100)	2/2 (100)	NS
Central venous catheter removal	42/44 (95)	5/6 (83)	NS
Surgical debridement/drainage	25/41 (61%)	2/7 (28%)	NS
<b>Outcome</b>			
7-day mortality	6 (5)	7 (22)	<0.01
30-day mortality <sup>§</sup>	23/114 (20)	12/30 (40)	0.03
In-hospital mortality	36 (29)	17 (53)	0.01

400  
 401 Data are numbers (%) unless indicated otherwise. IQR: interquartile range. NS: not  
 402 significant.

403 <sup>‡</sup> time elapsed from the day of first positive blood culture to start of appropriate therapy.

404 <sup>\*\*</sup> includes patient receiving vancomycin for at least 48h.

405 <sup>†</sup> in mg/l.

406 <sup>‡</sup> percentages refer only to episodes with a removable primary or deep-seated focus of infection. Two peripheral  
 407 catheters had already been removed before MRSA bacteremia was diagnosed and were therefore not counted.

408 <sup>§</sup> evaluable number of patients for that parameter.

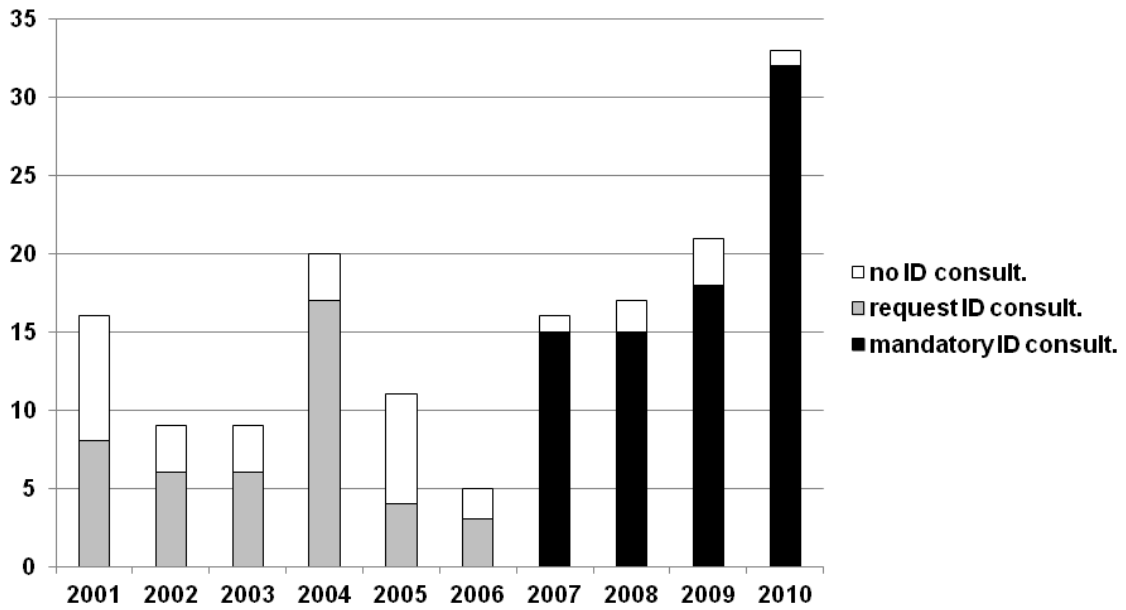
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411 **Figure 1.** Annual incidence of MRSA bacteremia episodes with or without infectious  
 412 diseases (ID) consultation according to institutional policy.

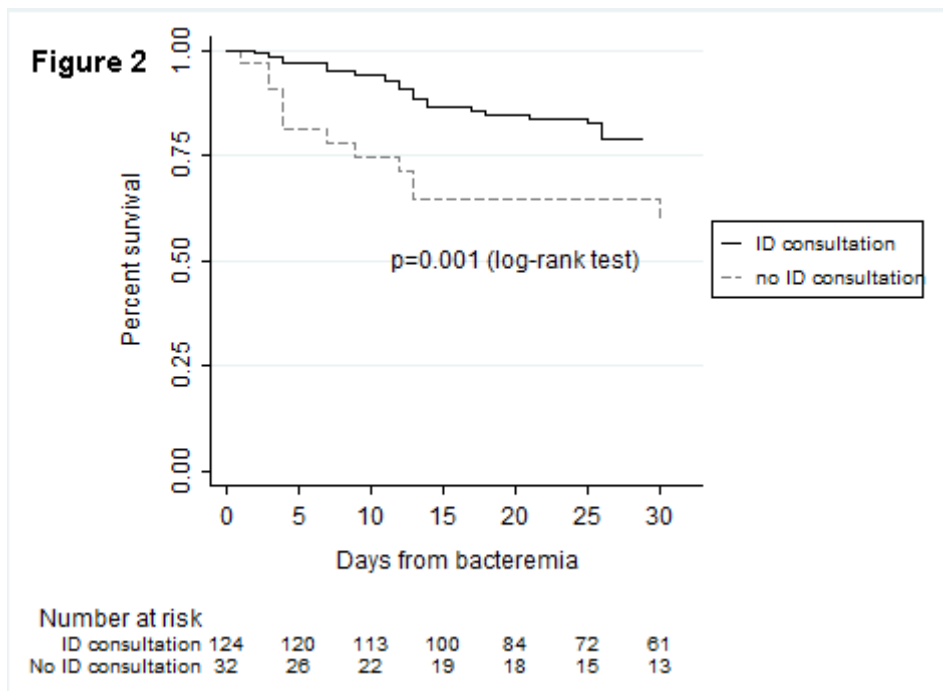
**Figure 1.**

Number of episodes



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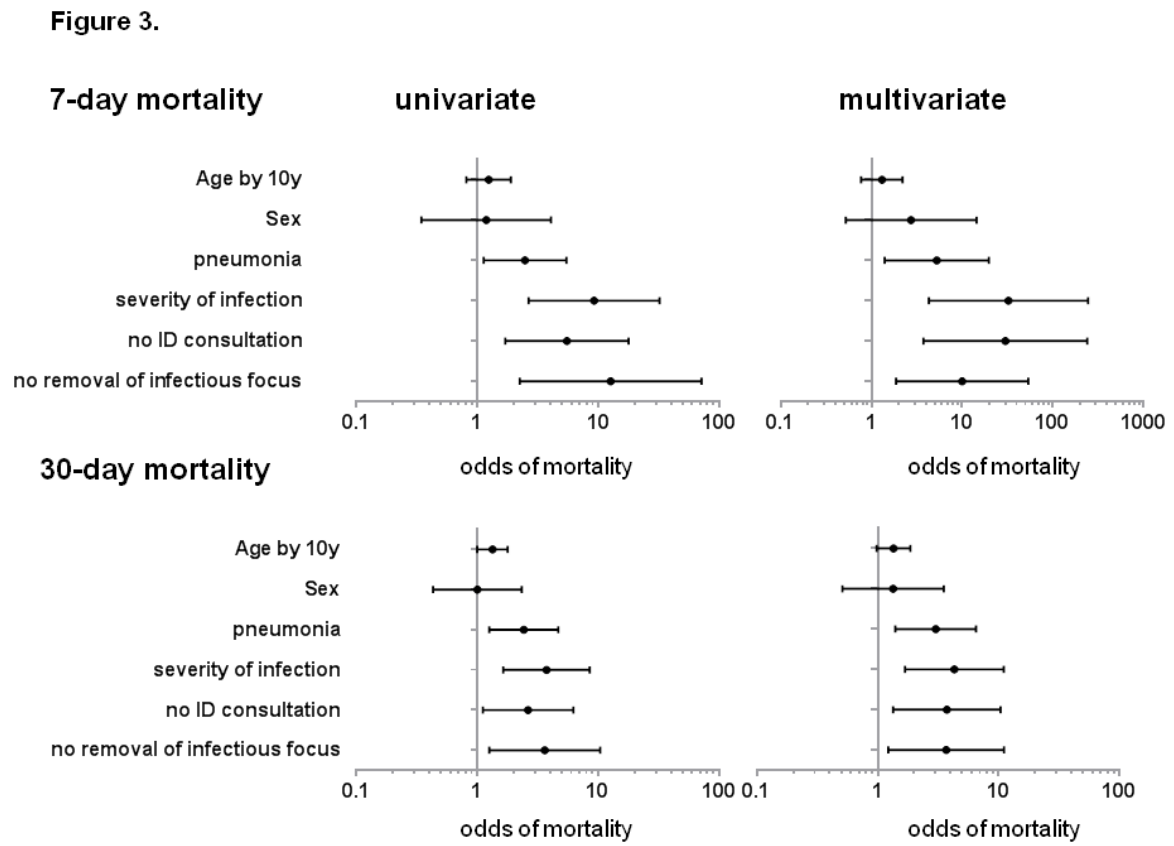
414 **Figure 2.** Kaplan-Meier survival curves.



415

416 **Figure 3.** Univariate and multivariate analyses of predictors of 7-day and 30-day mortality.

417 Each dot and horizontal bar indicates odds ratio and 95% confidence interval.



418