



## *Staphylococcus aureus* nasal colonization among dental health care workers in Northern Germany (StaphDent study)

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### ABSTRACT

Methicillin-resistant *Staphylococcus aureus* (MRSA) can colonize dental patients and students, however, studies on the prevalence of MRSA and methicillin-susceptible *S. aureus* (MSSA) among dental health care workers (DHCW) including use of personal protective equipment (PPE) are scarce. We conducted an observational study (StaphDent study) to (I) determine the prevalence of MRSA and MSSA colonization in DHCW in the region of Mecklenburg Western-Pomerania, Germany, (II) resolve the *S. aureus* population structure to gain hints on possible transmission events between co-workers, and (III) clarify use of PPE. Nasal swabs were obtained from dentists (n = 149), dental assistants (n = 297) and other dental practice staff (n = 38). Clonal relatedness of MSSA isolates was investigated using *spa* typing and, in some cases, whole genome sequencing (WGS). PPE use was assessed by questionnaire. While 22.3% (108/485) of the participants were colonized with MSSA, MRSA was not detected. MSSA prevalence was not associated with size of dental practices, gender, age, or duration of employment. The identified 61 *spa* types grouped into 17 clonal complexes and four sequence types. Most *spa* types (n = 47) were identified only once. In ten dental practices one *spa* type occurred twice. WGS data analysis confirmed a close clonal relationship for 4/10 isolate pairs. PPE was regularly used by most dentists and assistants. To conclude, the failure to recover MRSA from DHCW reflects the low MRSA prevalence in this region. Widespread PPE use suggests adherence to routine hygiene protocols. Compared to other regional HCW MRSA rates the consequent usage of PPE seems to be protective.

**Abbreviations:** DHCP, dental health care professionals; DHCW, dental health care workers; HCP, health care professionals; HCW, health care workers; MSSA, methicillin-sensitive *Staphylococcus aureus*; MRSA, methicillin-resistant *Staphylococcus aureus*; *S. aureus*, *Staphylococcus aureus*; PPE, personal protective equipment.

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## 1. Introduction

The worldwide spread of methicillin-resistant *Staphylococcus aureus* (MRSA) in hospitals, nursing homes and in the general population is of particular concern (Aslam et al., 2018; Köck et al., 2011; Tong et al., 2015). While the proportion of MRSA among all *S. aureus* isolates carried by the general population is around 1% (Holtfreter et al., 2016; Köck et al., 2016; Mehraj et al., 2014), it accounts for 13.3% of all *S. aureus* isolates in German hospitals (Layer et al., 2019). Other European countries have reported MRSA prevalences between 0.0% (Sweden) and 2.1% (Belgium) in the general population (den Heijer et al., 2013). In the hospital setting, steady or decreasing prevalences have been observed in a number of European countries, including Germany, since the early 2000s (Layer et al., 2019; Lee et al., 2018).

In contrast to MRSA, MSSA colonization is very common. For Northern Germany, *S. aureus* colonization rates between 21 and 41% have been reported for the general population (Holtfreter et al., 2016; Köck et al., 2016; Mehraj et al., 2014). Staphylococcal carriage is a risk for endogenous infections (Datta and Huang, 2008; Eiff et al., 2001; Wertheim et al., 2004). Moreover, persistent carriers spread the bacteria to other persons by direct contact from wounds or colonized skin, droplets, shared equipment or surfaces, and pets (Knox et al., 2012; Mork et al., 2020; Sakr et al., 2018). Hence, professional groups with close and frequent contact to MRSA carriers, i.e. hospital staff, ambulance personnel, and nursing home staff, have an increased risk of acquiring MRSA (Albrich and Harbarth, 2008; Price et al., 2017). Risk factors for MRSA acquisition outside the hospital settings include direct contact to persons from countries with high MRSA rates and intensive husbandry (Buenaventura-Alcazaren et al., 2020; Köck et al., 2016; van Dulm et al., 2020). MRSA may also be carried by dental healthcare workers (DHCWs), students and patients, and can be recovered from dental surfaces (Apolonio-Alonso et al., 2011; Horiba et al., 1995; Kurita et al., 2006; Martínez-Ruíz et al., 2014; Petti and Polimeni, 2011; Roberts et al., 2011). However, studies on the prevalence of MRSA and methicillin-susceptible *S. aureus* (MSSA) among DHCW are scarce (Albrich and Harbarth, 2008; Petti and Polimeni, 2011; Reddy, 2010).

Pathogen transmission in healthcare settings is prevented by hand hygiene and near-patient surface disinfection, along with use of PPE (Albrich and Harbarth, 2008; Pittet et al., 2000). Dentists in Western-Pomerania, Northern Germany, have demonstrated high compliance with these basic measures, as recommended by the Commission of Hospital Hygiene and Infection Prevention at the Robert Koch-Institute (Hübner et al., 2012; Kommission für Krankenhaushygiene und Infektionsprävention (KRINKO) beim Robert Koch-Institut, 2006).

We conducted an observational study among DHCWs (StaphDent study), firstly to determine the prevalence of MRSA and MSSA colonization among DHCWs in the region of Mecklenburg Western-Pomerania, Germany; secondly, to examine strain types in this occupational group for hints on possible transmission events, and thirdly, to record the use of basic PPE in dental practice.

## 2. Materials and Methods

### 2.1. Study design and recruitment

The prevalence of MRSA and MSSA carriage among dentists and their staff was determined between April and September 2016 in Mecklenburg Western Pomerania, Germany. The primary objective was to detect the prevalence of MRSA. The secondary objectives were the prevalence of MSSA, their genetic diversity, identification of factors that may promote staphylococcal colonization and self-assessment of basic hygiene measures in dental practices. Selection of dental practices was randomized with voluntary anonymous participation. The study protocol was approved by the local ethics committee of the University of Greifswald (registration no. BB 051/16).

Out of 1017 registered practices in the 6 districts of Mecklenburg Western-Pomerania, 455 were randomly selected, informed by phone about the study and asked to participate. To ensure commitment, participants' information, declaration of consent, questionnaire and swab were sent by mail. All participants had to give written consent as prerequisite for inclusion. To ensure anonymization, participant names were not documented and only an incomplete postcode lacking the last digit was recorded. If a copy of the final microbiological report was requested, and the name was transmitted for this purpose, anonymization was performed according to the same procedure following sample analysis in the laboratory. This protects the identification of the participating person. Members of a practice were given the same number to enable referring findings to a practice while maintaining anonymity.

A questionnaire was used to record the profession, age, sex and duration of employment for each participant as well as the number of employees in their practice. Moreover, frequency of use of gloves, mouth-nose protection, protective goggles and protective clothing over work clothing was self-reported by each participant. Finally, risk factors for colonization with MSSA/MRSA were assessed (Table S1).

### 2.2. Microbiological identification of *S. aureus*

Nose swabs were taken by the study participants themselves with sterile cotton swabs (Transsystem® with Amies agar gel medium, HAIN Lifescience, Nehren, Germany). They were given detailed written instructions on how to swab the nasal vestibule and on the proper packaging and shipping of the samples. The cotton swab was transferred to the laboratory within 24 hours and processed within 1 hour upon arrival. Swabs were streaked onto Mannitol Salt Agar (Becton Dickinson, Heidelberg, Germany) to enable selective growth of *S. aureus* as well as on MRSA CHROMagar (MAST Diagnostica, Reinfeld, Germany) to identify MRSA. Afterwards, the swab was transferred into CASO broth (Carl Roth, Karlsruhe, Germany) and incubated for 24 h at  $36 \pm 1$  °C. 100 µl of these cultures were streaked onto Mannitol Salt Agar and MRSA CHROMagar. To identify suspected colonies of *S. aureus*, two coagulase tests (Pastorex™ Staph-Plus, BioRad, Feldkirchen, Germany and Slidex Staph Plus®, Biomérieux, Nürtingen, Germany) were performed.

### 2.3. Spa genotyping

Spa genotyping was conducted according to published protocols using the primers spa-1113f and spa-1514r (Harmsen et al., 2003; Holtfreter et al., 2016). Closely related spa types (costs  $\leq 3$ ) were grouped into spa clonal complexes (spa CCs) using the BURP algorithm (Mellmann et al., 2007). Afterwards, spa CCs were allocated to multi-locus sequence type (MLST) CCs using the SpaServer database ([www.spaserver.ridom.de](http://www.spaserver.ridom.de)), experimental assessment of MLST in a subset of samples (see below), and/or the scientific literature (Grumann et al., 2011; Holtfreter et al., 2007; Holtfreter et al., 2016).

### 2.4. MLST

MLST analysis was performed on a subset of 14 MSSA isolates as previously reported (Enright et al., 2000), and STs were identified using the MLST database <https://pubmlst.org/saureus/> and Ridom SeqSphere software. MLST was conducted to validate spa type singletons (n = 11) and to group strains with short spa repeat sequences (n = 3).

### 2.5. Minimum spanning tree

Spa types were clustered using the minimum spanning tree (MST) algorithm of the spa typing plug-in of the BioNumerics software (version 7.1; Applied Maths, Ghent, Belgium) with default settings.

## 2.6. Whole genome sequencing (WGS)

Whole genome sequences of 20 selected MSSA isolates were generated by de novo assembly of Illumina MiSeq reads as previously reported (Trübe et al., 2019). Whole genome alignment was generated based on the maximum common genome of all 20 strains using Roary v3.12.0 software. Pairs differing in <30 nucleotides were subjected to pair-wise alignments using Geneious 10.0.5 (Biomatters Ltd., Australia). Virulence, resistance and biocide gene screening was carried out using resources from the Center for Genomic Epidemiology (<https://cge.cbs.dtu.dk/services>) and an in-house database (Malberg Tetzschner et al., 2020; Zankari et al., 2012). This Whole Genome Shotgun project has been deposited at DDBJ/ENA/GenBank (see Table S2 for accession numbers).

## 2.7. Statistical analysis

Proportions are reported as descriptive statistics for categorical data. Associations between categorical variables were analyzed using Pearson Chi-Square Test.

## 3. Results

### 3.1. Cohort description

Out of 455 contacted dental practices in Mecklenburg Western Pomerania, Germany, 127 practices agreed to participate. However, only 105 practices actually participated (response rate 23.1%). Nasal swabs were obtained from a total of 454 participants, including dentists (30.7%), dental assistants (61.2%), dental receptionists (4.7%) and dental laboratory staff (3.1%). Average age was  $43.6 \pm 12.6$  years for all occupational groups without significant differences between the professional groups. 87.4% of participants were female. With one exception (Asian), all participants were Caucasian.

### 3.2. Prevalence of MRSA and MSSA

MRSA were not isolated from any of the 485 participants. MSSA isolates were detected in 108 participants (22.3%) (Table 1). MSSA prevalence tended to be higher in dentists (23.5%) and their assistants (23.6%) than among employees at patient reception (8.7%) or in the laboratory (6.7%). After grouping medical staff (dentists and dental assistants) and non-medical staff (receptionists and dental technicians), this difference became significant (Chi-Square test,  $p \leq 0.05$ ).

MSSA prevalence did not correlate with practice size, i.e. the number of medical staff in the dental practice ( $p = 0.339$ , Table 1), even if only practices in which all employees participated in the screening were included (Table S3). However, there was a trend for a higher prevalence in smaller practices. Indeed, after grouping practices into those with up to 5 employees versus those with more than 5 employees the trend became significant (31.5 vs. 18.0%;  $p = 0.015$ , Table S3). In this study, MSSA colonization did not correlate with sex (21.9% in women, 24.6% in men) or age; neither was MSSA prevalence influenced by length of employment. We also stratified the data by the geographical region (county) of the practices, but again observed no major differences (Table 1).

Apart from practice-related parameters, all study participants were assessed for risk factors for MSSA/MRSA colonization. Direct contact with persons working in outpatient care, persons requiring dialysis, persons being in chronically need of care, and persons having direct professional contact with animals for meat production were identified as risk factors for MSSA colonization (Table S1).

### 3.3. Genotyping of MSSA isolates

A total of 105 MSSA strains were *spa* typed; the remaining three isolates were not available for analyses. The *spa* typing revealed a

**Table 1**

Prevalence of *S. aureus* in DHCW in the StaphDent study.

Variable	% (No <i>S. aureus</i> -positive/total No)	p value <sup>1</sup>
Total	22.3 (108/485)	
<b>Occupation<sup>2</sup></b>		0.174
Dentist	23.5 (35/149)	
Dental assistant	23.6 (70/297)	
Dental receptionist	8.7 (2/23)	
Dental technician	6.7 (1/15)	
<b>Employees per practice<sup>3</sup></b>		0.339
2	36.4 (4/11)	
3	27.5 (22/80)	
4	20.3 (14/69)	
5	26.3 (21/80)	
6	17.7 (11/62)	
7	19.1 (9/47)	
8-10	19.0 (12/63)	
11-15	15.5 (9/58)	
16-25	40.0 (6/15)	
≤5	25.4 (61/240)	0.099
>5	19.2 (47/245)	
<b>Sex</b>		0.641
Female	21.9 (93/424)	
Male	24.6 (15/61)	
<b>Age (yrs)</b>		0.599
16-19	37.5 (3/8)	
20-29	28.2 (20/71)	
30-39	21.7 (25/115)	
40-49	21.3 (23/108)	
50-59	22.5 (29/129)	
60-69	15.4 (8/52)	
>69	0.0 (0/2)	
<b>Length of employment (yrs)<sup>4</sup></b>		0.327
1-3	25.8 (25/97)	
4-10	25.0 (21/84)	
> 10	19.6 (57/291)	
<b>Geographical region (Counties)</b>		0.097
Mecklenburg lake district	24.0 (36/150)	
Western Pomerania - Greifswald	17.5 (20/114)	
Rostock	18.0 (23/128)	
North-West Mecklenburg	28.6 (16/56)	
Western Pomerania - Rügen	38.7 (12/31)	
Ludwigslust - Parchim	16.7 (1/6)	

<sup>1</sup> Pearson Chi-Square Test.

<sup>2</sup> One participant did not report his/her profession.

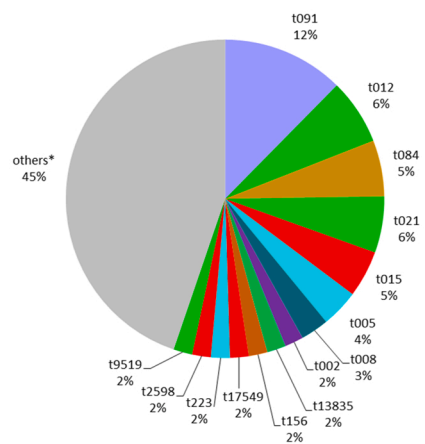
<sup>3</sup> In some practices not all employees participated in the study.

<sup>4</sup> Length of employment within the same practice (seniority); 13 participants did not report their length of employment.

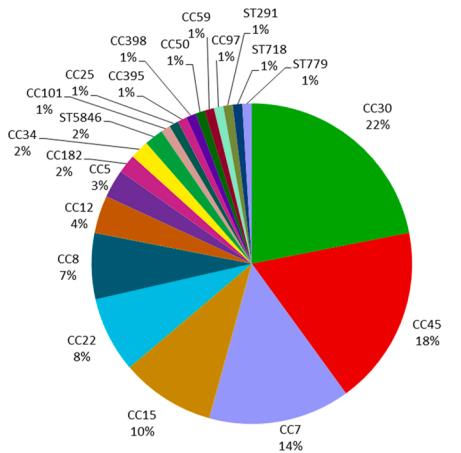
diverse MSSA population among dental staff. A total of 61 *spa* types were detected, most of them ( $n = 47$ ) only once (Fig. 1A). The most prevalent *spa* types in the StaphDent cohort were t091 (12.4%), t012 (6.7%), t021 (5.7%), t084 (5.7%), and t015 (4.8%). *Spa* types grouped into 17 clonal complexes (CC) and 4 sequence types (STs) (Fig. 1B). The diversity as well as the clonal linkage of the *spa* types within the respective CC was visualized with a minimum spanning tree (Fig. 1C). The lineages CC45, CC30 and CC8 contained the largest number of different *spa* types (12, 11, and 6, respectively). In contrast, 13 out of 15 CC7 isolates belonged to *spa* type t091.

To estimate whether certain *spa* types or CCs are more common amongst dental staff, we compared our findings with the SHIP-TREND-0 cohort, a large-scale population-based study in Western Pomerania (Holtfreter et al., 2016). The *spa* type prevalence was highly concordant in both studies, except for *spa* type t091 which was more prevalent in the StaphDent cohort (12.4 vs. 5.2%, Chi Square test,  $p \leq 0.01$ ) (Fig. 2A). Moreover, several usually rare *spa* types (t9519, t2598, t13835, t17549)

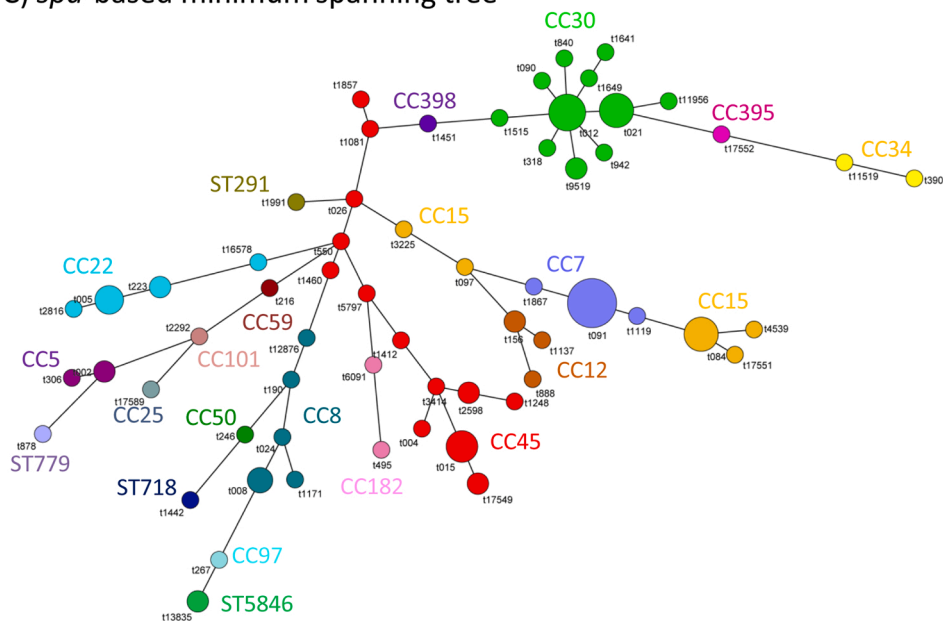
A) *spa* types



B) Clonal complexes (CC)



C) *spa*-based minimum spanning tree



**Fig. 1.** The *S. aureus* population in the StaphDent cohort is highly diverse. A) The phylogenetic relationship of all *S. aureus* isolates from the StaphDent cohort was determined by *spa* typing. *Spa* types are colour-coded according to their respective CC. B) Allocation of *spa* types to CCs was based on the BURP algorithm implemented in the Ridom StaphType software as well as the Ridom SpaServer database, and aided by MLST sequencing of selected strains. MLST CC nomenclature was deduced from *spa* CCs using the Ridom SpaServer database. Overall, a total of 61 *spa* types were grouped into 17 CCs. C) A minimum spanning tree was generated from *spa* typing data using the BioNumerics software. Each node represents a unique *spa* type. The number of *S. aureus* isolates per *spa* type is reflected by the size of each node, while the genetic distance between two bordering *spa* types is reflected by the distance between the two nodes (maximum neighbor distance, 1.00). Nodes are colour-coded according to the associated CC.

\*others, *spa* types occurring only once in the StaphDent cohort (t004, t024, t026, t090, t097, t190, t216, t246, t267, t306, t318, t495, t550, t840, t878, t888, t942, t1081, t1119, t1137, t1171, t1248, t1412, t1442, t1451, t1460, t1515, t1641, t1649, t1857, t1867, t1991, t2292, t2816, t3225, t3414, t3905, t4539, t5797, t6091, t11519, t11956, t12876, t16578, t17551, t17552, t17589)

occurred twice among dental staff. As expected, there was also a strong overlap in the most common MSSA CCs for both cohorts (Fig. 2B). CC7, which is dominated by t091, was again more prevalent in the StaphDent study. An in-depth analysis of the genome sequence of 2 CC7 isolate pairs (see below) revealed a combination of virulence and immune evasion factors that is typical for this lineage (Holtfreter et al., 2016; Monecke et al., 2009). They harbored the phage-encoded immune evasion cluster (*sak*, *scn*, *sep*), genes encoding pore-forming toxins (*lukDE*, *hlgABC*), and several extracellular proteases (*aureolysin*, *spIA*, *spIB*, *spLE*). Genes encoding multidrug efflux pumps involved in biocide resistance were commonly found, while genes conferring resistance towards antibiotics beyond *bla* were scarce (Table S4).

3.4. Prevalence of *spa* types in individual practices

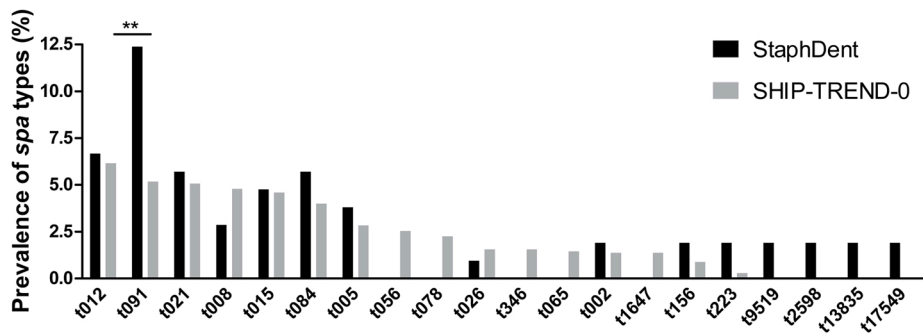
Due to their high diversity, most *spa* types occurred only once (47/61). 51 *spa* types were only found in a single dental practice. The remaining 10 *spa* types were found in multiple practices (Table S5). The

most frequently represented *spa* type t091 was detected in 11 practices, followed by t012 in 6 practices, as well as t015, t021, and t084 in five practices each. Notably, in ten out of 105 (9.5%) practices, one *spa* type each appeared twice, suggesting a tight clonal relationship of these isolates (Table S5). This included both common *spa* types, such as t012, t021, t084, and t091, as well as rare *spa* types, i.e. t2598, t9519, t13835, and t17549. This was unexpected since the likelihood for detecting even the most prevalent *spa* type t091 twice is below 3% (considering a colonization rate of 22.3% and a t091 prevalence of 12.4%).

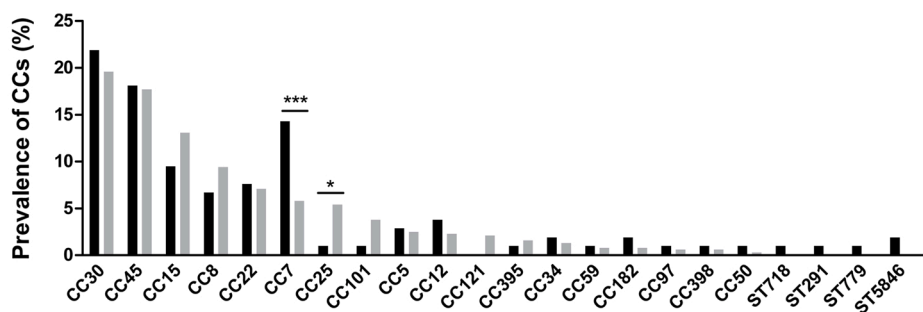
3.5. Clonal relationship of *S. aureus* isolates

To investigate whether isolates with identical *spa* type from the same practice were considered as closely clonally related, WGS data were used to initially screen the 20 isolates with respect to their maximum common genome (MCG) (Table S6). Based on the MCG analysis, six strain pairs which seemed closely related were subjected to a closer inspection using individual comparative whole genome alignments of the pairs.

## A) *spa* types



## B) Clonal complexes



This analysis revealed a rate of  $\leq 13$  SNPs in four cases, implying clonality (Table S7).

### 3.6. Use of PPE

Finally, compliance with PPE use was evaluated. A total of 80% of dentists wore gloves for every treatment, with a further 14% for the majority of treatments (Fig. 3A). Only 51% of dentists wore mouth-nose protection at each treatment, 24% for most treatments and 22% in cases of suspected infection. Three participants (2%) always worked without mouth-nose protection. Dental assistants were more likely to mouth-nose protection than physicians (Fig. 3B).

## 4. Discussion

Epidemiological data on the prevalence of MRSA and MSSA among DHCW are currently scarce (Petti and Polimeni, 2011). The StaphDent study is to our best knowledge first published study to analyze *S. aureus* carriage rates and strain types among DHCW in Europe.

### 4.1. Prevalence of MRSA among DHCW

None of the 485 participants in the study were colonized with MRSA, resulting in an MRSA prevalence  $\leq 0.2\%$ . Thus it can be assumed that MRSA does not have significant epidemiological impact for this occupational group in this region. Unfortunately, our findings can hardly be placed into a global perspective due to a lack of comprehensive studies (Petti and Polimeni, 2011). MRSA was not detected in any of 277 dentists and dental students in Denmark (Kjerulf et al., 2009). In contrast, MRSA was found in 4.2% of dentists and 1.6% of dental hygienists from the United States (Reddy, 2010). Reported MRSA colonization rates among dental students ranged from 3.1 in South Korea to roughly 20% in Mexico and the United States (Baek et al., 2016; Martínez-Ruiz et al.,

Fig. 2. Similar prevalence of the most common *spa* types and CCs in StaphDent and the population-based study SHIP-TREND-0. SHIP-TREND-0 is a large-scale population-based study in Western Pomerania (Germany), and represents a sub-region of the StaphDent recruitment area. Nasal *S. aureus* isolates were obtained from 1024 probands between 2008 and 2012 (Holtfreter et al., 2016). A) This graph depicts all *spa* types with  $n \geq 2$  in the StaphDent cohort ( $n = 14$ ) and the 14 most common *spa* types in the SHIP-TREND-0 study. B) This graph displays all CCs with a prevalence  $\geq 1\%$  in either StaphDent or the SHIP-TREND-1 cohort. Overall, we observed a strong overlap in the most common *spa* types and CCs between both cohorts. Statistics: The prevalence of individual *spa* types or CCs in both cohorts was compared using the Chi Square test. \*,  $p \leq 0.05$ . \*\*,  $p \leq 0.01$ . \*\*\*,  $p \leq 0.001$ .

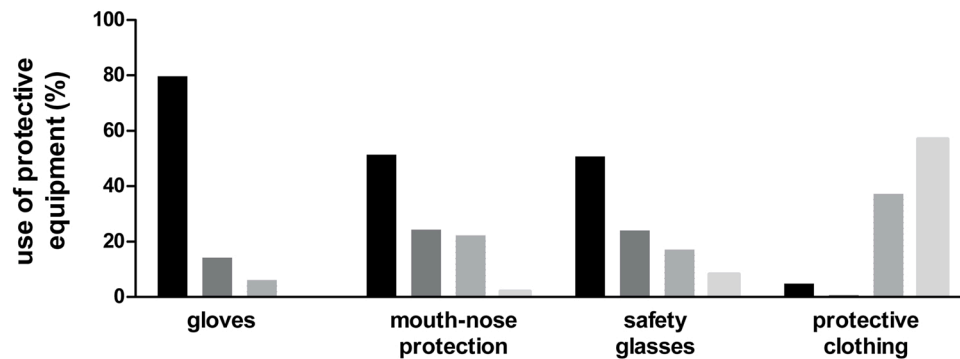
2014; Roberts et al., 2011). These variable MRSA rates among DHCW and dental students from different geographical areas might be explained by varying MRSA prevalence in the community and different hygiene standards in healthcare institutions (Albrich and Harbarth, 2008; Petti and Polimeni, 2011). Moreover, each of these studies used different MRSA detection methods, which hampers a direct comparison with our data.

Our reported MRSA carriage rate among DHCWs ( $\leq 0.2\%$ ) was considerably lower than those among HCWs and hospital patients but similar to the rates observed for the general population in the same geographical region with 0.34% (Holtfreter et al., 2016). In a risk-adapted admission screening of patients ( $n = 3375$ ) at the Greifswald University Medical Center, the MRSA prevalence after culture-based diagnosis was 3.7% on average across all medical disciplines (Hübner et al., 2009). HCW in Western-Pomerania in the HICARE project had the following prevalence rates for MRSA nasal carriage: Outpatient care services 4.0% (sample size  $n = 150$ ), nursing homes 2.1% (sample size  $n = 1383$ ), rehabilitation clinics 0.6% (sample size  $n = 84$ ; unpublished data).

High MRSA rates among HCWs were also frequently reported for other geographical regions (Albrich and Harbarth, 2008). For instance, the MRSA prevalence among HCW in non-outbreak situations was 4.6% in the Dutch-German EUREGIO (Deurenberg et al., 2016). Generally, higher rates are observed among nursing staff than medical staff, presumably due to the close care contacts (Dulon et al., 2014). In contrast, the MRSA prevalence among HCWs and patients was comparable to the general population in some surveys, probably depending on compliance with basic hygiene measures and use of PPE (Chen et al., 2015; Wu et al., 2019). Similarly, in German rehabilitation centers the MRSA prevalence among HCW was only slightly higher (Schubert et al., 2019) than the general population (0.4% vs. 0.34%) (Holtfreter et al., 2016).

The relatively high prevalence of MRSA for HCWs, especially in outpatient settings, is probably explained by the frequent and close

### A) Dentists



### B) Dental assistants



**Fig. 3.** Use of personal protective equipment by dentists and dental assistants. The use of personal protective equipment was self-reported by dentists (A) and dental assistants (B) using a questionnaire. Study participants reported whether they used gloves, mouth-nose protection, safety glasses and protective clothing at each treatment, in the majority of treatments, only if infection was suspected or never.

contact with patients in this setting, where the colonization status is not always known. The longer and sometimes unprotected exposure to high-risk groups may explain the higher MRSA prevalence in HCW compared with dental staff. In addition to the lower contact frequency with MRSA carriers, and the use of PPE in dental practices might also be a factor in avoiding MRSA transmission (Dancer, 2009; Gorwitz et al., 2008; Pittet et al., 2000).

#### 4.2. Prevalence of MSSA among DHCW

The observed MSSA prevalence of 22.3% in the StaphDent cohort is lower than the previously reported prevalence in the SHIP-TREND cohort (27.2%) (Holtfreter et al., 2016). Several factors may have influenced the comparably low MSSA prevalence. Firstly, our cohort was restricted to DHCW, which differ in several aspects from the general population. Secondly, mannitol salt agar has lower sensitivity to detect MSSA than other selective agars (Han et al., 2007). Finally, the self-swabbing might not have been taken thoroughly enough. Regardless, the MSSA prevalence in our StaphDent cohort was similar to carriage rates reported by Mehraj et al. for Northern Germany, while a higher colonization rate was reported by Köck et al. (Köck et al., 2016; Mehraj et al., 2014). On an international scale, similar rates were for instance reported for the UK (25.4%) and France (21.1%), lower rates

for Hungary (12.1%) and Austria (15.7%) (den Heijer et al., 2013).

Several studies have demonstrated that - similar to MRSA - the prevalence of MSSA increases in patients or professional workers in health care settings. For instance, residents in nursing homes in central Germany had an MSSA carriage rate of 36.6% (Daeschlein et al., 2006). Notably, regular nose swabs from physicians in the University Medical Center Greifswald revealed colonization rates of up to 100% after operating on open chronic wounds. Moreover, these physicians demonstrated repeated and recalcitrant strong nasal colonization with changing clones (up to four different clones/year) (Daeschlein et al. unpublished). These data clearly show that repeated and prolonged exposure to MSSA can lead to an increased colonization rate.

#### 4.3. High diversity of the *S. aureus* population in DHCW

*Spa* typing of the *S. aureus* isolates revealed a highly diverse population structure consisting of 61 *spa* types clustering into 21 CCs/STs, but with some clustering of *spa* types in certain practices. The StaphDent cohort (sampled in 2016) strongly resembled the *S. aureus* population found in the general population in the same area (sampled in 2008-2012) with some fluctuations likely due to the smaller sample size in StaphDent. In line with this, highly similar prevalences of *spa* types and corresponding CCs have been reported in two other German studies

(Becker et al., 2017; Mehraj et al., 2014). Moreover, similar *S. aureus* population structures were also found in several European and US studies (Muthukrishnan et al., 2013; Ruimy et al., 2009; Sakwinska et al., 2009; Sangvik et al., 2011).

*Spa* type t091 and the corresponding CC7 were significantly over-represented in the StaphDent cohort. This *spa* type was detected in 11 practices, in two of them twice. Whether this is due to a recent expansion of this *spa* type in the general population of the study region (and hence also in the StaphDent cohort) or to a selection advantage of this clone in DHCWs or their working environment remains to be clarified. An in-depth analysis of the genome sequence of 2 CC7 provided no hints towards genetic features that might explain the high prevalence of CC7 in this study. The isolate pairs revealed a combination of virulence and immune evasion factors that is commonly found in this lineage (Holtfreter et al., 2016; Monecke et al., 2009).

#### 4.4. Accumulation of *spa* types in individual practices

We detected the same *spa* type twice in 10 out of 105 practices. WGS data analysis of these strains indicated a close clonal relationship for four pairs, which exhibited a repertoire of 3-13 SNPs during pairwise genomic alignment. Since up to 30 SNPs were reported for strains isolated from a single person over a 13-month period, these pairs were judged as descendants from a common progenitor (Young et al., 2012). We suggest two scenarios. Firstly, transmission events could occur between co-workers within the same practice, either by direct contact, airborne inhalation or via contaminated surfaces. Secondly, transmission events could occur due to intense social contacts of co-workers. It is possible that spouses or children may work within the same practice, but due to the anonymization this could not be clarified for the ten practices concerned. In line with this, in 18-28% of households 2 or more members are colonized with closely related MSSA isolates (Busato et al., 1998; Knox et al., 2012; Stone et al., 2009).

#### 4.5. Study limitations

Because swabs were taken only from the nasal cavity, it is possible that additional carriage sites such as skin, pharynx or perineum, which are less frequently colonized than the nose, might have been colonized with MSSA or even MRSA. Thus, the real prevalence of MSSA or MRSA could have been higher (Dancer and Noble, 1991). Nasal swabs were taken by volunteers themselves. Since it is known that the bacterial yield is influenced by swabbing technique and can be strongly increased upon theoretical teaching (Warnke et al., 2014), all subjects were instructed that swabs are to be obtained by repeating concentric brushing with slight pressure. Nevertheless, the observed lower colonization rate in non-medical staff vs. medical staff could have been influenced by differences in the swabbing technique. Moreover, sampling was done only once which does not allow differentiation between intermittent and permanent carriers. Finally, since only one isolate per sample was processed, probands carrying multiple strains were not identified in this study.

## 5. Conclusions

The MSSA colonization rate in the StaphDent cohort was slightly lower than in the local general population. The observed high diversity of the *S. aureus* population in DHCW argues against the same *spa* types spreading within dental practices and probably reflects the distribution within the general population. MRSA nasal carriage was not detected, resulting in an MRSA prevalence  $\leq 0.2\%$ . This is considerably less than rates among HCPs and hospital patients but similar to the rates observed for the general population in the same geographical region. That could be a hint, that regular use of PPE in dental practices may prevent the acquisition of MRSA. The suspicion that PPEs prevent the acquisition of MRSA is supported by the fact that prevalence of MRSA in outpatient

care service almost reached prevalence in hospitalized patients. Especially in out-patient care, the consistent use of personal protective equipment and hand disinfection is much more difficult than in the dental practice. During the COVID-19 pandemic the PPE has even gained importance to protect dental health care workers against aerogenically transmissible pathogens (Matuschek et al., 2020).

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## Declaration of Competing Interest

The authors report no declarations of interest.

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## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.ijmm.2021.151524>.

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