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Individual and institutional predisposing factors of MRSA surgical site infection and outcomes—a retrospective case-control-study in 14 European high-volume surgical centres

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Der dieser Arbeit zugrunde liegenden Datensatz wurde in der Arbeitsgruppe Klinische Antiinfektiva-Entwicklung und Epidemiologie seltener Infektionen der Universität zu Köln sowie von der SALT study group an 14 europäischen Zentren ermittelt und von Frau Priv.-Doz. Dr. Sibylle Mellinghoff zur Verfügung gestellt. Die Daten der Uniklinik Köln wurden durch mich in der oben genannten Arbeitsgruppe unter der Anleitung von Priv.-Doz. Dr. Sibylle Mellinghoff ermittelt. Hierfür erfolgte die Auswertung von Arztbriefen, mikrobiologischen, pathologischen und radiologischen Befunden aus den digitalen Patient*innenakten und aus dem digitalen Archiv der Uniklinik.

Der Datensatz wurde durch mich mittels SPSS® (IBM Statistics 27) ausgewertet. Das Erstellen von Grafiken und Tabellen wurde mithilfe von Word und Excel durchgeführt. Unterstützend standen mir hierbei Priv.-Doz. Dr. Sibylle Mellinghoff, Dr. Blasius Liss und Dr. Jan-Hendrik Naendrup zur Seite. Das veröffentlichte Paper wurde von mir eigenständig verfasst, im Anschluss erfolgte eine Überarbeitung und Optimierung zusammen mit meinen Koautor*innen (Jan-Hendrik Naendrup, Caroline Bruns, Annika Y. Classen, Jon Salmanton-García, Harald Seifert, Rosanne Sprute, Jannik Stemler, Sarah V. Walker, Oliver A. Cornely, Blasius J. Liss und Sibylle C. Mellinghoff).

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Für meine Eltern und Großeltern, die mir diesen Weg ermöglicht haben.

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List of abbreviations

AMR	antimicrobial resistance
EDCD	*European Centre for Disease Prevention and control*
HAI	health-care associated infections
EARS-Net	*European Antimicrobial Surveillance Network*
SSI	surgical site infections
S. aureus/SA	*Staphylococcus aureus*
MSSA	methicillin-sensible *Staphylococcus aureus*
MRSA	methicillin-resistant *Staphylococcus aureus*
PBP	penicillin-binding protein
SALT	*Staphylococcus aureus* surgical site infection rates in 5 European countries
EU	European Union
EEA	European Economic Area
ABS	antibiotic stewardship
ID	infectious disease

1. Zusammenfassung

Antibiotikaresistenzen stellen eine der größten Herausforderungen der modernen Medizin dar. Aufgrund ihrer verlängerten Behandlungsdauer, der erhöhten Morbidität sowie der damit verbundenen gesteigerten Gesundheitskosten verursachen sie beträchtliche individuelle und gesamtgesellschaftliche Belastungen. Aus diesem Grund wurden nationale und internationale Surveillance Systeme etabliert. Heute berichten diese an das Europäische EARS-Net (*European Antimicrobial Surveillance Network*), welches durch die europäische Gesundheitsbehörde ECDC (*European Center for Disease Prevention and Control*) koordiniert wird. Circa 70% der Infektionen mit Antibiotika-resistenten Erregern sind nosokomial, im Krankenhaus erworbene Infektionen. Eine Prävalenzstudie aus dem Jahr 2016/2017 zum Zeitpunkt dieser Studie zeigte, dass circa 6,5% aller Patient*innen in Krankenhäusern der Akutversorgung in Europa an einer nosokomialen Infektion erkrankt waren. Hierunter bilden postoperative Wundinfektionen eine große Gruppe. Solche Wundinfektionen werden am häufigsten durch *Staphylokokkus aureus* verursacht (*S. aureus)*, ein Erreger der natürlichen menschlichen Hautflora. Aufgrund verschiedener Resistenzmechanismen zeigt er teils eine Widerstandsfähigkeit gegenüber gängigen Antibiotika, insbesondere gegenüber Betalaktam-Antibiotika. Diese resistente Variante wird als Methicillin-resistenter *S. aureus* (MRSA) bezeichnet. Zuletzt war der MRSA-Anteil unter *S. aureus* Nachweisen in Europa rückläufig auf circa 15% (2022). Verglichen mit Methicillin-sensiblem *S. aureus* (MSSA) ist MRSA mit einem schlechteren Outcome verbunden.

Diese Arbeit hat zum Ziel die Inzidenz von postoperativen Wundinfektionen durch MRSA in Europa zu erfassen und Länder- sowie Zentrums- und Abteilungs-abhängige Unterschiede zu untersuchen. Darüber hinaus sollen Risikofaktoren und das klinische Ergebnis im Vergleich zu MSSA bestimmt werden. Hierfür erfolgt die Analyse einer Subkohorte der europaweiten SALT Studie (*Staphylococcus aureus* surgical site infection rates in 5 European countries; NCT03353532) bestehend aus Patienten mit postoperativen MRSA-Wundinfektionen aus 14 operativen Zentren in Frankreich, Deutschland, Italien, Spanien und dem Vereinigten Königreich.

Im Jahr 2016 wurden bei insgesamt 178.903 Patient*innen, die sich einer invasiven Operation unterzogen, 104 Fälle einer MRSA-Infektion dokumentiert, was einer Inzidenz von 0,06% entspricht. Im internationalen Vergleich zeigte sich eine signifikante Ungleichverteilung: In Spanien lag die Inzidenz mit 58 von 67.934 Fällen deutlich höher, während sie in Deutschland mit 16 von 46.443 Fällen signifikant niedriger war (beide $P < 0,05$). Innerhalb der Länder wurden ebenfalls Unterschiede beobachtet. In Krankenhäusern mit etablierten Programmen für Antibiotic Stewardship (ABS) oder infektiologischer Beratung (3 von 14 Zentren) traten

signifikant weniger MRSA-Fälle auf (17 von 43.556 Fällen) im Vergleich zu Zentren ohne solche Programme (61 von 83.048 Fällen; $P < 0,05$). Die betroffenen Patient*innen litten überwiegend an chronischen kardiovaskulären Erkrankungen, Diabetes mellitus und soliden Tumoren. Im Vergleich zu Patient*innen mit MSSA-Wundinfektionen waren MRSA-Patienten in einer bivariaten Analyse signifikant älter, adipöser und wiesen eine höhere Morbidität auf (jeweils $P < 0,05$). Darüber hinaus zeigte sich, dass Operationen im Zeitraum zwischen 18 und 24 Uhr signifikant häufiger mit MRSA-Wundinfektionen assoziiert waren (17 von 104 Fällen) im Vergleich zu Operationen zu anderen Zeiten (62 von 640 Fällen, $P < 0,05$).

Zusammenfassend findet sich in Europa und den individuellen Ländern eine niedrige Inzidenz von postoperativen Wundinfektionen durch MRSA. Es bestehen dennoch Unterschiede zwischen den Nationen und den Zentren mit etablierten ABS-Programmen oder infektiologischer Beratung. Dies verdeutlicht den Bedarf an einer breiteren Implementierung solcher Maßnahmen. Trotz der Größe dieser Kohorte, die zu den umfangreichsten Studien zu postoperativen MRSA-Wundinfektionen zählt, bleiben die Aussagen hinsichtlich spezifischer Prozeduren und besonders gefährdeter Patientengruppen durch die geringe Fallzahl eingeschränkt. Zukünftige Forschung sollte daher gezielt auf die Identifikation und Prävention von Risikofaktoren für MRSA-Infektionen fokussieren.

2. Introduction

2.1. Antimicrobial resistance and health-care associated infections

Antimicrobial resistance (AMR) is one of the greatest challenges in modern medicine. *The European Centre for Disease Prevention and control* (ECDC) recently assessed the burden of infections with antibiotic-resistant pathogens. From 2016 to 2020 there were between 30.000 and 38.000 attributable deaths in Europe each year. 70% of all infections due to resistant bacteria were health-care associated infections (HAI). The investigated period shows an increasing trend in the number of those infections.[1] In addition to consequences as higher mortality, longer hospital stays, increased number of complications and the associated costs[2], we could face more particular obstacles for example in case of necessary immunosuppression by chemotherapy or due to organ transplantation. These concerns led to the establishment of national surveillance systems which report to the *European Antimicrobial Surveillance Network* (EARS-Net) which is coordinated by the ECDC. In 2008 the surveillance of antimicrobial resistance has been included in European law.[3]

2.2. Surgical site infections

A point prevalence survey revealed that 6,5% of patients in acute care hospitals in Europe had at least one HAI in 2016/2017. Surgical site infections (SSI) are among the most frequent HAI and constitute an important criterion in health research.[45] SSI are, like HAI, associated with greater disease burden.[6]

2.3. Staphylococcus aureus

Staphylococcus aureus (*S. aureus*) is the most common causative microorganism of surgical site infections.[47] It is important to distinguish between methicillin-sensitive (MSSA) and methicillin-resistant *Staphylococcus aureus* (MRSA). The latter has appeared increasingly since the broad use of antibiotics – especially methicillin - in the 1960s.[89] Most *S. aureus* stems are resistant against simple penicillin. They produce so-called penicillinases, which split the beta-lactam ring of penicillin. The methicillin-resistant form additionally produces a modified penicillin-binding-protein (PBP2a) causing resistance against all beta-lactam antibiotics due to low affinity.[1011] Further resistance acquisition through transposition and plasmid integration is possible.[12] Therapeutic options are already limited, today we observe additional resistance against fluoroquinolones and rifampicin. After initial spread of MRSA with increasing incidence of invasive infections we now observe a decreasing trend all over Europe. The latest EARS-Net report suggests a decrease of MRSA proportions among *S. aureus* from 17.8% (2018) to 15.2% (2022) in invasive isolates.[13] The distinction between MSSA und MRSA is crucial for therapy and clinical course regarding outcome due to increased length of hospitalization, more complications and higher mortality in case of MRSA.[141516]

2.4. Objectives

Regarding AMR most published data concern all health-care associated infections. Especially in EARS-Net only invasive specimens (blood cultures or cerebrospinal fluid) are included. The following analysis is limited to surgical site infections and refrains from using only indicator procedures. The Europe-wide SALT (*Staphylococcus aureus* surgical site infection rates in 5 European countries) study recently analysed overall *S. aureus* SSI incidence in France, Germany, Italy, Spain, and UK for all invasive surgeries at 14 high-volume centres, defined as executing more than 10,000 procedures annually.[17,18] Given the impact of MRSA on SSI outcomes, we report an in-depth subgroup analysis of patients with MRSA SSI within the SALT patient cohort to assess incidence rates of SSI by MRSA and to determine related factors and clinical outcome compared to MSSA, including country-specific, institutional, and patient determinants.

3. Publication

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JAC-Antimicrobial Resistance

Individual and institutional predisposing factors of MRSA surgical site infection and outcomes—a retrospective case-control-study in 14 European high-volume surgical centres

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Objectives: To assess incidence rates of surgical site infections (SSI) by MRSA and to determine related factors and clinical outcome compared to MSSA, including country-specific, institutional and patient determinants.

Patients and methods: We performed a subgroup analysis of the Europe-wide SALT (NCT03353532) study population with MRSA SSI from 14 centres in France, Germany, Italy, Spain and the UK.

Results: An overall MRSA SSI incidence of 0.06% ($n=104$) was found in 178 903 patients undergoing invasive surgery in 2016. Frequently observed comorbidities were chronic cardiovascular disease, diabetes and solid tumours. Compared to the overall MRSA SSI incidence, incidence rates were significantly higher in Spain (58 of 67 934 cases) and lower in Germany (16 of 46 443 cases; both $P<0.05$). Centres with antibiotic stewardship (ABS) and infectious disease (ID) consultation programmes ($n=3/14$) had lower MRSA rates (17 of 43 556 cases versus 61 of 83 048 cases, $P<0.05$). In bivariate analyses, MRSA SSI patients were significantly older, had higher BMI and more comorbidities compared to MSSA ($P<0.05$ each). Surgery performed between 6:00 and 12:00 pm led to higher MRSA proportions among *S. aureus* SSI (17 of 104 cases versus 62 of 640 cases, $P<0.05$).

Conclusions: This study shows low overall and country-specific incidence rates of MRSA SSI in Europe. We could show significant differences between countries as well as between centres with established ABS and ID consultation programmes were observed. The number of those programmes seems too small against this background.

Introduction

Surgical site infections (SSI) are among the most frequent healthcare-associated infections (HAI).[1,2] They are associated with prolonged hospitalization, poor clinical outcome and higher treatment costs.[3,4] MSSA is the most common causative microorganism in the context of SSI.[2,5] Despite its decreasing prevalence in Europe, MRSA continues to be of great importance due to increased morbidity, mortality and treatment costs in SSI patients compared to MSSA.[6]

The Europe-wide SALT (*Staphylococcus aureus* surgical site infection rates in five European countries) study recently analysed overall *S. aureus* SSI incidence in France, Germany, Italy, Spain and the UK for all invasive surgeries at 14 high-volume centres, defined as executing more than 10 000 procedures annually.[7] Given the impact of MRSA on SSI outcomes, we report an in-depth

subgroup analysis of patients with MRSA SSI within the SALT patient cohort. We evaluate patient and institutional determinants of MRSA incidence as well as overall and country-specific infection rates.

Patients and methods

Study design

This analysis was based on the dataset of the SALT study.[7,8] SALT is a case-control study, comprising microbiologically proven SA SSI cases and matched uninfected controls without documented clinical or microbiological evidence of SSI (Table S2, available as Supplementary data at JAC-AMR Online) nested within a retrospective multinational, multicentre cohort of 178 903 patients undergoing invasive surgery at participating centres in France, Germany, Italy, Spain and the UK in 2016. Participating centres were Central University Hospital of Limoges, Central Regional University Hospital of Tours, Central Departmental Hospital of Vendée in France; University Hospitals of Munich, Bonn, Jena and Cologne in Germany; Hospital Clinic of Barcelona, General University Hospital Gregorio Marañón, Hospital del Mar Medical Research Institute, La Fe University and Polytechnic Hospital, University Hospital Ramón y Cajal Madrid in Spain; Central Manchester University Hospitals in UK and University of Udine and Santa Maria Misericordia University Hospital in Italy.

The primary objectives of the present analyses were to assess overall and country- and surgical speciality-specific incidence rates of MRSA SSI compared to MSSA SSI. Secondary objectives were to determine patient and institutional factors associated to MRSA SSI as well as to investigate the influence of MRSA SSI on clinical outcome compared to MSSA SSI. Exploratory objectives were the description of procedure-specific incidence of MRSA SSI and the impact of antibiotic stewardship (ABS) and ID consultation programmes on MRSA SSI incidence as well as their clinical outcome compared to MSSA SSI.

Patient selection

From the SALT cohort, all 104 patients with MRSA SSI were included (Table S1). A total of 640 patients with MSSA SSI served as comparison group for bivariate analyses and, out of these, 104 cases served as controls for multivariate analyses. Twenty cases excluded from the SALT cohort due to missing matches were not included in our analysis.

Data assessment

Regarding data capture we refer to the published report of the SALT main study.[8] The following data were captured from all identified MRSA SSI patients as well as MSSA SSI patients: age, sex, BMI, American Society of Anaesthesiologists (ASA) score, comorbidities, length of hospitalization, required admission to ICU and length of ICU stay, reason for admission and attribution of admission to SSI (in case of ICU stay), necessity for surgical revision or re-admission, survival at day 30 and at day 90 after surgery, antibiotic treatment including its duration, patient functional status at admission and at final discharge, and death attributable to SSI as defined by the treating physician. If re-admission was necessary, reason for re-admission and attribution to SSI, duration of hospitalization and length of ICU stay as well as all antibiotic treatment and its duration were recorded. We further captured SA as causative pathogen from clinical specimens obtained during surgery or blood cultures including day of susceptibility testing, presence of resistance patterns (i.e. resistance to methicillin) and type of SSI according to ECDC criteria.[9]

Data on ABS programmes and infectious disease (ID) consultation were captured retrospectively by the American CDC Checklist for Core Elements of Hospital Antibiotic Stewardship[10] and defined 'established' if introduced at least 1 year before January 2016.

Statistical methods

MRSA SSI rates were determined for each country and each surgical specialty (e.g. vascular surgery) as well as individual surgical procedures (e.g. insertion of arteriovenous graft). For each incidence rate, the 95% confidence intervals for a binominal proportion were calculated. The cohort of MRSA SSI cases was compared to the cohort of MSSA SSI cases using both descriptive statistics and a logistic regression analysis. The dependent variable was infection by MRSA. Within the MRSA SSI cohort, we present continuous variables as mean (standard deviation) and median (interquartile range) and compared those using Mann–Whitney *U*-test after checking for normality using Kolmogorov–Smirnov test. Categorical variables are presented as proportions and compared using the Chi-square test or Fisher's exact test. Cases with missing data were excluded from the respective calculations. To assess individual risk factors for MRSA SSI, a backward stepwise logistic regression analysis was performed. As a sensitivity analysis outcome measures were analysed in duplicate, once in the overall population and once in a subgroup of MRSA and MSSA patients matched one-to-one by a propensity score based on variables identified in the backward stepwise logistic regression analysis.

Statistical analysis and generation of all tables, listings and figures were performed using SPSS® (IBM Statistics 27). Statistical significance was defined as *P* value less than 0.05. All tests were two-tailed.

Ethics

The SALT study on which this retrospective study is based was submitted to the Research Ethics Commission of the University of Cologne (no. 17-078) for advice; the requirement for informed consent was waived due to the retrospective nature as well as the anonymous data capture strategy of this study. The study was registered at clinicaltrials.gov under NCT03353532.

Results

In total, 764 of 178 903 [0.43% (95% CI, 0.40%–0.46%)] patients undergoing invasive surgery in 2016 in the 14 included European centres developed SA SSI; of these, 104 [14.0% (95% CI, 11.4%–16.3%)] infections were caused by MRSA accounting for an overall MRSA SSI incidence of 0.06% (95% CI, 0.05%–0.07%).

Table 1 shows the country-specific incidence rates. The single centre in Italy did not report MRSA cases. The highest country-specific MRSA SSI incidence rates were reported in Spain [0.09% (95% CI, 0.07%–0.11%), $n=58$] and the UK [0.09% (95% CI, 0.04%–0.17%), $n=8$]. The lowest rates were reported in Germany [0.03% (95% CI, 0.02%–0.06%), $n=16$]. Compared among each other, these differences turn out to be significant in the case of Spain and Germany (both $P<0.05$).

Only three centres had established ABS programmes and ID consultation services, one in the UK and two in Germany (Table S4). Centres with ABS and ID consultancy programmes had both lower overall MRSA SSI incidences [0.04% (95% CI, 0.02%–0.06%) versus 0.07% (95% CI, 0.06%–0.09%), $P<0.05$] and lower proportions of MRSA SSI among SA SSI [6.3% (95% CI, 4.0%–10.0%) versus 21.6% (95% CI, 17.3%–27.0%), $P<0.05$]. Presence of ABS and ID consultation programmes did not significantly influence clinical outcomes. In these centres, re-admission rates and revision surgery rates were lower and 30 and 90 day survival were higher compared to centres without these services, whereas the necessity for ICU admission was higher (Tables S11 and S12).

Table 1. Overall incidence of MRSA SSI per country

Centre	Number of included patients $N=178\,903$[a]	Number and percentage of MRSA SSI [*n* (%)] $N=104$	Incidence rates of MRSA SSI [% (95% CI)]
France	35 974	22 (21.2)	0.06 (0.04–0.09)
Germany	46 443	16 (15.4)	0.03 (0.02–0.06)
Spain	67 934	58 (55.8)	0.09 (0.07–0.11)
UK	9168	8 (7.7)	0.09 (0.04–0.17)

Abbreviations: ID, infectious disease consultation service; Limoges, Central University Hospital of Limoges; Tours, Central Regional University Hospital of Tours; Vendée, Central Departmental Hospital of Vendée; LMU, University Hospital of Munich; UKB, University Hospital of Bonn; UKJ, University Hospital of Jena; UKK, University Hospital of Cologne; HCB, Hospital Clinic of Barcelona; HGGM, General University Hospital Gregorio Marañón; IMIM, Hospital del Mar Medical Research Institute; LaFe, La Fe University and Polytechnic Hospital; RyC, University Hospital Ramón y Cajal Madrid, NHS Manchester, Central Manchester University Hospitals NHS.

[a]Including the Italian centre.

The highest specialty-specific incidence rates were observed in orthopaedic/trauma surgery [0.1% (95% CI 0.1%–0.1%), $n=31$] and vascular surgery [0.1% (95% CI, 0.1%–0.2%), $n=15$] (Table S5, Figure 1). In both specialties, patients were significantly more likely to develop MRSA SSI than patients in other specialties (both $P<0.05$).

Regarding individual procedures, minimal invasive surgery of the bile duct had the highest procedure-specific incidence rate (2.3% [95% CI, 0.3%–15.8%], $n=1$) (Table S5). In orthopaedic and trauma surgery, highest procedure-specific incidence rates were observed in revision surgeries, replacement and removal of prosthetic joint of the upper limb [0.5% (95% CI 0.1%–3.7%), $n=1$], amputation and disarticulation of lower limb [0.3% (95% CI, 0.1%–0.8%), $n=4$], spinal fusion [0.3% (95% CI, 0.1%–1.1%), $n=2$] and primary total prosthetic replacement of hip joint [0.2% (95% CI, 0.1%–0.5%), $n=7$]. The highest cumulative incidence of MRSA SSI was observed in primary total prosthetic replacement of hip joint and insertion of arteriovenous graft [both, 6.7% (95% CI, 3.3%–13.8%), $n=7$].

Microbiological evidence was mostly obtained through wound swab (52.9%) or surgically obtained specimens (32.7%). Approximately 2% of infections were detected through blood culture (Table S3).

Patient characteristics are given in Table 2. Within the MRSA cohort, sex was evenly distributed (48.1% female, 51.9% male) and mean age was 65.9 (range, 21 to 95) years. Sixty (57.7%) of 104 MRSA SSI patients were overweight (BMI ≥25), 31 (29.8%) of these were obese (BMI ≥30). Most patients within the cohort had a mild or severe systemic disease (ASA 2–3). Frequently observed comorbidities were chronic cardiovascular disease (26.0%), diabetes (26.0%), solid organ malignancies (26.0%) and peripheral vascular disease (19.2%).

Bivariate analyses comparing MRSA SSI to MSSA cases showed that the MRSA SSI cohort was significantly older and had a higher BMI (both $P<0.05$) (Table 2). Furthermore, MRSA SSI patients more frequently had at least mild systemic disease (ASA ≥2, $P<0.05$) and were significantly more likely to have at least one comorbidity ($P<0.05$), such as peripheral vascular disease, chronic obstructive pulmonary disease, dementia, transient ischaemic attack or cerebrovascular accident and chronic kidney disease (all $P<0.05$). Surgery performed between 6:00 pm and 12:00 pm showed higher rates of MRSA compared to MSSA incidence rates ($P<0.05$), whereas a statistically significant difference in procedure duration was not found ($P=0.083$).

Risk factors for MRSA SSI compared to MSSA SSI are given in Table S6. We found age (OR 1.024; $P<0.001$), surgery from 6 to 12 pm (OR 1.310; $P=0.070$), chronic kidney disease (OR 2.148; $P=0.019$) and dementia (OR 3.190; $P=0.029$) to be predictive.

Regarding the outcome of MRSA SSI compared to MSSA (Table S7), mean length of hospitalization was significantly longer (24.9 versus 16.3 days; $P<0.05$). Need for re-admission and for revision surgery were higher in MRSA SSI (58.7% versus 49.4% of cases and 57.7% versus 47.8% of cases) without reaching statistical significance ($P=0.079$ and $P=0.062$). MRSA SSI patients where numerically less likely to be admitted to the ICU (17.3% versus 19.7% of cases, $P=0.482$). Overall survival after 30 and 90 days did not differ between MRSA and MSSA cases (Table S8). The observed differences did not prove to be significant after performing a propensity score matching (Tables S9 and S10), although hospitalization of patients with MRSA SSI continued to be longer than of patients with susceptible SA SSI (24.9 versus 19.7 days, $P=0.056$).

Discussion

This multicentre study shows a low overall and country-specific incidence of MRSA SSI in European high-volume surgical centres in line with the epidemiology of nosocomial MRSA infections in general.[11–14] The overall MRSA rate of 14% is comparable to current European MRSA rates among invasive SA isolates as previously reported by ECDC.[11] Our data show significant international differences.

The absolute numbers of MRSA SSI for each surgical procedure allow for exploratory analyses of procedures at risk for MRSA SSI and outcome-related assertions. In line with previous publications, MRSA SSI patients in our sample were older and had more underlying conditions than MSSA SSI patients.[15–17]

Procedure duration did not significantly affect the likelihood of MRSA SSI, whereas time of surgery affected MRSA SSI incidence rates. Patients undergoing surgery between 6:00 and 12:00 pm were more likely to develop MRSA SSI. On one hand, the time of the day and hours of work are known to affect behaviour and error rates of healthcare professionals.[18,19] Lower adherence to hygiene and safety protocols might thus have contributed to the higher MRSA SSI incidence rates in patients who underwent surgery between 6:00 and 12:00 pm. However, several trials, including a cluster-randomized trial of 138 691 patients, have failed to demonstrate an effect of increased surgeon work hours on SSI rates or other clinically important outcomes.[20] Patients operated during evening and night hours are structurally different from those during daytime and undergo different types of surgery (i.e. more acutely requiring surgery, fewer elective low-risk procedures). For the time-of-surgery subgroups, we saw no difference

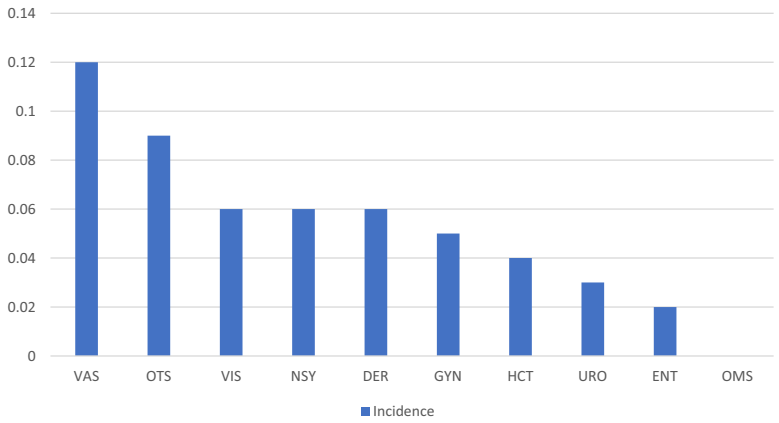

Figure 1. Incidence rates of MRSA SSI by category. Abbreviations: VAS, vascular surgery; OTS, orthopaedic and trauma surgery; VIS, visceral surgery; NSY, neurosurgery; DER, dermatological surgery; GYN, gynaecological surgery; HCT, heart and cardiothoracic surgery; URO, urological surgery; ENT, ear, nose and throat surgery; OMS, oral and maxillofacial surgery.

Table 2. Descriptive and bivariate analysis of demographics and patient characteristics

Characteristic	*S. aureus* SSI cases $N = 744$	MSSA SSI cases $N = 640$	MRSA SSI cases $N = 104$	Significance
Age [years]				
Mean (range)	58.1 (18–95)	56.8 (18–95)	65.9 (21–95)[a]	$P < 0.05$
Age groups [% (*n*)]				ns
18–29	9.5 (71)	10.6 (68)	2.9 (3)	
30–44	16.7 (124)	17.5 (112)	11.5 (12)	
45–59	20.4 (152)	20.6 (132)	19.2 (20)	
60–75	34.3 (255)	34.5 (221)	32.7 (34)	
>75	19.1 (142)	16.7 (107)	33.7 (35)	
Sex [% (*n*)]				ns
Female	48.1 (358)	48.1 (308)	48.1 (50)	
Male	51.9 (386)	51.9 (332)	51.9 (54)	
BMI [% (*n*)][b]			[a]	$P < 0.05$
<18.5	2.1 (13)	2.2 (12)	1.2 (1)	
18.5–24.9	32.5 (203)	33.4 (181)	26.5 (22)	
25.0–29.9	34.4 (215)	34.3 (186)	34.9 (29)	
30.0–34.9	20.8 (130)	20.7 (112)	21.7 (18)	
35.0–39.9	6.9 (43)	6.1 (33)	12.0 (10)	
>40	3.4 (21)	3.3 (18)	3.6 (3)	
ASA [% (*n*)][b]				ns
1	17.1 (101)	18.9 (94)	7.4 (7)	
2	41.2 (244)	39.8 (198)	48.9 (46)	
3	36.7 (217)	36.5 (182)	37.2 (35)	
4	4.9 (29)	4.6 (23)	6.4 (6)	
5	0.2 (1)	0.2 (1)	0.0 (0)	
ASA ≥ 2	82.9 (491)	81.1 (404)	92.6 (87)[a]	$P < 0.05$

Continued

Table 2. *Continued*

Characteristic	*S. aureus* SSI cases $N = 744$	MSSA SSI cases $N = 640$	MRSA SSI cases $N = 104$	Significance
Karnofsky performance status at admission [% (*n*)][b]				ns
90%–100%	38.0 (220)	37.8 (186)	39.1 (34)	
70%–80%	40.6 (235)	40.0 (197)	43.7 (38)	
50%–60%	14.5 (84)	15.4 (76)	9.2 (8)	
30%–40%	5.5 (32)	5.1 (25)	8.0 (7)	
10%–20%	1.4 (8)	1.6 (8)	0.0 (0)	
Comorbidities [% (*n*)]				
Cardiovascular				
Chronic cardiovascular disease	23.1 (172)	22.7 (145)	26.0 (27)	
Congestive heart failure	7.7 (57)	7.5 (48)	8.7 (9)	
Peripheral vascular disease	12.1 (90)	10.9 (70)	19.2 (20)[a]	$P < 0.05$
Pulmonal				
Chronic obstructive pulmonary disease	6.2 (46)	5.3 (34)	11.5 (12)[a]	$P < 0.05$
Haematological/oncological				
Leukaemia	0.4 (3)	0.3 (2)	1.0 (1)	$P = 0.147$
Lymphoma	2.2 (16)	2.5 (16)	0.0 (0)	
Solid tumour	22.3 (166)	21.7 (139)	26.0 (27)	
Neurological				
Dementia	2.3 (17)	1.4 (9)	7.7 (8)[a]	$P < 0.05$
Transient ischaemic attack or cerebrovascular accident	5.8 (43)	4.8 (31)	11.5 (12)[a]	$P < 0.05$
Hemiplegia	1.3 (10)	1.3 (8)	1.9 (2)	
Other internal				
Diabetes	21.0 (156)	20.2 (129)	26.0 (27)	$P = 0.177$
Liver disease	4.4 (33)	3.9 (25)	7.7 (8)	$P = 0.117$
Chronic kidney disease	7.8 (58)	6.4 (41)	16.3 (17)[a]	$P < 0.05$
Other				
HIV/AIDS	1.2 (9)	1.4 (9)	0.0 (0)	
Procedure duration (min)				
Mean (range)	156.5 (0–1640)	154.2 (0–1640)	171.0 (15–725)	$P = 0.083$
Time of surgery [% (*n*)]				
0 to 6 am	2.6 (19)	2.7 (17)	1.9 (2)	
6 am to 12 am	52.9 (393)	54.0 (345)	46.2 (48)	
12 am to 6 pm	33.9 (252)	33.6 (215)	35.6 (37)	
6 pm to 12 pm	10.6 (79)	9.7 (62)	16.3 (17)[a]	$P < 0.05$

Abbreviations: MSSA, methicillin-susceptible *Staphylococcus aureus*; ns, not significant.
[a]Statistically significant difference between MRSA SSI cases and MSSA SSI cases.
[b]For BMI calculation, only 625 cases were included; for ASA score calculation, only 592 cases were included; for Karnofsky performance status, only 579 cases were included and for time of surgery, only 743 cases were included due to missing data in the remaining cases.

in mean age (67.5 versus 65.2 years), but more patients were above the age of 75 years (41.2% versus 32.2%) and most had higher baseline morbidity (ASA ≥3%–80% versus 35%) (Table S13). While our data implicate an influence of time point of surgery, many other factors such as colonization-status are of high relevance and must be investigated in forthcoming trials.

Moreover, our analysis shows longer hospitalization, higher rates of revision surgery and re-admission to hospital of patients hospitalized with MRSA SSI, not only causing higher costs but precipitating additional individual sequelae such as secondary HAI.[2,21] MRSA SSI did not cause higher overall mortality.

Consistent with previous research,[22,23] the presence of ABS programmes and ID consultation services was associated with significantly lower incidence rates of MRSA SSI compared to MSSA SSI in our cohort. The paucity of centres with established ID consult services (three out of 14) is concerning, considering their established efficacy and the focus of our trial on high-volume centres with research expertise on SSI. Greater efforts are required to further disseminate ID expertise considering the current inhomogeneity of training programmes as well as the distribution of ID specialists.[24]

Although being one of the largest MRSA SSI cohorts,[25,26] limitations of our study are primarily the limited sample size

resulting in more vulnerable findings. Our findings need to be interpreted with caution due to the limited number of centres included per country. Our findings may not match established distributions of MRSA in Europe. The single participating Italian centre, e.g. did not report any SSI due to MRSA in 2016, while the single UK centre had a particularly high incidence. In general, the SA SSI cohort established by the SALT study is more suitable for cross-national analyses rather than for regional epidemiological comparisons. The limited patient number is most salient in the lacking robustness of MRSA effects on outcomes. While the unmatched cohort showed a significant difference in duration of hospitalization, we were not able to reproduce this finding in the matched cohort, which did not meet the significance threshold ($P=0.056$). Thus, conclusions regarding risk factors and outcomes drawn from our analyses may primarily add to the foundation of future studies.

This sub-cohort of the largest study of SSI in Europe confirms the low incidence of MRSA SSI, while highlighting its inhomogeneous extent even among leading surgical centres. As discussed, multiple factors influence the prevalence or MRSA SSI. Most concerning is the incomplete implementation of best practices approaches including ABS programmes and ID consultancy. Despite the inherent limitations, our findings support the urgent call for the establishment of these practices not only in high-volume surgical centres to further restrict the occurrence of multi-resistant pathogens.

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Transparency declarations

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Access to data

All data in the study were made fully accessible for all authors. The corresponding author is responsible for the final submission for publication.

Contributions

J.R., S.C.M. and B.L. conceptualized this subgroup analysis, authored the manuscript and performed the interpretation of data. B.L. designed the underlying SALT study (NCT03353532). S.C.M. and O.A.C. implemented the research and contributed to the design, data capture and analysis of results. C.B. supported the implementation of research and performed data management for the study mentioned previously. J.R. and the SALT

study group contributed data from European centres and edited the manuscript. J.H.N., C.B., A.Y.C., J.S.G., H.S., R.S., J.S. and S.V.W. contributed to interpretation of data and edited the manuscript. J.R. and B.L. verified cohort data and carried out statistical analyses. J.H.N. supported the statistical analyses.

Supplementary data

Tables S1–S13 are available as Supplementary data at *JAC-AMR* Online.

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4. Discussion

This sub-cohort from the largest study on SSI in Europe confirms the low incidence of MRSA-related SSI, while emphasizing their uneven distribution even among leading surgical centres. As discussed, various factors contribute to the prevalence of MRSA SSI. A particularly concerning issue is the incomplete adoption of best practice measures, such as ABS programs and infectious disease (ID) consultations.

4.1. Differences from existing European surveillance

Data on MRSA and SSI have been collected and evaluated centrally in Europe by the ECDC since surveillance systems were introduced. In 2023 those data were provided by all EU Member States and EEA countries for the first time.[13] The result is a large European cohort. The ECDC publishes annual reports which are made available to the public. Those reports usually present MRSA or SSI as sub-categories within larger topics such as antimicrobial resistance or healthcare-associated infections. Procedure-specific data is primarily provided through indicator procedures that represent various surgical categories. To identify specific areas requiring closer attention, we evaluated all surgical procedures and additionally patient-related factors.

4.2. International comparison

As described in the published work this multi-centre study shows a low overall and country-specific incidence of MRSA SSI in European high volume surgical centres in line with the epidemiology of nosocomial MRSA infections in general.[20212223] The overall MRSA rate of 14% is comparable to current European MRSA rates among invasive *S. aureus* isolates as previously reported by ECDC.[20] Our data show significant international differences. Highest incidence rates were observed in Spain (0.09% (0.07 – 0.11 95% CI) and UK (0.09% (0.04 – 0.17 95% CI), while lowest in Germany (0.03% (0.02 – 0.06 95% CI). In Spain and Germany, a relatively large number of surgical centres with resulting high case numbers (n = 67,934 and n = 46,443) were included, while in UK, only one centre participated with a total of approximately 9,000 cases. The single participating Italian centre did not report any SSI due to MRSA in 2016.

4.3. Antibiotic stewardship

In this study, we collected data solely on the case numbers from each centre, with minimal information on centre-specific characteristics. Consequently, it is not possible to draw conclusions regarding the underlying causes of the observed international variations or differences between individual centres. Only two factors were considered: first, the inclusion criterion limited the study to surgical centres performing over 10,000 procedures annually, reflecting a certain level of quality and expertise. Second, the presence or absence of standardized ABS programs was documented.

In 2023 the European Council adopted a recommendation to combat AMR which includes the better surveillance of AMR and antimicrobial consumption and concrete targets to reduce antimicrobial consumption by 20% and particular invasive infections like MRSA bloodstream infections by 15%.[24] Consistent with prior research[2526], the presence of ABS programmes and ID consultation services was associated with significantly lower incidence rates of MRSA SSI compared to MSSA SSI in our cohort. However, no improvement in outcome could be observed. A future study involving additional centres that have implemented such a service would need to re-examine this specific question. International guidelines still recommend decolonization in certain situations but have not yet included ABS as a preventive measure.[2728] Considering the low number of hospitals with ABS and ID consultancy programs across Europe (3 of 14 hospitals), we here support the demand for dissemination of such programs at every level of patient care. Particularly given the focus of our trial on high-volume centres with specialized research expertise in SSI.

4.4. Procedures at risk

Given the low number of cases in general, we observed incidences of an average of less than one percent for each surgical procedure. Most MRSA SSI occurred in orthopaedic trauma surgery (n = 31 cases (29.8%)), yet the incidence was 0.1% (0.1 – 0.1 95% CI). Since our sample size is considerably small, international and procedure-specific differences may not be representative. This also applies for the relatively high MRSA SSI incidence in minimally invasive surgery of the bile duct (2.3% (0.3 – 15.8 95% CI), but the small number of those procedures probably contributes more to this than the number of resulting MRSA SSI, also reflected in a wide confidence interval.

The results concerning procedure duration and time of day implicate an influence of surgery between 6 and 12 pm on MRSA SSI incidence rates, which has been discussed in the published paper. In summary this finding could be explained by less adherence to hygiene protocols. However, even larger trials could not prove a statistical correlation.[29] Further patient- and procedure-related factors are relevant and cannot be ruled out.

The question of which procedures are at risk cannot be adequately addressed. Moreover, previous findings show an increased risk to develop MRSA SSI in preoperatively colonized patients[3031]. Other treatment-associated factors could outweigh the actual procedure. Preoperative screening, application of an adequate decolonization regimen as well as preoperative antibiotic prophylaxis in colonized patients have been shown to prevent SSI efficiently.[32333435] Yet, several randomized controlled trials were unable to confirm this[36], but rather support ABS as a key factor.[37]

4.5. Patient-related risk factors

We were able to identify age and number of underlying conditions as independent patient-related risk factors. Despite the small number of cases, both variables appear to have a certain individual influence, as already analysed in previous studies.[383916] Then again, the actual causal link could rather be due to more frequent inpatient hospital treatment and antibiotic treatment. In addition it was not assessed if a patient lived in a long-term care facility prior to infection all leading to a higher risk of MRSA colonization and therefore infection.[3040] This example points out the difficulties to determine independent risk factors for MRSA SSI, since we can assume a lot of confounding and some variables have not been assessed at all.

4.6. Limitations

The primary limitations of our study are the relatively small sample size, which makes the findings more susceptible to variability, as previously noted. Additionally, the limited number of centres included per country necessitate cautious interpretation of our results. For example, while bivariate analyses in the unmatched cohort indicated that hospitalization was significantly longer for MRSA SSI cases compared to MSSA SSI cases, this result could not be confirmed

after matching (P = 0,056). Consequently, conclusions regarding risk factors and outcomes from this analysis should be viewed as contributing to the groundwork for future studies rather than providing definitive answers.

4.7. Conclusions

This sub-cohort, drawn from the largest study on SSI in Europe, corroborates the low incidence of MRSA-related SSI while underscoring their uneven distribution, even among leading surgical centres. As previously discussed, multiple factors contribute to the prevalence of MRSA SSI. While many of these factors are patient-related and largely beyond control, modifiable factors such as MRSA colonization and potentially predisposing elements like prior antibiotic use or hospital admissions were not considered in this analysis. The underlying causes of the observed differences between European surgical centres remain unclear. Of particular concern is the incomplete adoption of best practice strategies, including ABS programs and infectious disease consultancy. Despite the limitations of the study, these findings reinforce the urgent need for the widespread implementation of such practices, not only in high-volume surgical centres, to mitigate the spread of multi-resistant pathogens.

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6. Appendix

Supplemental Table 1. Inclusion and exclusion criteria

	Criteria
Inclusion	• Age 18 years or greater at the time of surgery
Exclusion	• Patients undergoing minimal invasive biopsies and eye surgery • SSI at the time of surgery • Cases with missing data defined as missing completely at random

Supplemental Table 2. Study site data per country

Characteristic	France	Germany	Italy	Spain	UK	Total
Number of centres	3	4	1	5	1	14
Number of included patients	35974	46443	19384	67934	9168	178,903

Supplemental Table 3. Microbiological data from *S. aureus* SSI cases

	S. aureus SSI [n (%)] N = 744	MSSA SSI [n (%)] N = 640	MRSA [n (%)] N = 104
Type of SSI			
Superficial incisional	354 (46.3)	307 (46.5)	47 (45.2)
Deep incisional	206 (27.0)	172 (26.1)	34 (32.7)
Organ space	204 (26.7)	181 (27.4)	23 (22.1)
Specimen type			
Aspirate	71 (9.5)	58 (9.1)	13 (12.5)
Blood culture	35 (4.7)	33 (5.2)	2 (1.9)
Sample obtained during surgery	200 (26.9)	166 (26.0)	34 (32.7)
Wound swab	438 (58.9)	383 (59.8)	55 (52.9)
Wound class			
Clean	373 (50.1)	314 (49.1)	59 (56.7)
Clean-contaminated	154 (20.7)	133 (20.8)	21 (20.2)
Contaminated	98 (13.2)	86 (13.4)	12 (11.5)
Dirty	61 (8.2)	56 (8.8)	5 (4.8)
Unknown	58 (7.8)	51 (8.0)	7 (6.7)

Supplemental Table 4. Overall incidence of MRSA SSI per centre and country

Centre	Number of included patients N = 178903	Number and percentage of MRSA SSI [n (%)] N = 104	Incidence rates of MRSA SSI [% (95% CI)] N = 104	ABS/ID on site
France	35974	22 (21.2)	0.06 (0.04 – 0.09)	
Limoges	9663	8 (7.7)	0.08 (0.04 – 0.17)	unknown
Tours	16697	11 (10.6)	0.07 (0.03 – 0.12)	unknown
Vendée	9614	3 (2.9)	0.03 (0.01 – 0.10)	no
Germany	46443	16 (15.4)	0.03 (0.02 – 0.06)	
LMU	4946	1 (1.0)	0.02 (0.00 – 0.14)	no
UKB	7109	6 (5.8)	0.08 (0.04 – 0.19)	no
UKJ	15581	4 (3.8)	0.03 (0.01 – 0.07)	yes
UKK	18807	5 (4.8)	0.03 (0.01 – 0.06)	yes
Spain	67934	58 (55.8)	0.09 (0.07 – 0.11)	
HCB	13041	7 (6.7)	0.05 (0.03 – 0.11)	no
HGGM	15344	21 (20.2)	0.14 (0.09 – 0.20)	no
IMIM	6555	7 (6.7)	0.11 (0.05 – 0.22)	unknown
LaFe	12810	12 (11.5)	0.09 (0.05 – 0.16)	no
RyC	20184	11 (10.6)	0.05 (0.03 – 0.10)	no
UK				
NHS Manchester	9168	8 (7.7)	0.09 (0.04 – 0.17)	yes
Italy				
Udine	19384	0 (0.0)	0.00	no

Abbreviations: ABS = antibiotic stewardship, ID = infectious disease consultation service, Limoges = Central University Hospital of Limoges, Tours = Central Regional University Hospital of Tours, Vendée = Central Departmental Hospital of Vendée, LMU = University Hospital of Munich, UKB = University Hospital of Bonn, UKJ = University Hospital of Jena, UKK = University Hospital of Cologne, HCB = Hospital Clinic of Barcelona, HGGM = General University Hospital Gregorio Marañón, IMIM = Hospital del Mar Medical Research Institute, LaFe = La Fe University and Polytechnic Hospital, RyC = University Hospital Ramón y Cajal Madrid, NHS Manchester = Central Manchester University Hospitals NHS, Udine = University of Udine and Santa Maria Misericordia University Hospital

Supplemental Table 5. Specialties and procedures with highest number and highest rate of MRSA SSI

Procedure	Number and percentage of MRSA SSI [n (%)] N = 104	Procedure specific incidence of MRSA SSI [% (95% CI)] N = 104
Dermatological surgery	10 (9.6)	0.1 (0.0 – 0.1)
Wound debridement	5 (4.8)	0.1 (0.1 – 0.3)
Incision and excision of skin and subcutaneous tissue	3 (2.9)	0.0 (0.0 – 0.1)
Skin autograft transplantation to head or neck	1 (1.0)	0.1 (0.0 – 0.8)
Facial plastic surgery	1 (1.0)	0.1 (0.0 – 0.7)
Ear, nose and throat surgery	2 (1.9)	0.0 (0.0 – 0.1)
Gynaecological surgery	12 (11.5)	0.1 (0.0 – 0.1)
Caesarean section	6 (5.8)	0.1 (0.0 – 0.2)
Breast excision and resection	3 (2.9)	0.1 (0.0 – 0.3)
Surgery on vagina and recto-uterine pouch	1 (1.0)	0.1 (0.0 – 0.7)
Plastic surgery of breast augmentation and reduction	1 (1.0)	0.1 (0.0 – 0.7)
Surgery on uterus and cervix uteri	1 (1.0)	0.0 (0.0 – 0.2)
Heart and cardiothoracic surgery	4 (3.9)	0.0 (0.0 – 0.1)
Revascularization of the heart	2 (1.9)	0.1 (0.0 – 0.4)
Open surgery of the lung and pleura (reconstruction and removal)	1 (1.0)	0.1 (0.0 – 0.4)
Atrial septum/valve repair surgery	1 (1.0)	0.0 (0.0 – 0.3)
Neurosurgery	7 (6.7)	0.1 (0.0 – 0.1)
Operations on scull, brain, meninges	3 (2.9)	0.1 (0.0 – 0.2)
Reconstruction of a nerve and nerve plexus	2 (1.9)	0.1 (0.0 – 0.2)
Access to the vertebral column, extradural	1 (1.0)	0.1 (0.0 – 1.0)
Operations on spinal cord and spinal cord structures		

	1 (1.0)	0.1 (0.0 – 0.6)
Oral and maxillofacial surgery	0 (0.0)	0.0
Orthopaedic and trauma surgery	31 (29.8)	0.1 (0.1 – 0.1)
Primary total prosthetic replacement of hip joint	7 (6.7)	0.2 (0.1 – 0.5)
Amputation and disarticulation of lower limb	4 (3.9)	0.3 (0.1 – 0.8)
Open repair of a fractured long tubular bone	4 (3.9)	0.1 (0.0 – 0.3)
Operations on bone	4 (3.9)	0.1 (0.0 – 0.2)
Operations on the vertebral column	3 (2.9)	0.1 (0.0 – 0.2)
Spondylodesis	2 (1.9)	0.3 (0.1 – 1.1)
Open reduction and internal fixation of a fracture or slipped epiphysis	2 (1.9)	0.1 (0.0 – 0.3)
Revision, replacement and removal of prosthetic joint of the upper limb	1 (1.0)	0.5 (0.1 – 3.7)
Reduction of a joint dislocation	1 (1.0)	0.3 (0.0 – 1.7)
Urological surgery	5 (4.8)	0.0 (0.0 – 0.1)
Open surgery on the urethra	1 (1.0)	0.3 (0.0 – 2.0)
Open surgery on the prostate	1 (1.0)	0.2 (0.0 – 1.3)
Transplantation of kidney	1 (1.0)	0.1 (0.0 – 0.6)
Minimally invasive operations on the prostate	1 (1.0)	0.1 (0.0 – 0.4)
Minimally invasive operations on the bladder	1 (1.0)	0.0 (0.0 – 0.2)
Vascular surgery	15 (14.4)	0.1 (0.1 – 0.2)
Insertion of arteriovenous graft	7 (6.7)	0.4 (0.2 – 0.8)
Ligation of blood vessels	2 (1.9)	0.7 (0.2 – 2.9)
Angioplasty	2 (1.9)	0.6 (0.2 – 2.3)
Surgery on lymph nodes and vessels	2 (1.9)	0.1 (0.0 – 0.3)
Open insertion of stent grafts	1 (1.0)	0.2 (0.0 – 1.3)
Visceral surgery	18 (17.3)	0.1 (0.0 – 0.1)
Open resection of large intestine	3 (2.9)	0.2 (0.1 – 0.6)

Operations on the abdominal wall	3 (2.9)	0.1 (0.0 – 0.3)
Open excision and resection of pancreas	2 (1.9)	0.3 (0.1 – 1.3)
Minimally invasive resection of large intestine	2 (1.9)	0.2 (0.1 – 0.8)
Minimally invasive surgery of the bile duct	1 (1.0)	2.3 (0.3 – 15.8)

Supplemental Table 6 Multivariate analysis of significant differences between MSSA and MRSA SSI cases (Logistic regression)

Factor	Significance	Odds ratio
Age	p=0.000	1.024
Surgery 6 pm to 12 pm	p=0.070	1.310
CKD	p=0.019	2.148
Dementia	p=0.029	3.190

Included variables

- Surgical category
- Age
- Procedure duration
- Diabetes
- Sex
- Smoking status
- Time of surgery
- Liver disease
- Solid tumour
- HIV/AIDS
- Chronic kidney disease (CKD)
- Chronic heart failure (CHF)
- Chronic cardiovascular disease (CVD)
- Chronic obstructive pulmonary disease (COPD)
- Peripheral vascular disease (PVD)
- Cerebrovascular accident/transient ischemic accident (CVA/TIA)
- Dementia
- Hemiplegia
- Connective tissue disease (CTD)
- Leukaemia
- Malignant lymphoma
- Peptic ulcer

Supplemental Table 7. Complications compared between MRSA and MSSA SSI cases

Complication	MRSA N = 104	MSSA N = 640	Significance
Mean hospitalization [days (range)]	24.89 (0 – 133)	16.26 (0 – 180)	p<0.05
ICU stay following surgery [% (n)]	17.3 (18)	19.7 (126)	p=0.569
Readmission to hospital [% (n)]	58.7 (61)	49.4 (316)	p=0.079
Revision surgery [% (n)]	57.7 (60)	47.8 (306)	p=0.062

Supplemental Table 8. Survival compared between MRSA and MSSA cases

Survival	MRSA N = 104	MSSA N = 640	Significance
30 days [% (n)]	96.2 (100)	97.3 (623)	p=0.519
90 days [% (n)]	89.4 (93)	91.9 (588)	p=0.405

Supplemental Table 9. Complications compared between MRSA and MSSA cases with propensity score matching

Complication	MRSA N = 104	MSSA N = 104	Significance
Mean hospitalization [days (range)]	24.89 (0 – 133)	19.66 (0 – 180)	p=0.056
ICU stay following surgery [% (n)]	17.3 (18)	21.2 (22)	p=0.482
Readmission to hospital [% (n)]	58.7 (61)	50.0 (52)	p=0.210
Revision surgery [% (n)]	57.7 (60)	48.1 (50)	p=0.165

Supplemental Table 10. Survival compared between MRSA and MSSA cases with propensity score matching

Survival	MRSA N = 104	MSSA N = 104	Significance
30 days [% (n)]	96.2 (100)	95.2 (99)	p=0.522
90 days [% (n)]	89.4 (93)	86.5 (90)	p=1.000

Supplemental Table 11. Complications of MRSA SSI compared between centres with and without established ABS and ID consultation programmes

Complication	ABS/ID on site N = 17	No ABS/ID on site N = 61	Significance
Mean hospitalization [days (range)]	28.18 (0 – 133)	26.05 (1 – 94)	p=0.569
ICU stay following surgery [% (n)]	23.5 (4)	19.7 (12)	p=0.740
Readmission to hospital [% (n)]	41.2 (7)	57.4 (35)	p=0.236
Revision surgery [% (n)]	41.2 (7)	55.7 (34)	p=0.288

Supplemental Table 12. Survival of MRSA SSI compared between centres with and without established ABS and ID consultation programmes

Survival	ABS/ID on site N = 17	No ABS/ID on site N = 61	Significance
30 days [% (n)]	100 (17)	95.1 (58)	p=0.591
90 days [% (n)]	100 (17)	88.5 (54)	p=0.202

Supplemental Table 13. Demographics and characteristics of patients with MRSA surgical site infections (SSI) undergoing surgery between 6 pm and 12 pm compared to other daytimes

Characteristic	Time of surgery 6 pm to 12 pm N = 17	All other daytimes N = 87
Age [years]		
Mean (range)	67.5 (27 – 95)	65.2 (21 – 93)
Age groups [% (n)]		
18 – 29	5.9 (1)	3.4 (3)
30 – 44	11.8 (2)	10.3 (9)
45 – 59	17.6 (3)	20.7 (18)
60 – 75	23.5 (4)	33.3 (29)
>75	41.2 (7)	32.2 (28)
Sex [% (n)]		
Female	35.3 (6)	50.6 (44)
Male	64.7 (11)	49.4 (43)
BMI [% (n)] *		
<18.5	10.0 (1)	0.0 (0)
18.5 – 24.9	40.0 (4)	24.6 (15)
25.0 – 29.9	20.0 (2)	32.8 (20)
30.0 – 34.9	10.0 (1)	26.2 (16)
35.0 – 39.9	20.0 (2)	11.5 (7)
>40	0.0 (0)	4.9 (3)
ASA [% (n)] *		
1	0.0 (0)	9.0 (7)
2	18.8 (3)	55.1 (43)
3	68.8 (11)	30.8 (24)
4	12.5 (2)	5.1 (4)
5	0.0 (0)	0.0 (0)
Karnofsky performance status at Admission [% (n)] *		
90 – 100%	40.0 (6)	38.9 (28)
70 – 80%	46.7 (7)	43.1 (31)
50 – 60%	0.0 (0)	11.1 (8)
30 – 40%	13.3 (2)	6.9 (5)
10 – 20%	0.0 (0)	0.0 (0)

* For BMI calculation, only 71 cases were included; for ASA score calculation, only 94 cases were included and for Karnofsky performance status, only 87 cases were included due to missing data in the remaining cases.[19]