Increase of vancomycin-resistant Enterococcus faecium strain type ST117 CT71 at Charité - Universitätsmedizin Berlin, 2008 to 2018

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Research

Keywords: Vancomycin-resistant Enterococcus faecium, whole genome sequencing, ST117, CT71, virulence factors, resistance genes

Posted Date: November 11th, 2019

DOI: https://doi.org/10.21203/rs.2.17129/v1

Version of Record: A version of this preprint was published on July 16th, 2020. See the published version at https://doi.org/10.1186/s13756-020-00754-1.

Abstract

In addition to an overall rise in vancomycin-resistant Enterococcus faecium (VREfm), an increase in certain other strain types has been reported in Germany over the past few years. Outbreak analyses at Charité - Universitätsmedizin Berlin revealed the frequent occurrence of VREfm ST117 CT71 isolates in 2017 and 2018. To investigate whether ST117 CT71 have emerged in recent years or whether these strains have been circulating for a longer time, we retrospectively analyzed non-outbreak strains that occurred between 2008 and 2018 to identify frequent sequence types (STs) and cluster types (CTs). Methods In total, 120 VREfm isolates obtained from clinical and surveillance cultures from the years 2008, 2013, 2015, and 2018 were analyzed. Thirty isolates per year comprising the first 7 to 8 non-outbreak isolates of each quarter of the respective year were sequenced using whole genome sequencing. MLST and cgMLST were determined as well as resistance genes and virulence factors. Risk factors for VREfm ST117 were analyzed in a multivariable analysis with patient characteristics as possible confounders. Results The percentage of VREfm of type ST117 increased from 17% in 2008 to 57% in 2018 (p=0.012). In 2008, vanA genotype accounted for 80% of all ST117 isolates compared to 6% in 2018. VanB CT71 first appeared in 2018 and predominated over all other ST117 at 43% (p<0.0001). The set of resistance genes and virulence factors in CT71 (msrC, efmA, ermB, dfrG, and aac(6')-Ii) and virulence factors (acm, esp, hyl, ecbA and sgrA) was also found in other ST117 non-CT71 strains, mainly in CT36. The study population did not differ among the different calendar years analyzed in terms of age, gender, length of stay, or ward type (each p>0.2). Conclusion This study revealed an increase in ST117 strains from 2008 to 2018, accompanied by a shift toward CT71 strains with the vanB genotype in 2018. We did not detect resistance or virulence traits in CT71 that could confer survival advantage compared to other CTs among ST117 strains. To date, it is not clear why ST117 and in particular strain type ST117 CT71 predominates over other strains.

Background

In recent years, Vancomycin-resistant enterococci (VRE) have been on the rise among hospitalized patients in Germany (1). Infections with VRE may result in an increased length of stay, higher mortality, and greater costs of hospitalization (2). Risk factors for colonization or infection by VRE include long periods of hospitalization, increased antibiotic consumption, co-morbidities, immunosuppression, and exposure to patients colonized or infected with VRE (3). Patients colonized with VRE and the patient environment may represent reservoirs for transmission because of the tenacity of VRE and its long survival time on dry surfaces (3, 4). Vancomycin resistance is mediated through different genotypes of a gene cluster, *vanA* to *vanN*, which are located on plasmids or in the chromosome (5, 6). Vancomycin-resistant *Enterococcus faecium* (VREfm) is able to acquire plasmids and insertion elements rapidly. Consequently a variety of resistance and virulence genotypes have emerged (7).

In recent years, the German National Reference Centre for Staphylococci and Enterococci has reported the frequent occurrence of VREfm strains of sequence type ST117 as determined by multi-locus sequence typing (MLST). Of their collection of 91 isolates from blood samples in 2016, more than half were ST117 (8). Further analysis of ST was based on core genome multi-locus sequence typing (cgMLST), which identified frequent subclusters CT71 and CT36 (8).

Outbreak analyses at Charité - Universitätsmedizin Berlin (Charité) also revealed the frequent occurrence of VREfm ST117 CT71 isolates in 2017 and 2018. In order to understand the local epidemiology and strain characteristics, we investigated whether ST117 (and more specifically ST117 CT71) has only emerged in recent years or whether these strains have instead been circulating for a longer time and have been identified more often through the broad use of molecular typing methods.

Thus, we retrospectively analyzed trends in ST and CT types among non-outbreak strains in the past decade.

Methods

Study population

We retrospectively analyzed VREfm cultures, clinical and surveillance, routinely collected at Charité, a 3000 bed, acute care hospital, at five-year intervals in 2008, 2013, and 2018. First, 7–8 consecutive non-outbreak isolates per quarter from individual cases from all wards at Charité were included. Because a recent publication suggested an increase in CT71 in Germany between 2015 and 2016 (9), isolates collected in 2015 were included according to the protocol mentioned above, resulting in 30 isolates per year and a total number of 120 isolates. Charité screening protocols required the identification during the stay on the ward of all admission cultures from previously known VRE carriers and from all patients admitted to hematology/oncology wards as well as cultures from patients who shared a room with a VRE carrier. We retrieved epidemiological data from the patient data management system and included patient age and sex, date of sampling, ward, length of stay (LOS) at the time of specimen collection, and specimen collection site.

Bacterial isolates and DNA extraction

Determination of VRE was performed using chromID® VRE agar plates (bioMérieux, Marcy-l´Étoile, France) and disc diffusion tests MASTDISCS® (5 µg Vancomycin, Mast Group Ltd., Bottle, United Kingdom). In addition, we tested for the presence of *van* genes using PCR. Vitek®2 System (bioMérieux, Marcy-l´Étoile, France) or MALDI-TOF MS (Bruker Daltonics, Bremen, Germany) have been used for identification and antimicrobial susceptibility testing since 2013. VREfm isolates were stored as cryocultures, subcultured on blood agar and incubated overnight at 37°C. DNA extraction was performed using the UltraClean Microbial DNA isolation kit following the manufacturer's instructions (Qiagen, Hilden, Germany). The quantity and purity of the DNA was measured by QuantiFluor ONE dsDNA System (Promega GmbH, Mannheim, Germany) and Eppendorf Biophotometer (Eppendorf AG, Hamburg, Germany).

Whole genome sequencing and bioinformatics analyses

Short read sequencing libraries were generated from genomic DNA using the Nextera XT DNA library preparation kit (Illumina Inc., San Diego, USA) and were sequenced on the MiSeq system (Illumina Inc., San Diego, USA) with 250-cycle paired-end chemistry according to the manufacturer's instructions. Isolates were sequenced to reach 100-fold coverage. After sequencing quality-trimming, *de novo* assembly with the Velvet assembler and gene-by-gene comparison approach using the SeqSphere+ software version 4.1.9 (Ridom GmbH, Muenster, Germany) were performed. For the gene-by-gene comparison, the *E.faecium* cgMLST task template with default parameters (suggested threshold: ≤ 20 alleles difference) and reference genome NC_017022.1 was used to extract MLST and cgMLST data as described previously (10). The quality of the samples and sequencing runs was checked using Fast QC (https://github.com/s-andrews/FastQC), and Illumina Analysis Viewer (http://emea.support.illumina.com/sequencing/sequencing_software/sequencing_analysis_viewer_sav/downloads.html). The ResFinder and VirulenceFinder web server (http://www.genomicepidemiology.org) was used to identify resistance genes and virulence factors, using a threshold of 90% minimum sequence identity and 60% minimum length identity cut-off.

In parallel, the recently published ASA³P analysis pipeline was used (11). Briefly, raw sequencing reads were quality clipped with Trimmomatic (12) and *de novo* assembled with SPAdes (13). Contigs were rearranged using MeDuSa (14) and annotated with Prokka (15). The ST clade was determined using BLAST+ and the PubMLST.org database. Antibiotic resistance genes and virulence factors were analyzed with the use of CARD database (16) and VFDB (17).

Statistical analysis

Either number and percent or median and interquartile range were calculated for descriptive analysis. Differences were tested using the Chi-square test or Wilcoxon rank-sum test. To analyze risk factors for the occurrence of ST117, we used a logistic regression model for multivariable analysis with patient age and sex, calendar year, type of ward, length of stay (LOS) at the time of specimen collection, and specimen collection site as possible confounders. Parameters with a significance of $p \leq 0.05$ were entered into the model. All tests of significance were two-tailed, and $p<0.05$ was considered statistically significant. All statistical analyses were performed using SPSS (IBM SPSS statistics, Somer, USA) and SAS (SAS Institute, Cary, USA).

Ethics

The bacterial isolates were obtained during routine diagnostics and all samples were anonymized. Ethical approval and informed consent were thus not required.

Results

Characteristics of VREfm isolates

All 120 VREfm isolates were sequenced, with an average coverage ranging from 41- to 121-fold. The percentage of good targets based on the core genome ranged from 95.2% to 99.8% with an average of 99.0%. STs as well as CTs were determined for all strains. Regarding classification into ST, each consecutive year saw a higher percentage of isolates that were ST117, rising from 16.7% in 2008 to 56.7% in 2018 (p=0.012). In total, 43 (35.8%) of the 120 *E. faecium* isolates were classified as ST117. In addition to ST117 strains, we detected strains assigned to ST203 (11.7%), ST80 (7.5%), ST78 (9.2%), ST192 (8.3%), ST17 (6.7%), and others (each ≤ 5%) (Fig. 1). While ST117, ST203 and ST80 were identified in all years, the number of isolates belonging to ST203 and ST80 increased until 2015 but decreased subsequently from 2015 to 2018. Beside the increase in ST117, we also observed a sharp rise in isolates assigned to ST78 between 2015 and 2018 as well as a higher diversity of STs in 2008 than in 2018 (Fig. 1).

When classifying the strains with a higher resolution into cgMLST, there was a clear shift of dominant CTs from CT164 in 2008 to CT71 in 2018. We did not find any CT71 isolates in 2008, 2013, or 2015 although there was a variety of other CTs such as CT24, CT36 and CT190 (Fig. 2). In contrast, 43% of isolates from 2018 were CT71 strains (13/30, p<0.0001). Of all 120 isolates of the years studied, CT71 (11%) was the most common CT, followed by CT36 and CT162 (both 8%), and CT164 and CT894 (both 6%).

Antimicrobial resistance and virulence factors of ST117 strains

Resistance genes and virulence factors for all 43 ST117 strains were identified using ResFinder, Virulence Finder, VFDB, and CARD, all of which indicated various resistance genes and virulence factors (Additional file 1: Table S1). Resistance genes for macrolides, lincosamides, and streptogramin B (*msrC*, *ermB* and *efmA*) were detected in all ST117 strains. Additionally, all strains harbored resistance genes for trimethoprim (*dfrF and dfrG*) and aminoglycosides (*aac(6')-aph(2")*, *aph(3')-III*, *ant(6)-Ia and aac(6')-Ii*). While almost all Non-CT71 strains had several genes conferring resistance to

aminoglycosides, we found only one such gene in CT71 strains. Some isolates featured resistances to amphenicol (*cat*) and tetracycline (*tet(M)*) which were absent in CT71 strains. Among all ST117 strains, 74% (32/43 isolates) displayed the *vanB* genotype and the *vanA* 26% (11/43 isolates). There was a shift from *vanA* to *vanB* between 2008 and 2018, with 80% (4/5 isolates) and 67% (6/9 isolates) *vanA* in 2008 and 2013, to 100% (11/11 isolates) and 94% (16/17 isolates) *vanB* in 2015 and 2018, respectively (Additional file 2: Figure S1). All CT71 strains harbored *vanB*.

All ST117 strains carried the virulence factor *acm*, which encourages cell wall-anchored collagen adhesion and has characteristics typical of a microbial surface component recognizing adhesive matrix molecules (MSCRAMM) and *sgrA* to stimulate surface adhesion. Moreover, nearly all ST117 strains were characterized by the presence of *ecbA* (98%, 42/43 isolates), the *E. faecium* collagen binding protein A, as well as the enterococcal surface protein *esp* (95%, 41/43 isolates) to promote biofilm formation. The spreading factor hyluronidase *hyl* was detected in more than half of the ST117 strains (78%, 33/43 isolates). Occasionally, the virulence factor *scm* (14%, 6/43 isolates), the second collagen adhesin of *E. faecium*, occurred. All CT71 strains presented the same set of virulence factors: *acm*, *esp*, *hyl*, *ecbA*, and *sgrA* (30%, 13/43 isolates). This set of virulence factors was also detected in another 15 non-CT71 strains, a total of 28 isolates out of 43 (65%). These 15 strains belonged mainly to CT36 (21%, 9/43 isolates). The virulence factors of non-ST117 strains showed no striking difference from ST117 strains.

Patient characteristics

All VREfm cases from the years 2008, 2013, 2015 and 2018 were analyzed and came to a total of 120 cases. We investigated patient and isolate details. These included age, sex, LOS, LOS at the time of specimen collection, type of ward, and site of specimen collection. VREfm samples were comprised of rectal swabs (n=76, 63%), blood cultures (n=7, 6%), urine samples (n=15, 13%), wound swabs (n=5, 4%), stool samples (n=9, 8%), nasal- and throat swabs (n=2, 2%), and other clinical cultures (n=5, 4%). Rectal swabs, throat swabs, and nasal swabs were considered screening specimens, all others were considered clinical specimens. Wards were divided into four categories: intensive care unit, hematology/oncology, surgery, and others. The latter category included standard care wards such as nephrology, cardiology and gastroenterology. Interdisciplinary wards with an intensive care unit were also assigned to this group. Multiple assignment was not allowed. In single quarters of each year, a variety of different wards were represented. The VREfm cases did not differ among calendar years with regard to age (in total median across all calendar years 66 years, IQR 53-75, p=0.839), gender (in total male 52% and female 48%, p=0.223), LOS (in total median 33 days, IQR 14-64%, p=0.209), or the above mentioned ward type. Between 2008 and 2018, there was no difference in intensive care unit, hematology/oncology, surgery, or others (p=0.945, p=0.825, p=0.867 and p=0.729). In contrast, LOS at the time of specimen collection and site of specimen collection differed in various calendar years. In 2008, most of the samples were obtained as clinical cultures (n=25, 83.3%), while in 2013 (n=4, 13.3%), 2015 (n=6, 20%), and 2018 (n=7, 23.3%) screening cultures were more frequent. Urine accounted for the majority of clinical cultures. The LOS at the time of specimen collection decreased from 2008 (18.5 days; IQR 4-40) to 2018 (1.5 days; IQR 0-21) and is consequently of significance, p=0.011.

Risk factors for the frequent occurrence of ST117 strains

Table 1 shows patient characteristics for ST117 and non-ST117 carriers in each year. Non-ST117 comprised all strains other than ST117, including those which could not be assigned to a known ST type. Regarding ward type, 54% of all CT71 strains were collected in ICUs, which comprised five different ICUs located in different buildings across the city. Most

samples were obtained from rectal swabs and stool samples. Urine samples accounted for 6% of the total number of samples, including 4 samples (13%) in 2008, no sample in 2013 or 2015, and 3 samples (10%) in 2018.

Table 1 Patient characteristics grouped as non-ST117 and ST117 carriers indicated by year (2008-2018) and by patient characteristics of CT71 carriers in 2018.

Year Total number of isolates	**2008** N=30		**2013** N=30		**2015** N=30		**2018** N=30		
Strain type No. (%)	**Non-ST117** 25 (83)	**ST117** 5 (17)	**Non-ST117** 21 (70)	**ST117** 9 (30)	**Non-ST117** 18 (60)	**ST117** 12 (40)	**Non-ST117** 13 (43)	**ST117** 17 (57)	**CT71** 13 (43)
Age in years, Median (IQR)	62 (46-72)	69 (56-76)	68 (57-76)	68 (53-71)	72.5 (54-74)	64 (47-72)	60 (54-66)	69 (52-77)	69 (52-75)
Sex, No. (%)									
Male	15 (60)	3 (60)	9 (43)	5 (56)	6 (33)	6 (50)	6 (46)	13 (77)	10 (77)
Female	10 (40)	2 (40)	12 (57)	4 (44)	12 (67)	6 (50)	7 (54)	4 (23)	3 (23)
LOS in days, Median (IQR)	53 (26-76)	23 (4-74)	32 (15-60)	47 (26-59)	31 (16-52)	34 (15-48)	14 (5-66)	16 (8-55)	40 (16-60)
LOS specimen collection in days, Median (IQR)	19 (6-37)	4 (4-42)	11 (2-24)	19 (11-26)	4.5 (1-12)	5 (1-18.5)	1 (0-42)	2 (0-12)	5 (1-21)
Type ward, No. (%)									
Intensive care unit	10 (40)	2 (40)	9 (43)	5 (56)	10 (56)	3 (25)	4 (30)	8 (47)	7 (54)
Hematology/oncology	9 (36)	1 (20)	8 (38)	3 (33)	4 (22)	7 (59)	5 (40)	3 (18)	3 (23)
Surgery	3 (12)	1 (20)	1 (5)	1 (11)	1 (5)	1 (8)	4 (30)	0 (0)	0 (0)
others	3 (12)	1 (20)	3 (14)	0 (0)	3 (17)	1 (8)	0 (0)	6 (35)	3 (23)
Site of specimen collection, No. (%)									
Screening cultures	4 (16)	1 (20)	19 (90)	7 (78)	13 (72)	11 (92)	12 (92)	11 (65)	9 (69)
Clinical cultures	21 (84)	4 (80)	2 (10)	2 (22)	5 (28)	1 (8)	1 (8)	6 (35)	4 (31)

Multivariable risk factor analysis for ST117

The multivariable analysis supported a strong association of ST117 with the calendar year. Samples from 2018 were more than 9 times more likely to be type ST117 than in 2008 (OR 9.4, 95%CI 2.3-37.7, p=0.002). A similar association was found for urine as specimen collection site and ST117 strains (OR 10.6, 95%CI 1.4-82.5, p=0.024). CT71 was not an independent risk factor for ST117. Because CT71 did not appear until 2018, the calendar year could not be estimated in the model.

Discussion

This retrospective analysis revealed that the percentage of VREfm ST117 strains at Charité more than tripled between 2008 and 2018. When CT71 first appeared in 2018, it comprised more than 40% of all ST117 strains. In comparison, VREfm prevalence at Charité rose from 1.2% in 2016 to 1.4% in 2018. Thus, an overall increase of VRE may not be the only explanation for the rise of ST117/CT71.

Previous publications have also reported a dramatic increase of ST117. Liese et al. reported the frequent occurrence of ST117, ST80, ST17, and ST192 strains in outbreak analyses from a German university hospital between 2010 and 2016, with ST117 strains appearing frequently only at the end of 2015 and 2016 (18). The German National Reference Centre for Staphylococci and Enterococci reported the same STs as Liese et.al. as well as an increase in ST117 in Germany in recent years (8). An increase in ST117 was also observed in other European countries such as Denmark (19), Switzerland (20), Norway (21), the Netherlands (22, 23), Spain (24), and Portugal (25).

In this study, different CTs of ST117 strains were identified; in 2018, however,CT71 clearly predominated. The analysis was comprised of non-outbreak isolates only, which were collected in different wards. Recent publications indicate the spread of CT71 throughout Germany in hospitals in different geographical regions without any presumed patient transfer (9, 26). The recent predominance of ST117 CT71 both in outbreak and non-outbreak strains leads to a question: What could be facilitating the spread of this particular clonal lineage? Compared to other CTs among ST117 strains, we did not detect resistance or virulence traits in CT71 that could confer survival advantage. The detected resistance genes (*msrC*, *efmA, ermB*, *dfrG*, and *aac(6')-Ii)* and virulence factors (*acm*, *esp*, *hyl*, *ecbA* and *sgrA*) of CT71 strains have already been reported in connection with high risk *Enterococcus* strains (19, 20, 27, 28). The same set of virulence factors as in CT71 strains was also found in 15 other ST117 non-CT71 strains, mainly CT36, a CT frequently identified in 2015 (33%). So perhaps it is not a single trait that is responsible for the dominance and spread of specific strain types, but a combination of particular virulence factors.

Lee et al. has also reported the detection of the virulence factors *acm* and *sgrA* in connection with the predominance of an outbreak strain type ST173 (29). Surprisingly, they identified fewer virulence factors in that outbreak strain than in the other strains. Falgenhauer et al. detected *acm*, *hyl*, and *esp* as well as the *efaAfm* gene in CT71 strains, the latter of which contributes to cell wall adherence (26). Although we used two databases for the detection of virulence factors, there may be virulence factors that have not yet been reported.

The analysis of patient characteristics does not provide an explanation for the predominance of either ST117 or CT71 strains. Only the year of specimen collection and urine as the site of specimen collection increased the chance of finding ST117.

Even though urine as sample collection site is generally regarded as a clinical culture, the sampling site itself does not necessarily indicate that the patients had a urinary tract infection.

In contrast to most previous publications, we aimed to investigate isolates outside of reported outbreaks and without apparent epidemiological links. Even though certain clones predominated in different years, continuous outbreak scenarios seem unlikely because the strains were found in three geographically distinct hospital buildings without an apparent epidemiological link between the patients. There may be ongoing inter-hospital spread, which would corroborate recent findings of Falgenhauer et.al., who also detected near-identical isolates (≤10 cgMLST alleles) of ST117 CT71 *vanB* clones in different hospitals across the Rhine-Main area of Germany (26). Inter-hospital spread would either require the direct movement of patients between the different hospitals or unrecognized vectors linking the strains.

Community-acquired VREfm and VREfm associated with animals differ genetically from hospital-acquired VREfm isolates (30), but healthcare independent populations, livestock, food, or water may nonetheless act as a reservoir. Moreover, horizontal gene transfer may facilitate the spread of VREfm through the exchange of mobile genetic elements

such as transposons or plasmids, or a crossover between chromosomal and plasmid DNA through insertion elements (IS elements)(31). Zhou et al. have demonstrated that both cgMLST and transposon analysis for the detection of horizontal gene transfer is important in order to understand the complex transmission routes and outbreaks of VREfm (22). Pinholt et al. have reported a clonal expansion of one specific VREfm clone based on a *vanA*-plasmid that was transferred via horizontal gene transfer to already existing hospital-adapted vancomycin-susceptible *E.faecium* and, thus, generated new VREfm (19). The exchange of genomic material between VRE and VSE may be responsible for the dissemination of *vanB* resistance in Germany (32).

The general increase of VREfm in Germany was accompanied by an increase in *vanB*-type strains (8) and by a shift from *vanA* to *vanB* genotype, which has been reported since 20 15/2016 (18, 32). We saw the same effect in our study, with an increase in *vanB* CT36 in 2015 and *vanB* CT71 in 2018.

Limitations of the study are the relatively small number of samples and the lack of information on patient factors both outside and inside of the hospital, such as comorbidities, antibiotic therapy, and admission to other health care institutions. In addition, the introduction of active surveillance cultures for VRE between 2008 and 2018 may have resulted in a systematic selection bias.

Conclusion

In conclusion, this retrospective analysis reports frequencies of specific VREfm strains in a German university hospital over time. An increase in ST117 strains from 2008 to 2018 was accompanied by a shift to *vanB* CT71 strains in 2018. This shift seems to be independent of intra-hospital transmissions, as epidemiologically unrelated isolates were examined. We found neither specific virulence factors nor alterations in the patient mix to explain the increase of ST117 CT71. To date, it is not clear why ST117, and strain type ST117 CT71 in particular, predominates over other strains. In addition to epidemiological data, further studies to understand the complex spread of VREfm strain types need to take into account horizontal gene transfer in VREfm as well as potentially unrecognized vectors such as VSEfm or other bacterial lineages, and interactions with the intestinal microbiome.

Abbreviations

cgMLST: Core genome multi locus sequence typing

Charité: Charité - Universitätsmedizin Berlin

CT: Cluster type

MLST: Culti locus sequence typing

ST: Sequence type

VRE: Vancomycin-resistant *Enterococcus*

VREfm: Vancomycin-resistant *Enterococcus faecium*

Declarations

Acknowledgments

The authors would like to thank Oliver Schwengers for his support in using ASA³P.

Authors´ contributions

AK and PG were responsible for the concept of the study. FM and AW wrote the manuscript. AW carried out the generation of the experimental data and the whole genome sequencing. FM and AW were responsible for bioinformatic data analysis. FS was involved in analyzing the results. All authors contributed substantially to the work and approved the final version of the manuscript.

Funding

This research did not receive grants from funding agencies in the public, commercial, or not-for-profit sectors.

Availability of data and materials

All data generated or analyzed in the course of this study have been included in this published article and its supplementary information files.

Ethics approval and consent to participate

Personal data were anonymized.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Additional File Legends

Additional file 1: Table S1. Resistance genes and virulence factors of 43 ST117 strains. Resistance genes: *msrC*: Macrolide, Lincosamide and Streptogramin B resistance; *efmA*, *ermB*: Macrolide resistance; *dfrF*, *dfrG*: Trimethoprim resistance; *aac(6')-aph(2"), aph(3')-III, ant(6)-Ia, aac(6')-Ii*: Aminoglycoside resistance; *cat*: Amphenicol resistance; *tetM*: Tetracycline resistance;

Virulence factors: *acm*: Cell wall-anchored collagen adhesin; *esp*: Enterococcal surface protein; *hyl*: Hyaluronidase; *ecbA*: *E. faecium* collagen binding protein A; *sgrA*: surface adhesion; *scm*: second collagen adhesin of *E. faecium.*

Additional file 2: Figure S1. Proportion of *vanA* and *vanB* genotype of ST117 strains from 2008-2018.

Figures

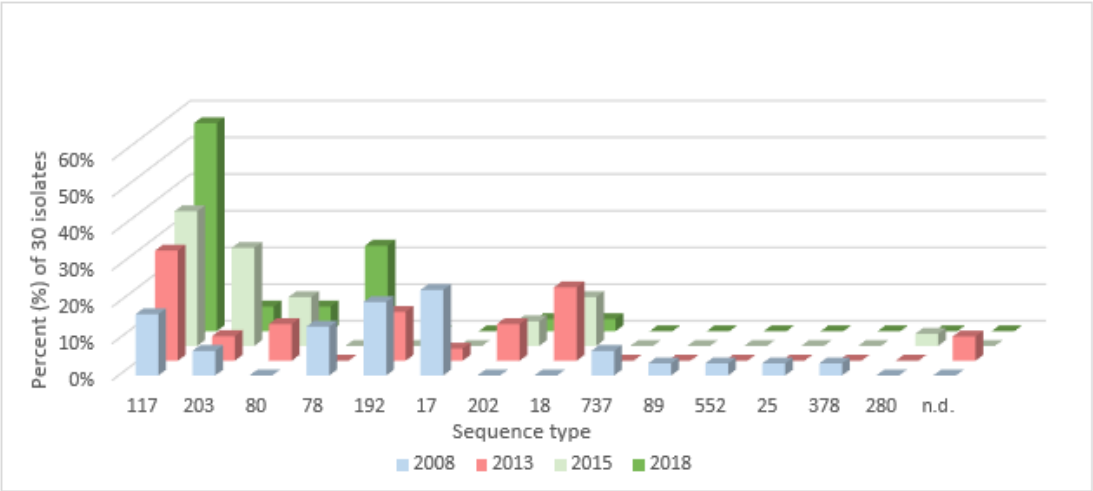

Figure 1

Frequency of different STs in percent for the period 2008 to 2018 with 30 isolates per year (n.d. denotes ST not defined, comprises different strains).

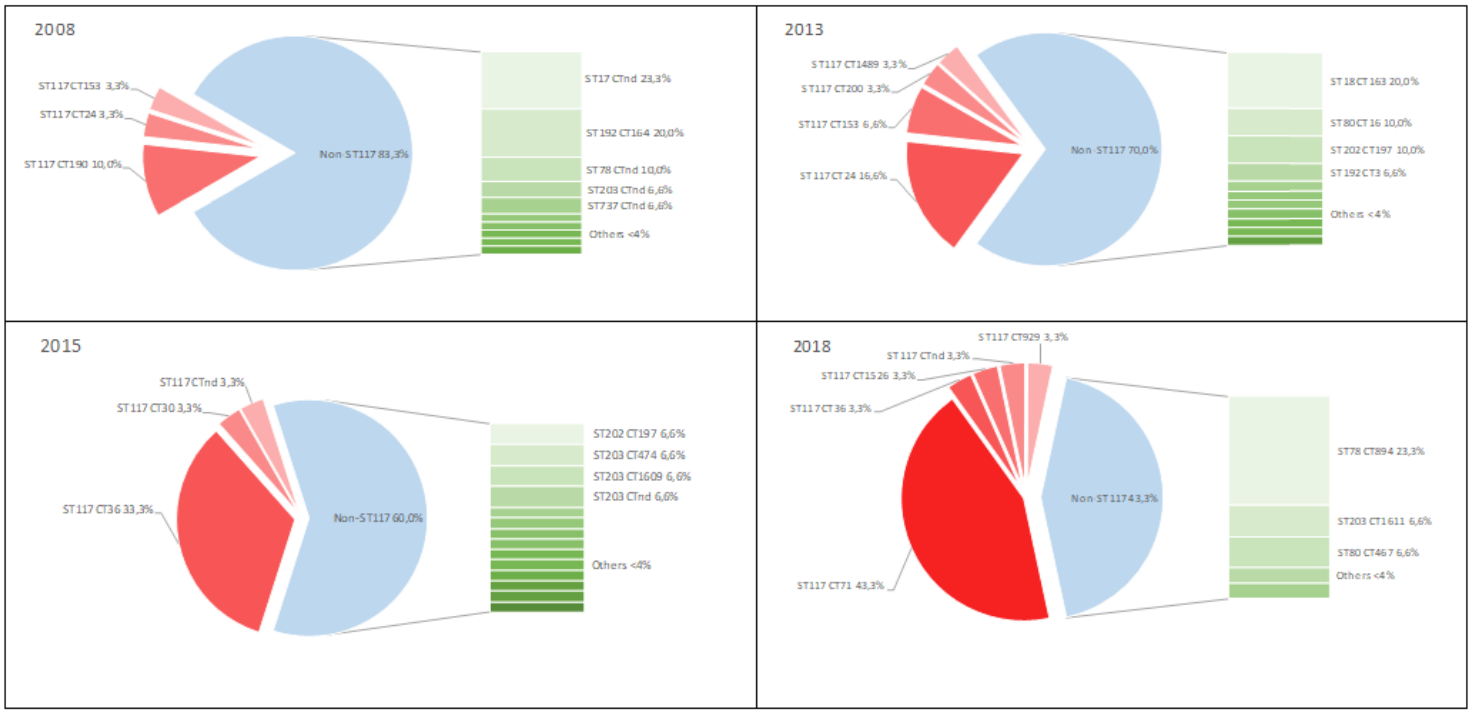

Figure 2

Increase in ST117 strains (marked red) in 2008, 2013, 2015 and 2018. Pie chart: percentage of ST117 strains and non-ST117 strains (marked light blue) based on 30 isolates per year, occurrence of different CTs within ST117; bar chart: occurrence of various CTs (marked green) within the non-ST117 group.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Additionalfile1TableS1.pdf

- Additionalfile2FigureS1.pdf