



Limited evidence of nosocomial methicillin-resistant *Staphylococcus aureus* transmission in a low-prevalence tertiary care centre: a five-year genomic epidemiology study

Aila Caplunik-Pratsch^{a,*}, Bärbel Kieninger^a, Stefan Hansch^a,
Sascha D. Braun^{b,c,d}, Anca Rath^a, Barbara Lenker^a, Jürgen Fritsch^a,
Anja Eichner^a, Stefan Monecke^{b,c,d}, Wulf Schneider-Brachert^{a,e}

^a Department of Infection Prevention and Infectious Diseases, University Hospital Regensburg, Franz-Josef-Strauss-Allee 11, Regensburg, Germany

^b Leibniz Institute of Photonic Technology (IPHT)/Leibniz Center for Photonics in Infection Research (LPI), Jena, Germany

^c InfectoGnostics Research Campus, Jena, Germany

^d Center for Translational Medicine (CETRAMED), Jena University Hospital, Friedrich Schiller University Jena, Jena, Germany

^e Institute of Microbiology and Hygiene, University Regensburg, Regensburg, Germany

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SUMMARY

Background: Methicillin-resistant *Staphylococcus aureus* (MRSA) has traditionally been considered a nosocomial pathogen. However, declining MRSA prevalence in many European countries has raised questions about the relative contribution of nosocomial transmission to MRSA epidemiology in low-prevalence healthcare settings. We aimed to characterize MRSA population structure and transmission dynamics in a German tertiary care hospital.

Methods: We conducted a retrospective genomic epidemiology study at a tertiary care hospital in Germany, including first MRSA isolates per patient and year collected between 2020 and 2024. Whole-genome sequencing and core genome multi-locus sequence typing were performed. Clusters were defined using a threshold of ≤ 10 allelic differences and assessed using epidemiological data.

Results: A total of 518 MRSA isolates from individual patients were analysed, of which 70.8% were screening-derived. The most frequent sequence types (STs) were ST22, ST398, and ST225. Only 58 of 518 isolates (11.2%) formed 23 genetic clusters, which were predominantly small (median size 2). Epidemiological assessment identified links to the study hospital, households, and external healthcare facilities, whereas several clusters had no identifiable epidemiological link. Only one cluster was compatible with probable in-hospital transmission. ST398 isolates were significantly less likely to originate from clinical samples (odds ratio = 0.34; $P = 0.0004$) and were exclusively detected as singletons.

Conclusions: In this low-prevalence setting, MRSA epidemiology was characterized by limited evidence of sustained nosocomial transmission despite cocirculation of multiple

* Corresponding author. Address: Aila Caplunik-Pratsch, Department of Infection Prevention and Infectious Diseases, University Hospital Regensburg, Franz-Josef-Strauss-Allee 11, 93053 Regensburg, Germany. Tel.: +49 9419444897.

E-mail address: aila.caplunik-pratsch@ukr.de (A. Caplunik-Pratsch).

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healthcare-associated, livestock-associated, and community-associated lineages. These findings suggest that MRSA cases are primarily driven by external introductions rather than sustained in-hospital transmission and support more targeted, lineage- and context-adapted infection prevention strategies.

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Introduction

The epidemiology of methicillin-resistant *Staphylococcus aureus* (MRSA) has undergone substantial changes in recent years. In several European countries, including Germany, declining MRSA rates have been observed, particularly among invasive isolates [1,2], raising questions about whether current infection prevention and control (IPC) strategies remain appropriate in contemporary low-prevalence settings.

Historically, MRSA has been regarded primarily as a nosocomial pathogen, and infection prevention strategies have focused on interrupting in-hospital transmission through measures such as admission screening and contact precautions [3]. However, the effectiveness of some of these measures has been increasingly questioned, and evidence supporting routine contact precautions remains inconsistent across healthcare settings [4,5], particularly when their potential unintended consequences are considered [6]. At the same time, accumulating evidence indicates that MRSA populations in contemporary hospital settings comprise not only healthcare-associated MRSA (HA-MRSA) lineages, but also by community-associated MRSA (CA-MRSA) and livestock-associated MRSA (LA-MRSA) strains, as well as repeated introductions from external healthcare facilities [7–9]. This increasing heterogeneity raises the question to what extent ongoing nosocomial transmission still contributes to MRSA epidemiology in low-prevalence settings.

Whole-genome sequencing (WGS) has substantially improved the investigation of MRSA transmission and enables high-resolution assessment of transmission dynamics in hospital epidemiology [8–10].

The relative contribution of nosocomial transmission to MRSA epidemiology remains incompletely understood, particularly in low-prevalence settings. We therefore used an integrated genomic and epidemiological approach to characterize MRSA population structure and transmission dynamics in a German tertiary care hospital.

Methods

Study design and setting

This retrospective observational study was conducted at the University Hospital Regensburg, Germany, a tertiary-care academic medical centre serving a large catchment area in Eastern Bavaria that includes substantial rural and agricultural regions.

All MRSA isolates detected in routine microbiological diagnostics at the Institute of Clinical Microbiology and Hygiene, University Hospital Regensburg, between January 2020 and December 2024 were considered for inclusion.

At our institution, risk-adapted MRSA screening and infection prevention measures are routinely implemented in accordance with the recommendations of the German

Commission for Hospital Hygiene and Infection Prevention (KRINKO) for the prevention and control of MRSA [3]. Details regarding the institutional MRSA screening and infection prevention strategy are provided in [Supplementary Material S1](#).

The University Hospital Regensburg participates in the German national nosocomial infection surveillance system (KISS; Krankenhaus-Infektions-Surveillance-System), including MRSA-KISS surveillance [11]. Hospital-wide MRSA epidemiological data for the study period (2020–2024) were collected by the Department of Infection Prevention and Infectious Diseases as part of routine MRSA-KISS surveillance.

In accordance with MRSA-KISS definitions, MRSA cases included both patients with newly detected MRSA and patients with previously known MRSA colonization or infection identified upon admission ('imported' MRSA cases). Nosocomial MRSA cases were defined as patients with first MRSA detection occurring more than 72 h after hospital admission.

Annual MRSA prevalence, incidence density of nosocomial MRSA cases per 1,000 patient-days, and MRSA screening intensity (screening swabs per 100 patients) were calculated according to MRSA-KISS methodology [11].

Isolate selection

The first MRSA isolate per patient and calendar year was identified using the laboratory information system. Screening isolates were defined as nasal swabs obtained as part of routine admission screening, whereas all other specimens, including wound swabs collected during screening procedures, were classified as clinical isolates. If multiple MRSA isolates were detected within the same year, only the first isolate was included; when unavailable for sequencing, the next available isolate from the same year was used. A patient-year approach was chosen to account for potential strain replacement or acquisition over time.

Microbiological identification and routine diagnostics

Clinical specimens were processed in the routine diagnostic microbiology laboratory according to standard procedures. Identification of *S. aureus* was performed using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (Bruker Microflex, Bruker Daltonics, Mannheim, Germany).

Antimicrobial susceptibility testing and interpretation were performed according to EUCAST guidelines using the BD Phoenix system (BD Diagnostics, USA).

MRSA isolates were forwarded to the sequencing laboratory of the Department of Infection Prevention and Infectious Diseases (outbreak laboratory) for further analysis.

MRSA identification was reconfirmed by real-time polymerase chain reaction using a LightCycler MRSA assay, targeting *mecA* and the *S. aureus*-specific *nuc* gene [12,13]. Isolates lacking *mecA* detection were retained to allow identification of alternative methicillin resistance determinants such as *mecC*.

Whole-genome sequencing

WGS was performed from DNA extracted from 24-hour-old pure cultures using the QIAamp DNA Mini Kit (Qiagen, Germany). Sequencing libraries were prepared using the Nextera XT Library Preparation Kit (Illumina, USA) and sequenced on Illumina MiniSeq or NextSeq Dx550 platforms (2 × 150 bp paired-end reads). Raw reads were quality-controlled and processed using the AQUAMIS pipeline [14].

Genome assembly

Raw sequence reads were initially assembled using SKESA. However, detection of *spa* types from these assemblies proved incomplete for a substantial subset of isolates. Therefore, all isolates were reassembled using SPAdes, and the SPAdes assemblies were used for all subsequent genomic analyses [15].

Core genome multi-locus sequence typing (cgMLST) and phylogenetic analysis

cgMLST was performed using Bruker MBioSEQ Ridom Typer (version 11.1.0; Bruker Daltonics, Bremen, Germany) based on the *S. aureus* cgMLST scheme comprising 1861 target genes [16].

Isolates differing by ≤10 cgMLST alleles were considered part of the same genomic cluster [17].

spa typing

spa typing was performed in Ridom Typer based on the polymorphic X region of the *S. aureus spa* gene.

SCCmec typing and microarray-based in silico characterization

For isolates assigned to genomic clusters, SCCmec typing was performed in silico using a previously described virtual microarray approach based on WGS data [18]. SCCmec types were assigned according to established interpretation criteria [19].

Detection of resistance and virulence genes

Detection of antimicrobial resistance genes and selected virulence determinants was performed using the integrated gene detection tools implemented in Ridom Typer.

Panton–Valentine leukocidin (PVL) positivity was defined as the presence of both *lukF*-PV and *lukS*-PV genes.

The immune evasion cluster (IEC) was defined by the detection of at least one IEC-associated gene (*scn*, *sak*, *chp*, or *sea*).

Epidemiological data analysis

For isolates belonging to genomic clusters, available epidemiological data were reviewed to identify possible transmission events. Patient records and hospital administrative data were assessed for spatial and temporal links, including ward location and overlapping hospital stays. The epidemiological assessment and link categorization were performed by one investigator (A.C.-P.). If no plausible link within the study hospital was identified, prior healthcare exposure in external

hospitals was additionally assessed. Based on the overall epidemiological assessment, clusters were classified as associated with the study hospital, household transmission, external healthcare exposure, mixed epidemiological patterns, or no identifiable epidemiological link.

For clusters associated with the study hospital, epidemiological links were further categorized as ‘probable’, ‘unclear’, or ‘no identifiable link’ based on predefined spatial and temporal criteria. ‘Probable’ transmission was defined as detection in patients on the same ward with overlapping inpatient stays or stays occurring within 30 days. Cases with only partial spatial or temporal concordance were classified as ‘unclear’, whereas cases without an identifiable relationship were classified as having ‘no identifiable link’. For clusters not associated with the study hospital, this categorization was considered not applicable.

Statistical analysis

Statistical analyses were performed using R statistical software (R Foundation for Statistical Computing, Vienna, Austria). Categorical variables were compared using Fisher’s exact test. These tests were used to assess associations between categorical variables such as ST, isolate source, and cluster occurrence. A *P*-value <0.05 was considered statistically significant. Given the exploratory epidemiological nature of the study, no adjustment for multiple testing was applied.

Ethics approval

The study protocol was approved by the Ethics Committee of the University of Regensburg (approval number 26-4516-104, approved 10 February 2026).

Results

Epidemiology of MRSA cases at University Hospital Regensburg (2020–2024)

According to MRSA-KISS surveillance data, 1016 MRSA cases were documented at University Hospital Regensburg during the study period (2020–2024) (Supplementary Table S1). MRSA prevalence remained low (0.51–0.77%), and the incidence density of nosocomial MRSA cases was consistently low (0.03–0.07 per 1,000 patient-days). Screening intensity varied between years and declined in 2024 (Supplementary Table S1).

WGS cohort

Among the MRSA cases documented during the study period, 673 annual first isolates were identified, of which 550 (81.7%) underwent WGS (Supplementary Table S2). Analyses of overall population structure were based on first isolates per patient during the entire study period (*N* = 518), whereas temporal analyses used annual first isolates (*N* = 550). The difference reflects repeated inclusion of patients with isolates in more than one study year. Longitudinal genotypic data are provided in Supplementary Table S3.

Overall clonal structure of MRSA isolates (first isolates of entire study period, N = 518)

The clonal population structure of the 518 first isolates per patient is illustrated in Figure 1.

A total of 44 distinct STs and 67 spa types were identified. The predominant STs were ST22 (17.0%), ST398 (16.6%), ST225 (14.7%), and ST1 (9.1%), followed by ST5, ST8, ST6, and ST45.

All isolates were confirmed as MRSA by detection of *mec* genes, predominantly *mecA* (507/518, 97.9%), while *mecC* was identified in 11 isolates (2.1%).

The distribution of predominant MRSA STs and associated major spa types is summarized in Table I, while detailed isolate-level molecular typing data are provided in Supplementary Table S6.

Temporal variation of MRSA subtypes (annual first isolates, N = 550)

To assess temporal variation in clonal distribution, 550 annual first isolates were analysed (Supplementary Table S3; Supplementary Figure S1).

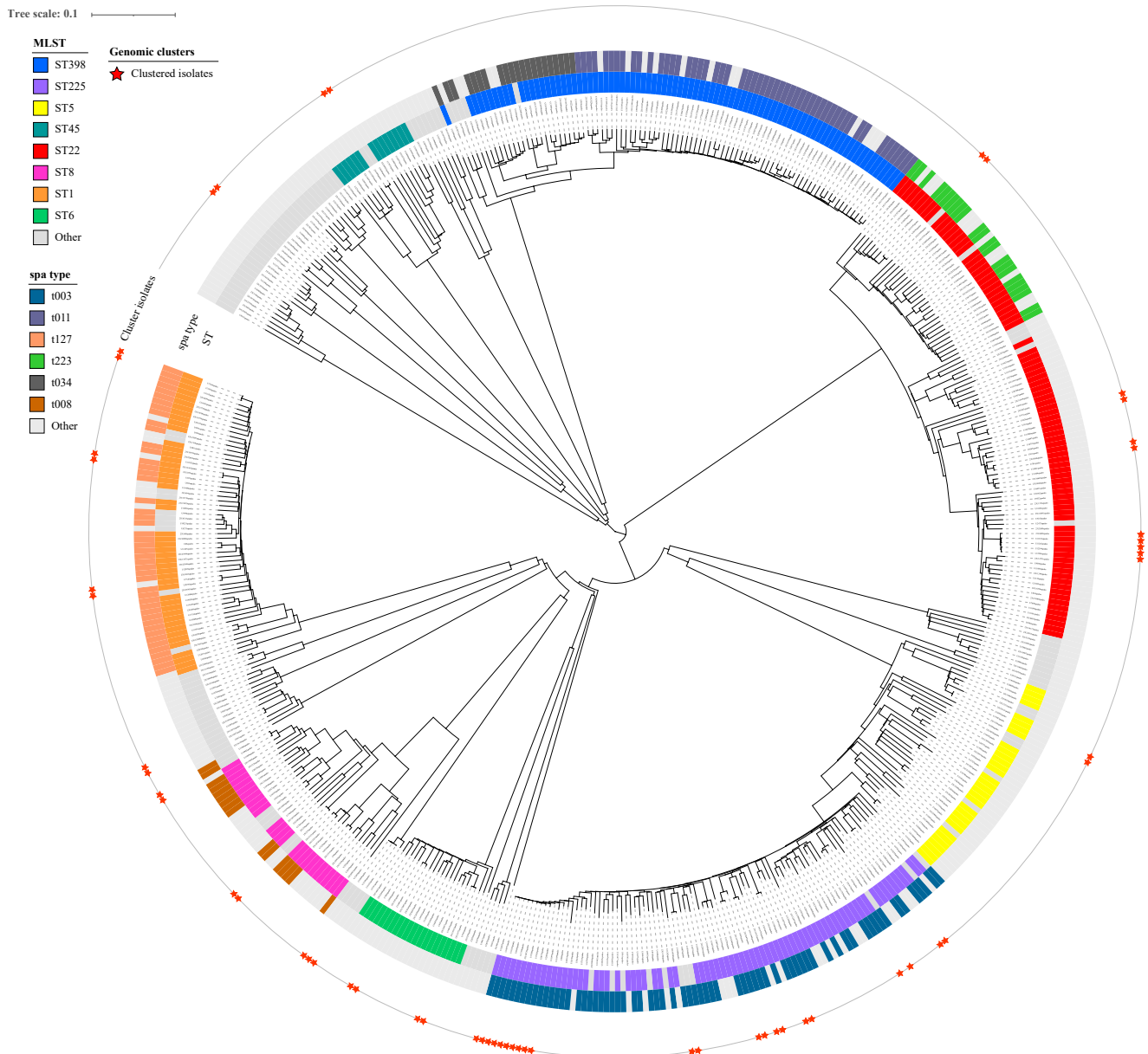


Figure 1. Phylogenetic structure of methicillin-resistant *Staphylococcus aureus* (MRSA) isolates with genomic clusters. Circular midpoint-rooted phylogenetic tree of the 518 first MRSA isolates recovered from individual patients during the study period. Genetic distances are based on core genome multi-locus sequence typing (cgMLST) allelic differences. The tree was visualized using iTOL. Concentric annotation rings indicate sequence types (STs; inner ring) and spa types (outer ring). Distinct colours represent the eight most prevalent STs and the six most prevalent spa types, while less frequent types are shown in grey. Isolates belonging to genomic clusters (≤ 10 cgMLST allelic differences) are indicated by red stars. MLST, multi-locus sequence typing.

Table 1

Distribution of the predominant MRSA sequence types and their major spa types ($N = 518$), 2020–2024

ST	Major spa type(s) ($\geq 10\%$ within ST)	N	%
ST22	t223 (22/88), t379 (9/88), other spa types (57/88)	88	17.0
ST398	t011 (53/86), t034 (18/86), other spa types (15/86)	86	16.6
ST225	t003 (56/76), other spa types (20/76)	76	14.7
ST1	t127 (40/47), other spa types (7/47)	47	9.1
ST5	t002 (15/32), other spa types (17/32)	32	6.2
ST8	t008 (14/27), other spa types (13/27)	27	5.2
ST6	t304 (15/21), other spa types (6/21)	21	4.1
ST45	t330 (4/14), t026 (2/14), other spa types (8/14)	14	2.7
Other STs	Mixed	127	24.5

Data are presented as number of isolates, with percentage in parentheses. STs accounting for $\geq 2.5\%$ of all isolates are shown individually; all remaining STs, including isolates without assignable ST, are grouped as 'Other STs'. Spa types representing $\geq 10\%$ of isolates within a given ST are listed; less frequent spa types are summarized as 'other spa types'. Complete isolate-level molecular typing data are provided in [Supplementary Table S6](#).

MRSA, methicillin-resistant *Staphylococcus aureus*; ST, sequence type.

Eight major STs accounted for the majority of isolates throughout the study period. ST398 decreased from 24.0% in 2020 to 11.9% in 2024. ST225 remained relatively stable between 2020 and 2022 (17–19%) but declined to approximately 10% in 2023 and 2024. ST1 increased moderately over time, reaching 11.9% in 2024. The proportion of ST22 fluctuated between 15% and 19% and was highest in 2024 (19.3%). The remaining STs showed only minor year-to-year variation.

Among patients with more than one annual first isolate (29/518, 5.6%), most showed stable genotypic characteristics over time. ST remained unchanged in 86.2% of patients. Unchanged STs were generally associated with low cgMLST distances, whereas ST changes corresponded to markedly higher genetic distances ([Supplementary Table S5](#)).

Resistance genes

Among the detected resistance determinants, characteristic lineage-associated resistance patterns were observed ([Supplementary Figure S2](#)). Resistance determinants associated with macrolide–lincosamide–streptogramin B resistance were detected in 41.9% of isolates, tetracycline resistance genes in 33.4%, trimethoprim resistance genes in 32.8%, and fusidic acid resistance determinants in 9.1%.

Tetracycline resistance determinants were predominantly associated with ST398, whereas ST225 was almost uniformly *erm(A)*-positive. ST1 was characterized by *erm(C)*, and trimethoprim resistance was predominantly mediated by *dfrrB*. Fusidic acid resistance genes were mainly detected in ST5 and ST8. Among five ST121 isolates, two carried *fusC*; however, both lacked *eta*, *etb*, and *dfrrG* and thus did not show the characteristic genetic profile of the recently described European FAR-MRSA ST121 clone [20].

Virulence genes

Virulence gene analysis also demonstrated distinct lineage-associated patterns ([Supplementary Figure S3](#)). PVL genes were detected in 63 of 518 isolates (12.2%) and *tsst-1* in 44 of 518 isolates (8.5%), whereas IEC-associated genes were present in 408 of 518 isolates (78.8%).

PVL genes were detected predominantly in ST8 and were absent in ST398. In contrast, IEC-associated genes were highly

prevalent overall (408/518, 78.8%) but were detected in only 8 of 86 ST398 isolates (9.3%).

Distribution of screening and clinical isolates

Among the 518 first MRSA isolates per patient, 367 (70.8%) were screening-derived and 151 (29.2%) were clinical isolates. ST398 was significantly less likely to be associated with clinical isolates than with screening-derived isolates (7.9% vs 20.2%; odds ratio [OR] = 0.34, $P = 0.001$; [Supplementary Table S4](#)). Among the 518 first isolates, 10 (1.9%) originated from blood cultures and belonged to ST22 ($N = 3$), ST1 ($N = 2$), ST225 ($N = 2$), ST152 ($N = 1$), ST80 ($N = 1$), and ST5 ($N = 1$). No bloodstream isolate was assigned to ST398. PVL-positive isolates were significantly more common among clinical isolates than among screening-derived isolates (24.5% vs 7.1%; OR = 4.24, $P = 1.9 \times 10^{-7}$), whereas IEC-positive isolates were also more frequent among clinical isolates (84.8% vs 76.3%; OR = 1.73, $P = 0.034$).

cgMLST cluster analysis and epidemiological findings

cgMLST analysis identified 23 genetic clusters among the 518 MRSA first isolates included in the study, comprising 58 of 518 MRSA isolates (11.2%), whereas 460 isolates (88.8%) remained genetically unrelated at the predefined threshold of ≤ 10 allelic differences. Cluster size ranged from 2 to 10 isolates (median 2). The three largest clusters comprised ten, five, and three isolates, respectively.

Clusters were predominantly observed among isolates belonging to ST225, ST22, and several less frequent STs. Notably, no cluster was identified among ST398 isolates, which were exclusively detected as singletons. Compared with other STs, ST398 isolates were significantly less likely to form genetic clusters (Fisher's exact test, $P = 1.9 \times 10^{-5}$). In contrast, ST225 isolates were significantly more frequently represented in clusters than other STs ($P = 4.3 \times 10^{-5}$).

SCCmec types were identical within all clusters except one, in which closely related SCCmec subtype variants were observed.

Epidemiological assessment revealed heterogeneous patterns of potential transmission. Based on predefined spatial and temporal criteria, epidemiological links within the study

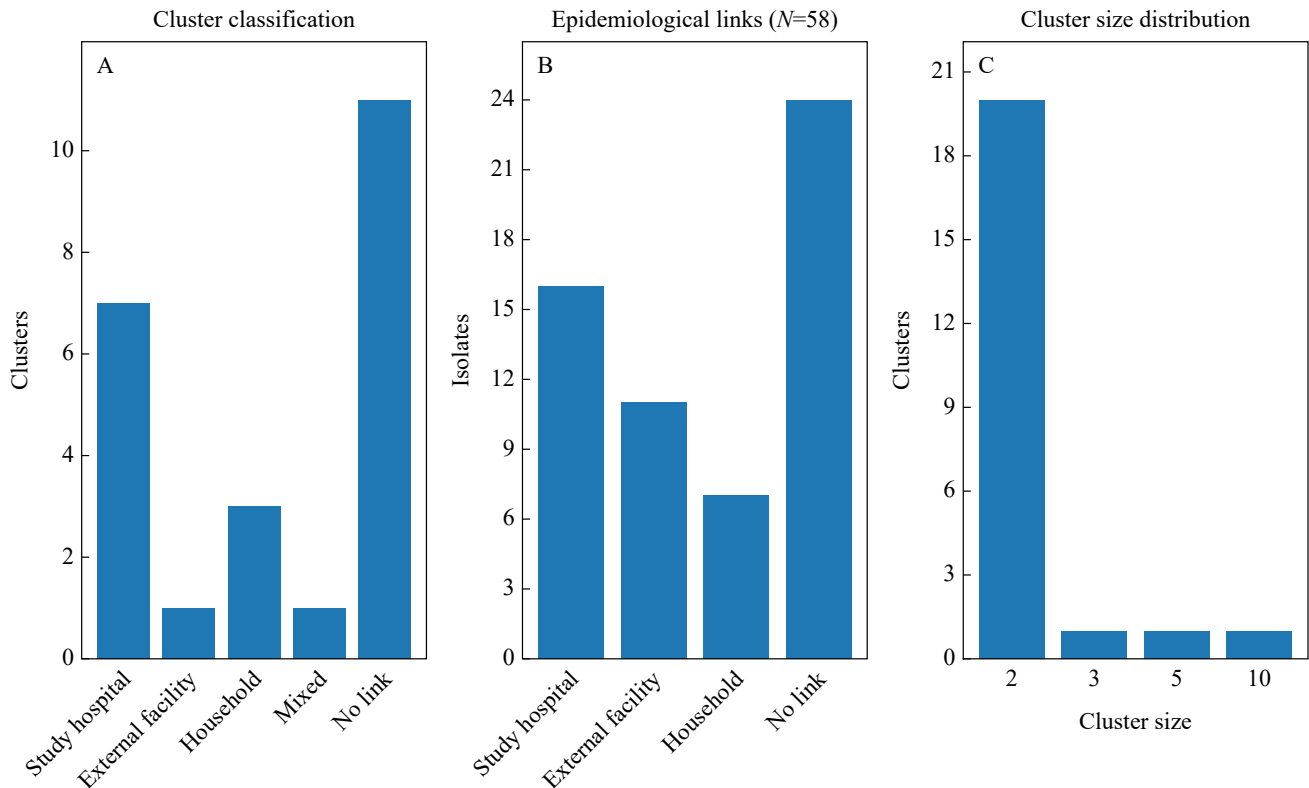


Figure 2. Epidemiological context of core genome multi-locus sequence typing (cgMLST)-defined methicillin-resistant *Staphylococcus aureus* (MRSA) clusters. (A) Number of genetic clusters according to their predominant epidemiological setting. (B) Distribution of isolates by epidemiological linkage. Isolates from mixed clusters were assigned according to their individual epidemiological links. (C) Cluster size distribution showing the number of isolates per cluster.

hospital were categorized as probable, unclear, or no identifiable link. Of the 23 clusters, seven were associated with the study hospital, three were consistent with household transmission, one cluster was predominantly linked to a specific department of an external healthcare facility, one cluster showed a mixed epidemiological pattern, and 11 clusters showed no identifiable epidemiological link between cases.

The largest cluster (ST225; $N = 10$) was predominantly associated with a specific department of an external healthcare facility, with 9 of 10 isolates linked to this setting. The second-largest cluster (ST22; $N = 5$) showed a mixed epidemiological pattern, comprising two isolates compatible with probable transmission at the study hospital (same ward with overlapping inpatient stay), two isolates linked to an external healthcare facility, and one isolate without an identifiable epidemiological link. The third-largest cluster (ST1535; $N = 3$) was consistent with household transmission.

Among clusters associated with the study hospital, only one cluster showed overlapping inpatient stays on the same ward, representing the strongest epidemiological evidence for in-hospital transmission. In the remaining clusters, isolates were either detected on the same ward but separated by more than 30 days or occurred during temporally overlapping hospitalizations without ward concordance.

The distribution of clusters and the corresponding number of isolates by epidemiological setting are shown in Figure 2, while detailed cluster characteristics and the distribution of epidemiological links within clusters are provided in Supplementary Table S7.

Discussion

This study combined WGS with epidemiological analysis to investigate the role of nosocomial transmission in the contemporary MRSA epidemiology of a tertiary care hospital in Germany. Despite the large number of isolates analysed, only a small proportion formed genomic clusters compatible with recent transmission, and epidemiologically plausible links were identified for only a minority of these clusters. Notably, ST398 isolates were exclusively detected as singletons and showed no evidence of clustering, suggesting limited onward transmission of this lineage within our hospital.

Although 44 STs were identified, the population structure was dominated by four major lineages (ST22, ST398, ST225, and ST1), indicating that a limited number of lineages accounted for a substantial proportion of MRSA isolates. The predominance of ST22 and ST225 is consistent with the current epidemiology of HA-MRSA in Germany [2,21], whereas the comparatively high proportion of ST398 likely reflects the inclusion of agricultural regions with intensive livestock farming within our hospital catchment area [22,23]. The relatively high prevalence of ST1 is consistent with the regional emergence of the European CC1-MRSA-IV lineage previously reported from Bavaria [24]. Moderate temporal changes in lineage frequencies were observed but should be interpreted cautiously, as they may partly reflect changes in screening intensity rather than true epidemiological shifts.

The distribution of screening-derived and clinical isolates in our dataset further highlights lineage-specific differences.

While ST22 and ST225 occurred with similar frequencies among screening-derived and clinical isolates, ST398 was significantly overrepresented among screening isolates, indicating that it was primarily detected through colonization screening rather than as a cause of clinical infection. Consistent with its predominance among screening-derived isolates, no bloodstream isolate in our dataset belonged to ST398. Although the number of bloodstream isolates was small due to the first-isolate-per-patient design, invasive infections were observed only among other lineages. A similar distribution between screening-derived and bloodstream isolates has been reported from a livestock-dense region in Germany [25].

In contrast, Larsen *et al.* described an increasing proportion of ST398 among MRSA bloodstream isolates in Denmark [26]. However, because that study included only bloodstream isolates, direct comparison with our findings is limited.

Consistent with previous studies, resistance and virulence determinants showed distinct lineage-associated distributions (Supplementary Figures S2 and S3) [27]. PVL-positive MRSA isolates were more frequent among clinical isolates, whereas IEC genes were uncommon in ST398, reflecting the limited human adaptation of classical LA-MRSA [27–29].

The observed differences between lineages in host adaptation, virulence determinants, and clinical associations raised the question whether transmission dynamics also differ between MRSA lineages. To further explore transmission dynamics, we performed cgMLST-based cluster analysis combined with detailed epidemiological assessment. Only a limited proportion of isolates formed genomic clusters at the pre-defined threshold of ≤ 10 allelic differences. Although no universally accepted cgMLST threshold for defining MRSA transmission clusters exists, the cut-off of ≤ 10 allelic differences used in this study is consistent with previous genomic epidemiology studies and supported by observations of limited within-host genomic variation [17,30].

Among the 518 first patient isolates included in the study, 23 clusters comprising 58 isolates (11.2%) were identified, whereas most isolates remained genetically unrelated. Most clusters were small, indicating that extended transmission chains were uncommon in our setting.

Integration of genomic and epidemiological data revealed heterogeneous patterns among clusters. Only a minority were compatible with potential transmission within the study hospital, whereas several were associated with external healthcare facilities or household transmission. Notably, only a single cluster showed epidemiological evidence compatible with probable in-hospital transmission, defined by overlapping inpatient stays on the same ward.

However, our epidemiological linkage criteria primarily captured transmission associated with documented ward stays and may therefore have missed transmission through other routes within the hospital. In particular, genetically related isolates from patients admitted to the same ward more than 30 days apart could reflect environmental persistence or indirect transmission chains involving unrecognized colonized patients or healthcare workers. As admission screening was risk-based rather than universal, asymptomatic carriers without known risk factors and potential intermediate carriers in transmission chains may have remained undetected. Likewise, clusters involving patients admitted to different wards could potentially reflect transmission through healthcare personnel, shared mobile equipment, or contacts in diagnostic or

interventional areas outside the patients' wards. Environmental reservoirs and healthcare workers have previously been implicated in MRSA transmission across patients and hospital wards [31]. As environmental sampling, healthcare worker screening, and detailed data on patient movements outside the ward were not available, the contribution of these potential transmission routes could not be assessed.

The overall low proportion of clusters with a clear epidemiological link nevertheless suggests that sustained nosocomial transmission played only a minor role in our setting. This interpretation is further supported by the observation that repeated MRSA detection in individual patients was usually associated with stable genotypic profiles and low cgMLST distances, consistent with within-host persistence, whereas changes in ST were rare and corresponded to markedly higher genetic distances, indicating acquisition of a distinct MRSA lineage. In a UK-based teaching hospital, Blane *et al.* identified multiple genomic clusters, but only a subset could be linked to in-hospital transmission, with many cases reflecting community or pre-admission exposure [8,10,31]. Similarly, limited evidence for nosocomial transmission has been reported in a study from the Netherlands focusing on epidemiologically defined contacts [10]. In contrast, Kinnevey *et al.* observed more extensive clustering and evidence of widespread in-hospital transmission in a single-centre study in Ireland [31]. Several factors may explain the observed variation in the frequency of probable in-hospital transmission across studies, including variations in study design, infection prevention policies, MRSA prevalence, and region-specific circulating lineages.

In our dataset, clustering differed markedly between MRSA lineages. Whereas clusters were predominantly observed among ST225, ST22 and several less frequent STs, all ST398 isolates occurred as singletons. Previous studies suggest that LA-MRSA ST398 may have a lower propensity for sustained nosocomial transmission than classical HA-MRSA lineages [32,33], although hospital transmission has been documented [34]. However, ST398 is genetically and epidemiologically heterogeneous [35–37]. Consequently, the absence of genomic clustering among ST398 isolates in our cohort should not be extrapolated to all ST398 populations, particularly to the human-adapted lineages described in other geographic regions.

Overall, our findings suggest that MRSA epidemiology in our setting was driven predominantly by repeated external introductions rather than sustained in-hospital transmission. Importantly, many genomic clusters lacked epidemiological support, underscoring that genomic relatedness alone is insufficient to infer transmission and highlighting the importance of integrating WGS with epidemiological data when interpreting potential transmission events [8,38].

The low level of epidemiologically supported in-hospital transmission observed in our study over a 5-year period has important implications for future infection prevention strategies. These findings raise questions about whether current control measures adequately address the dominant pathways of MRSA dissemination in contemporary low-prevalence settings. In Germany, infection control policies are largely shaped by KRINKO recommendations, including risk-adapted admission screening and contact precautions for all MRSA patients [3]. These recommendations, introduced in 2014 during a period of higher MRSA prevalence, may warrant re-evaluation in contemporary low-prevalence settings. In contrast, international

guidelines increasingly support more individualized, risk-based approaches with targeted use of contact precautions and consideration of unintended consequences [39,40]. Recent discussions have highlighted the limited high-quality evidence supporting routine contact precautions for endemic MRSA and emphasized the need for better data on contemporary transmission dynamics [41]. Our findings contribute to this debate by providing genomic and epidemiological evidence from a contemporary low-prevalence setting. The predominance of repeated external introductions relative to epidemiologically supported in-hospital transmission in our cohort suggests that transmission pathways outside the hospital currently contribute substantially to the observed MRSA burden. At the same time, the continued low level of in-hospital transmission may partly reflect the effectiveness of existing infection prevention measures. Together, these findings highlight the importance of understanding the relative contribution of different transmission pathways when designing MRSA control strategies. Together with previous studies [32,33], these observations support a more differentiated approach to MRSA infection prevention that takes lineage-specific transmission dynamics into account.

The strengths of this study include the integration of WGS with detailed epidemiological data collected over a five-year period, allowing comprehensive assessment of MRSA transmission dynamics. Nevertheless, several limitations should be considered. The retrospective design, incomplete capture of exposures outside the study hospital, and predefined epidemiological linkage criteria focused on ward-based contacts may have led to underestimation of indirect transmission pathways. In addition, the risk-adapted MRSA screening strategy may have influenced the observed distribution of MRSA lineages, while asymptomatic carriers without known risk factors and intermediate carriers in transmission chains may have remained undetected. Furthermore, the study was conducted under routine infection prevention measures, including contact precautions for patients with known MRSA colonization or infection, which may have influenced the observed frequency of nosocomial transmission. Incomplete WGS coverage of annual first isolates may also have influenced the observed lineage frequencies and the detection of genomic clusters. Finally, the findings reflect a single-centre setting and may not be fully generalizable to other regions with different MRSA epidemiology.

Taken together, sustained nosocomial transmission appeared to play only a minor role in MRSA epidemiology in our setting, with most cases likely reflecting repeated external introductions. Our findings support the integration of genomic and epidemiological data to better understand lineage-specific transmission dynamics and to guide more targeted infection prevention strategies in contemporary low-prevalence settings.

CRediT authorship contribution statement

Aila Caplunik-Pratsch: Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Bärbel Kieninger:** Writing – review & editing, Software, Data curation. **Stefan Hansch:** Writing – review & editing, Formal analysis. **Sascha D. Braun:** Writing – review &

editing, Software, Formal analysis. **Anca Rath:** Writing – review & editing. **Barbara Lenker:** Writing – review & editing. **Jürgen Fritsch:** Writing – review & editing, Supervision, Resources. **Anja Eichner:** Writing – review & editing, Resources, Investigation. **Stefan Monecke:** Writing – review & editing, Methodology, Investigation. **Wulf Schneider-Brachert:** Writing – review & editing, Supervision, Resources, Conceptualization.

Informed consent

The requirement for informed consent was waived by the Ethics Committee due to the retrospective nature of the study.

Clinical trial

Not applicable.

Consent for publication

Not applicable.

Data availability

The whole-genome sequence data generated in this study have been deposited in the National Center for Biotechnology Information (NCBI) under BioProject accession number PRJNA1467943.

Ethical approval

This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of the University of Regensburg (approval number 26-4516-104; approved 10th February, 2026).

Declaration of AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors used ChatGPT (OpenAI) to assist with language editing and improving the clarity of the manuscript. The authors critically reviewed and revised all suggestions and take full responsibility for the final content of the published article.

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Conflict of interest statement

The authors declare that they have no competing interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jhin.2026.09.025>.

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