Meticillin-susceptible *Staphylococcus aureus* transmission among healthcare workers, patients and the environment in a large acute hospital under non-outbreak conditions investigated using whole-genome sequencing

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Running Title: Transmission of MSSA under non-outbreak conditions

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Abbreviations: CC; clonal complex, ST; sequence type; HCW; healthcare worker, MSSA; meticillin-susceptible *S. aureus*, NPE; near patient environment, RIG; related isolate group, TEs; transmission events, WGS, whole-genome sequencing; cgMLST, core-genome multilocus sequence typing

ABSTRACT

Background: The role of meticillin-susceptible *Staphylococcus aureus* (MSSA) colonization of healthcare workers (HCWs), patients and the hospital environment in MSSA transmission events (TEs) is poorly understood.

Aims: We recently investigated these roles for MRSA under non-outbreak conditions in a large hospital with a history of endemic MRSA over two years using whole-genome sequencing (WGS). Numerous potential MRSA TEs were identified. Here we investigated MSSA TEs from the same sources during the same two-year hospital study.

Methods: HCW (*N*=326) and patient (*N*=388) volunteers on nine wards were tested for nasal and oral MSSA colonization over two years. Near-patient environment (*N*=1,164), high-frequency touch sites (*N*=810) and air (*N*=445) samples were screened for MSSA. Representative MSSA and clinical isolates were sequenced and analysed by core-genome multilocus-sequence typing (cgMLST). Closely related isolates (≤24 allelic differences) were segregated into related-isolated groups (RIGs). Potential TEs involving MSSA in RIGs from HCWs, patients and patient infections were identified in combination with epidemiological data

Findings: In total, 635 MSSA were recovered: clinical isolates (*N*=82), HCWs (*N*=170), patients (*N*=120), environmental isolates (*N*=263). Twenty-four clonal complexes (CCs) were identified among 406/635 MSSA sequenced, of which 183/406 segregated into 59 RIGs. Numerous potential HCW-to-patient, HCW-to-HCW and patient-to-patient TEs were identified, predominantly among CC5-MSSA, CC30-MSSA and CC45-MSSA. HCW, patient, clinical and environmental isolates were identified in 33, 24, six and 32 RIGs, respectively, with 19/32 of these containing MSSA related to HCW and/or patient isolates.

Conclusions: WGS detected numerous potential hospital MSSA TEs involving HCWs, patients and environmental contamination under non-outbreak conditions.

Keywords: MSSA, meticillin-susceptible *Staphylococcus aureus*, hospital transmission, whole-genome sequencing, MSSA colonization, environmental contamination, non-outbreak conditions, oral colonization, nasal colonization.

Introduction

Meticillin-resistant *Staphylococcus aureus* (MRSA) bloodstream infections (BSIs) have declined in the USA and Europe including Ireland since 2011, while BSI rates for meticillin-susceptible *S. aureus* (MSSA) have remained steady or increased[1]. The European Antimicrobial-Resistance Surveillance Network reported a 20% increase in MSSA BSIs between 2014-2018[2]. MRSA hospital transmission events (TEs) represent only a proportion of *S. aureus* transmissions. MRSA receive more focus in hospitals and the literature due to reduced treatment options. However, MSSA also cause severe infections and represent a higher proportion of the *S. aureus* bioburden in particular settings[3,4]. Investigating the prevalence and transmission dynamics of MSSA in hospitals among healthcare workers (HCW), patients and environment sources is necessary to inform infection prevention and control (IPC) policy and interventions to minimize all *S. aureus* TEs.

We recently investigated the transmission dynamics of MRSA under non-outbreak conditions in nine wards of a large acute adult Dublin hospital with a history of endemic MRSA over two-years using whole-genome sequencing (WGS)[5]. The study focused on potential TEs between HCWs, patients and near-patient environments (NPEs), extended ward environments, and the air. Numerous potential HCW-to-patient, HCW-to-HCW, patient-to-patient TEs and environmental contamination by HCW/patient strains were identified involving MRSA from multiple multilocus-sequence typing (MLST) clonal complexes (CCs) clustered into related isolate groups (RIGs) determined by core-genome (cg)MLST)[5]. Isolates within individual RIGs were closely related and exhibited ≤24 cgMLST allelic differences. Few studies have investigated the hospital transmission dynamics of MSSA and MRSA under non-outbreak conditions[6].

This study aimed to investigate the transmission dynamics of MSSA recovered in the same nine hospital wards during the same two-year time-period as the MRSA study using WGS. Detailed information regarding TEs involving MSSA and MRSA can be used to identify emerging clones and transmission pathways and to inform more effective IPC strategies[7].

Methods

Study design

This study was undertaken in nine wards (A-I) of a large-acute hospital in Dublin, Ireland and was approved by the Beaumont Hospital Medical Research Ethics Committee (reference number, 17/01). HCWs and ward patients were recruited subject to previously-described inclusion criteria and with informed consent[3,5]. Previous nasal MRSA or MSSA colonization status of participants was unknown to the researchers. Participant sampling was undertaken during three phases: phase I, May 2017 to mid-October 2017; phase II, late October 2017 to May 2018; phase III, August 2018 to March 2019. Eight of the nine wards consisted of four 6-bed bays, one 4-bed bay, and one 2-bed bay and five single-bed rooms. One ward consisted of two 4-bed bays and one 2-bed bay. Clinical MSSA isolates (e.g. from surgical site infections) from study ward patients were also investigated.

Participant and environmental sampling

Isolate recovery was described previously[3,5]. Briefly, participant samples were taken from the anterior nares using sterile transport swabs and from the oral cavity using a phosphate-buffered saline rinse[3,5,8]. Environmental sampling was undertaken in parallel with participant sampling to provide a snapshot of the MSSA environmental burden. Environmental sampling included NPEs and the wider ward environment (Table SI) as described previously[3,5]. Air sampling (500 L) was undertaken once per sampling phase using an EM0100A air sampler (Oxoid/Thermo Scientific, Fannin Healthcare, Dublin, Ireland) as described previously[5]. Environmental surface samples were taken using contact plates[9].

Microbiological methods

SaSelect chromogenic agar (Colorex, E&O laboratories, Bonnybridge, UK) was used to culture participant samples and for air and contact plate sampling[4,5,10]. *Staphylococcus aureus* identification was confirmed using the tube-coagulase test and the Pastorex StaphPlus latex-agglutination kit (BioRad, Marnes la Coquette, France)[11,12]. MSSA were screened for the absence of *mecA* by PCR as previously described[13]. Antimicrobial-susceptibility profiling including meticillin-susceptibility confirmation using 30-µg cefoxitin disks (Oxoid, Basingstoke, UK) was undertaken as previously described using a panel of 23 antimicrobial agents and heavy metals by disk diffusion using the European Committee on Antimicrobial Susceptibility Testing methodology and interpretive criteria[13,14]. Isolates were deemed multidrug resistant (MDR) if they exhibited resistance to ≥3 clinically used antibiotic classes[15].

Whole-genome sequencing

One isolate per HCW, patient and environmental site per sampling phase was selected for WGS unless antimicrobial-susceptibility profiles from multiple isolates from the same participant/site were different. Genomic DNA extracted from MSSA isolates was assessed for quality as previously described[16]. Sequencing libraries prepared using the Nextera DNA Flex Library Preparation Kit (Illumina, Eindhoven, The Netherlands), underwent paired-end sequencing using the 500-cycle MiSeq Reagent Kit v2 (Illumina). Libraries were scaled to exhibit an average coverage of 100× and sequencing run quality was assured by cluster density and Q30 assessment. Resulting fastq files were submitted for genome assembly and the *S. aureus* cgMLST scheme (1861 loci) using the BioNumerics software version 8 pipeline (Applied Maths, BioMérieux, Belgium) as previously described[5]. Variation between isolate cgMLST profiles within each CC was investigated using the categorical differences algorithm and the UPGMA method in BioNumerics to generate best-fit, circularised UPGMA trees. Isolates within each CC exhibiting ≤24 cgMLST allelic differences were deemed closely-related based on previously proposed relatedness thresholds[17,18] and clustered into RIGs[5]. HCW, patient or patient infection isolates deemed to be involved in individual potential TEs belonged to the same RIGs. All read datasets were submitted to the NCBI Sequence-Read Archive (BioProject-No. PRJNA818983).

Results

Healthcare workers

HCWs (*N*=326) were recruited as described previously[3], of which 121/326 (37.1%) yielded 170 MSSA during phases I (60/170), II (71/170) and III (39/170). In total, 50/121 (41.3%) colonized HCWs exhibited nasal carriage, 45/121 (37.2%) exhibited oral carriage and 26/121 (21.5%) exhibited both (Table SI). Twenty-one HCWs yielded MSSA during two sampling phases, 14 during phases I-II, two during phases II-III and five during phases I and III (Tables I and SI).

Patients, environmental sites, and clinical isolates

Patients (*N*=388) were recruited as described previously[3]. Patients were sampled during one sampling phase. Of these, 93/388 (24%) yielded 120 MSSA of which 45/93 (48.4%) exhibited nasal carriage, 21/93 (22.6%) exhibited oral carriage and 27/93 (29%)

exhibited both (Table SI). MSSA were recovered from 61/1164 (5.2%) NPE samples, 62/810 (7.7%) extended ward environment high-frequency touch sites and from 140/445 (31.5%) air samples. Eighty-two clinical MSSA from patient infections were recovered on the nine wards during the study. In total, 635 MSSA were recovered.

Isolates and antimicrobial-susceptibility

All 635 MSSA lacked *mecA* and were meticillin-susceptible. Eighty-six distinct antimicrobial-susceptibility profiles were detected among the 635 MSSA, including 47 MDR profiles exhibited by 91 isolates (14.3%) (Tables SI and SII).

Clonal complexes

In total 406/635 MSSA underwent WGS including 152/170 HCW isolates (121 HCWs), 94 patient isolates (91 patients), 39/82 clinical isolates and 121/263 environmental isolates. *In-silico* analysis detected 24 CCs with CC5 (18.4%), CC30 (15.7%) and CC1 (11%) the most prevalent (Table SI). In total 183/406 sequenced MSSA (45.1%) segregated into 59 RIGs; isolates within each RIG were closely related (≤24 cgMLST allelic differences). The remaining 223/406 sequenced isolates were deemed unrelated and assigned for convenience to RIG-0 (Table SI). Pairwise allelic differences between the 183 MSSA in RIGs are shown in Table SIII. The timeline for recovery of isolates in RIGs is shown in Figures 2a, (RIGs 1-28) and 2b (RIGs 29-59). Epidemiological information on isolates in RIGs is summarised in Table SIV. HCW, patient, patient infection and environmental MSSA were present in 33, 24, six and 32 RIGs, respectively, with 19/32 of the latter containing MSSA related to HCW and/or patient isolates.

RIGs containing isolates associated with potential TEs involving at least two isolates from an HCW, a patient or patient infection are described below. Details of RIGs including one isolate recovered from one of these sources with environmental isolates and RIGs containing environmental isolates only are provided in Table SI, SIV and Figure 2.

CC1-MSSA (RIG-8)

RIG-8 comprised three patient isolates recovered within five days starting with PO0717 in Ward H (3/4/2019), with the remaining isolates recovered five days later in wards H (PO0729) and C (PO0737) (Table S1 and Figures 1 & 2a).

CC5-MSSA (RIGs-9-11, 13 & 15)

RIGs 9 and 10 comprised two isolates each from two persistent-carrier HCWs sampled eight and 14 months apart, respectively. RIG-9 isolates HN0184.1 and HN0184.2 were recovered from HCW-0184 in Ward G in August 2017 and April 2018, respectively. RIG-10 isolates HN0044.1 and HN0044.2 were recovered from HCW-0044 in Ward A in June 2017 and August 2018, respectively (Tables I and SI, Figures 1 and 2a). RIG-11, the largest RIG in the study (*N*=21), included one patient isolate (PN0143) from Ward H (15/8/2017), recovered 13 days after an environmental isolate (EB0113, earliest RIG isolate) was recovered from the bedframe of a different patient in the same ward. RIG-11 contained 18 additional Ward H isolates from air samples (*N*=5), bedframes (*N*=6), bedside lockers (*N*=5) and mattresses (*N*=2) recovered over three weeks following the earliest isolate. Clinical isolate C119224 was the last RIG-11 isolate, recovered four months later (11/12/2017) in a different ward (Ward F) (Table SI, Figures 1 and 2a). RIG-13 comprised two HCW isolates (HO0244.1 and HO0590.1) from separate HCWs on the same date in Wards I and C, respectively. RIG-15 comprised three isolates from three HCWs including HN0340.1 in Ward F (11/01/2018), followed by HN0348.1 one day later in Ward H and HO0398.2e 47 days later in Ward I. All three isolates harboured a staphylococcal cassette chromosome element encoding *ccrAB4* and *fusC,* with 99.68% sequence similarity to *S. aureus* AR466 (GenBank accession no. CP029080.1)[19] (Table SI, Figures 1 and 2a).

CC15-MSSA (RIGs 16 & 18)

RIG-16 comprised three CC15/ST5033-MSSA air isolates (AHA0054.1, AHA0065.1 and AHA0053.1A) from Ward F in August 2017 and isolates HN0206.1 and HN0206.2 from HCW-0206 recovered in July and September 2017 in the same ward (Tables I and SI, Figures 1 and 2a). RIG-18 included a patient isolate (PN0297) recovered in Ward C in November 2017 and two air isolates (A101-05 and A1601-03) recovered from Ward C 14 months later. The two remaining RIG-18 isolates were recovered a week later from two patients (PO0629 and PO0631B.2) in Ward G (Table SI and Figures 1 an2a).

CC22-MSSA (RIGs 20-22)

RIG-20 comprised four ST737-MSSA starting with PN0697 from a patient in Ward C (22/03/2019), followed by a HCW isolate (HO0620.1) in Ward G (4/04/2019), followed by two additional HCW isolates (HO0674.1and HO0670.1) from separate HCWs in Ward C (10/4/2019 & 16/4/2019), (Table SI and Figures 1 & 2a). RIG-21 comprised four ST22-MSSA with the earliest isolate (EL0587) from a patient's locker in Ward H in February

2018, followed by a HCW isolate (HN0496.1) eight months later in October 2018 on Ward F, followed by a patient infection isolate (C2221) in Ward A in January 2019, followed four months later by a patient isolate (PN0743) in Ward H in April 2019 (Table SI and Figures 1 and 2a). RIG-22 comprised two ST22-MSSA (HN0318.1 and HN0318.2) from the same HCW over two sampling phases (December 2017 to August 2018) (Tables I and SI and Figures 1 & 2a).

CC398-MSSA (RIGs 24-27)

RIG-24 comprised two isolates (HN0378.1 and HN0384.1) from separate HCWs on Ward H seven days apart (Table SI, Figures 1 and 2a). RIG-25 comprised six isolates from Ward C including an ST398-MSSA patient isolate (PN0001) in May 2017, followed by two environmental isolates (EL0015 and AMA0004.1A) recovered 8-14 days later, followed by a HCW isolate (HN0024.1) 15 days later, followed a day later by an environmental isolate (EL0031) from another patient's NPE. The final RIG-25 isolate (C11430) was recovered from a patient infection eight months later in a different ward (Ward B) (Table SI, Figures 1 & 2a). RIG-26 comprised three isolates recovered from a HCW (HO0376.1) on Ward H in January 2018, an isolate from a second HCW (HO0598.1) 13 months later in Ward I and an isolate from a patient (PO0647) in Ward I two days after HCW isolate HO0598.1 (Table SI, Figures 1 & 2a). RIG-27 comprised four isolates including environmental isolate EL0333 recovered in November 2017 in Ward B, followed five days later by two isolates (PO0345 and PO0347) from separate patients in Ward A, followed three months later by a patient infection isolate (C171679) in Ward E (Table SI and Figures 1 & 2a).

CC30-MSSA (RIGs 29,31, 33, 35-36 & 39)

RIG-29 comprised two isolates (HO0312.1 and HN0342.1) recovered from separate HCWs in Wards A and F, respectively, 11-months apart (Tables SI, Figures 1 and 2b). RIG-35 comprised two isolates (PN0285 and PN0369) from separate patients in Wards C and H, respectively, between October 2017 and January 2018 (Tables SI, Figures 1 and 2b). RIG-36 comprised two isolates (HO0444.1 and HO0438.1) from separate HCWs on the same day in Ward E (Table SI). RIG-37 comprised three isolates starting with patient isolate PN0543 in Ward A (31/08/2018) followed four days later by another patient isolate (PN0547) in Ward A and a HCW (HO0474.1) in Ward B (Table SI, Figures 1 & 2b). Three RIGs each comprised two isolates recovered from persistent-carrier HCWs over two sampling phases:

RIG-31 (HCW-0282), RIG-33 (HCW-0076) and RIG-39 (HCW-0224) (Tables I and SI, Figures 1 and 2b).

CC45-MSSA (RIGs 40, 41,43, 45, 47, 50 & 51)

RIG-40 comprised two ST5036-MSSA (HN0422.1 and HN0260.3) from separate HCWs in Ward E in April 2018 and in March 2019, respectively, (Table SI and Figures 1 and 2b). RIG-41 comprised a patient isolate (PN0341) recovered in December 2017 in Ward B and a HCW isolate (HN0354.1) recovered 47 days later in Ward H. RIG-46 comprised a patient isolate (PO0455) recovered in April 2018 in Ward G and a HCW isolate (HN0434.1) recovered a month later in the same ward (Table SI and Figures 1 and 2b). RIG-48 comprised a HCW isolate (HO0588.1) recovered in February 2019 in Ward C and a patient isolate (PO0659) recovered 18 days later in Ward I. RIG-45 comprised four ST5031-MSSA including a patient isolate (PN0227) recovered in September 2017 in Ward E, two isolates from the same patient's NPE on the same day (EB0227 and EM0227) and a HCW isolate (HO0258.1) recovered a week later in Ward I (Table SI and Figures 1 and 2). RIG-51 comprised two ST508-MSSA (HO0234.1 and HO0248.1) from separate HCWs on the same day in Wards G and I, respectively. Three RIGs each comprised two isolates from persistent-carrier HCWs over two sampling phases: RIG-43 (HCW-0220), RIG-47 (HCW0016) and RIG-50 (HCW-0094) (Tables I and SI and Figures 1 and 2).

Additional RIGs (RIGs 52-59)

RIGs 52-59 comprised isolates belonging to infrequently observed MSSA CCs including ST1027 (RIG-52), ST59 (RIG-53), ST7 (RIG-54), ST8 (RIG-55) and ST188 (RIG-58), each comprising two isolates, ST72 (RIG-56) and ST109 (RIG-57), both comprising three isolates and ST97 (RIG-59) comprising four isolates (Table SI and SIV).

Persistent and intermittent MSSA carriage among HCWs

Of the 121/326 colonized HCWs, 21/121 (17.4%) yielded MSSA during two sampling phases. In the case of 10/21 HCWs, closely related MSSA of the same ST and exhibiting 0-13 cgMLST allelic differences were recovered during each phase indicating persistent carriage (Table I). Two further HCWs were colonized with two MSSA strains of the same CC/ST in each case, however the isolate pairs were not closely related; HCW-0138 yielded two CC15/ST582-MSSA with 217 cgMLST allelic differences and HCW-0260 yielded two CC45/ST5036-MSSA with 63 cgMLST allelic differences (Table I). The

remaining 9/21 HCWs harboured different MSSA during two sampling phases indicating loss and gain of different MSSA clones between samplings (Table I).

Discussion

This investigation formed part of a larger study exploring how *S. aureus* colonization of HCWs, patients and environmental contamination contribute to TEs in a large hospital under non-outbreak conditions. Oral and nasal *S. aureus* were recovered from volunteer patients and HCWs on nine wards during three sampling phases over a two-year period, together with isolates from extensive environmental sampling and patient infections on the same wards. WGS analysis and epidemiological data were used to identify potential TEs. We previously reported that 155 MRSA were recovered during the study and that nine CCs were identified among 110/155 sequenced MRSA of which 79/110 MRSA segregated into 17 RIGs[5]. Isolates within RIGs were closely related (≤24 cgMLST allelic differences). Numerous potential HCW-to-patient, HCW-to-HCW, patient-to-patient TEs and environmental contamination by HCW/patient MRSA were evident[5]. The present study reports an analysis of MSSA recovered from HCWs, patients, patient infections and the environment in the same nine hospital wards during the same two-year period.

In total, 635 MSSA were recovered from 121 HCWs (*N*=170), 93 patients (*N*=120), patient infections (*N*=82) and environmental samples (*N*=263) (Table SI). A subset of 406 MSSA were selected for WGS based on unique antimicrobial-resistance profiles and one isolate per patient or HCW (per sampling phase). These included 152, 94, 39 and 121 MSSA from HCWs, patients, patient infections and the environment, respectively. Of these, 183/406 MSSA grouped into 59 RIGs, each consisting of closely related isolates (≤24 cgMLST allelic differences) (Tables SI and SIV).

Seven MSSA from patient infections were identified in RIGs 11, 21, 25, 27, 52 and 59. RIG-11 comprised 21 CC5/ST5-MSSA including patient isolate PN0143, and 19 environmental isolates from the NPEs of eight other patients and five air samples in Ward H between 2nd-23rd August 2017. Clinical isolate C119224 was the last RIG-11 isolate, recovered in Ward F in December 2017. The large number of related environmental isolates suggests a heavy shedder in Ward H and the recovery of a closely related clinical isolate several months later suggests potential spread by an HCW. RIG-21 comprised four CC22/ST22-MSSA including NPE isolate EL0587 (February 2018) (Ward H), HCW isolate HN0496.1 (October 2018) (Ward F), clinical isolate C2221 (January 2019) (Ward A) and patient isolate PN0743 (April 2019) (Ward H). It is likely HCW-0496 or another undetected

HCW was responsible for transmission. In RIGs 25 and 27, the clinical CC398/ST398-MSSA isolates C11430 and C171679 were recovered eight and four months after the earliest recovered isolates in each RIG, respectively. HCW-0024 was a possible transmitter in RIG-25. In RIG-27 two patient isolates (PO0345 and PO0347) were recovered a week after the earliest recovered isolate. Considering the four-month timeline, it is unclear if transmission occurred via one of these patients or by an unknown HCW (Table SI and Figure 2a). RIG-52 consisted of two CC1027/ST1027-MSSA clinical isolates (C112296 and C111576) recovered a week apart in Wards C and H, respectively, in August 2017. An unknown HCW was likely responsible for transmission. The remaining 32 clinical isolates sequenced were unrelated by cgMLST to any other MSSA sequenced (Table SI).

Of the 121/326 colonized HCWs, 21/121 yielded MSSA during two sampling phases. For 10/21 HCWs, the same ST was exhibited by isolates recovered during two sampling phases between two and nine months apart. One of these 10 HCWs (HCW-0206) yielded isolates closely related to three air isolates recovered in Ward F in August 2017 one month after the first HCW isolate (HN0206.1), but 16 months before the second HCW isolate (HN0206.2) was recovered (Table SI, RIG-16). The remaining nine HCWs each yielded two closely related isolates during separate sampling phases that formed their own RIGs (RIGs 9, 10, 22, 31, 33, 39, 43, 47 and 50) (Tables I and SI). A further 11/21 HCWs exhibited loss and gain of different MSSA strains during successive sampling phases, ranging from three to 19 months apart (Tables I and SI). Three of these 11 HCWs during one sampling phase harboured isolates closely related to isolates in three other RIGs. RIG-15 comprised three CC5-MSSA including HO0398.2e (ST5) recovered in Ward I in March 2019, 14 months after isolates HN0340.1 & HN0348.1 (ST3130) were recovered from separate HCWs one day apart in Wards F and H. The two ST3130-MSSA exhibited zero cgMLST allelic differences, but both differed from the ST5-MSSA by five allelic differences. ST3130 is a single-locus variant of ST5. This is an example of slow variation occurring among MSSA and is in keeping with previous estimates for accumulation of mutations within MRSA[20]. RIG-40 comprised two CC45/ST5036-MSSA from HCWs in Ward E including HN0260.3 recovered in March 2019 and HN0422.1 during April 2018. RIG-56 comprised three CC72/ST72-MSSA including HN0088.2 from HCW-0088 recovered on the 7th December 2017 and H00320.1 and H00316.1 from separate HCWs recovered five days later (Tables I and SI).

Isolates in 26/59 RIGs containing at least two isolates from an HCW, patient or patient infection were involved in potential TEs (Table SIV). Of these, 6/26 RIGs (RIGs 11,

18, 21, 25, 27, 45) also contained environmental MSSA and while it is unclear if these isolates contributed towards TEs, they represent a risk for TEs. In total 9/26 RIGs included HCW isolates only (RIGs 13, 15, 24, 29, 36, 40, 51, 53 and 56), 7/26 RIGs included isolates from HCWs and patients only (RIGs 20, 26, 37, 41, 46, 48 and 55) and just two RIGs included patient isolates only (RIG-8 and RIG-35). This latter data supports a previous WGS study that reported a minority of *S. aureus* hospital acquisitions are likely to involve patient-patient transmission[3,21]. One RIG (RIG-52) comprised two clinical isolates and one RIG (RIG-59) comprised a patient carriage isolate and a patient infection isolate)

A comparison of the MSSA and MRSA populations sequenced from the overall study provides some interesting insights. The MSSA population was significantly more diverse with 24 CCs identified among 406 isolates sequenced, with CC5 (18.4%) predominant (Table S1). Only nine CCs were identified among the 110 MRSA sequenced, with the majority assigned to CC22 (70%)[5], reflecting the fact that CC22 MRSA predominate in Irish hospitals[1]. Only 22/406 (5.4%) MSSA sequenced were assigned to CC22. A comparison of the MSSA and MRSA by cgMLST revealed hardly any overlap. Of all 410 MSSA sequenced, only one ST22 HCW MSSA (HN0338.2) recovered in October 2018 (Table SI) clustered with a group of 24 closely related ST22 MRSA harbouring SCC*mec* IVh recovered between June 2017 and November 2018[5]. One of these MRSA (HN0338.1) was recovered eight months earlier than HN0338.2 from the same HCW in the same ward (Table SI)[5]. HN0338.1 (MRSA) and HN0338.2 (MSSA) were closely related (20 cgMLST allelic differences). These findings suggest loss of SCC*mec* IVh by MRSA HN0338.1 giving rise to MSSA HN0338.2. No other examples of potential loss/gain of SCC*mec* were evident among the MSSA and MRSA populations sequenced. Not all HCWs or patients in the hospital consented to participate in the study and it is possible that other examples of loss/gain of SCC*mec* may have been evident with a larger number of isolates. The diverse nature of the MSSA population identified over the two-year study provides ample opportunities for acquisition of SCC*mec* from MRSA circulating in the hospital, which could give rise to new MRSA clones. A previous study from this laboratory reported extensive genetic diversity among sporadic MRSA from Irish hospitals recovered over a 12-year period[22].

Currently hospital screening for *S. aureus* focuses on MRSA for high-risk patients. HCW screening is usually only considered upon identification of an epidemiological link between HCWs and MRSA from patient clusters. Screening of HCWs for MSSA is not normally undertaken. Here, the role of MSSA colonized HCWs in potential TEs involving

409 patients and other HCWs as well as environmental contamination was evident and the
410 colonization burden in HCWs (37.1%) was higher than in patients (24%). Of the 121 HCWs
411 and 93 patients colonized with MSSA, 45/121 (37.2%) and 21/93 (22.6%), respectively,
412 exhibited oral carriage only. Results from our contemporaneous study of MRSA from the
413 same hospital showed that of the 15 HCWs and 31 patients colonized with MRSA, 9/15
414 (60%) and 14/31 (45%), respectively, exhibited oral carriage only[3,5]. These findings
415 indicate that oral screening should be implemented as part of routine *S. aureus* screening
416 procedures.
417
418 *Limitations*
419 This was a single centre study restricted to specific wards. Although extensive
420 sampling was undertaken over three phases, for logistical reasons it was not continuous. Not
421 all HCWs or patients on the study wards provided consent and it is likely a significant
422 number of additional HCWs and patients were colonized with MSSA, which could have
423 contributed to TEs.
424
425 *Conclusions*
426 WGS and epidemiological data were used in this study and in our previous MRSA
427 study to monitor potential TEs in a large-acute hospital under non-outbreak conditions over
428 two years[5]. The findings highlight how dynamic MSSA/MRSA populations in colonized
429 HCWs, patients and environment contamination, and unidentified TEs including TEs
430 associated with patient infections may lead to outbreaks. The recent decreasing prevalence
431 of MRSA BSIs observed in many countries may be attributed to effective IPC measures,
432 however, such interventions have been less impactful on MSSA in the same hospitals[23].
433 Multicentre studies are required to establish if our findings are consistent across multiple
434 hospitals, including more clinical isolates to link actual infections with acquisitions from
435 other patients, HCWs and the environment. Surveillance and investigation of the dynamics
436 of MSSA/MRSA colonization of HCWs, patients and environmental contamination should
437 inform on-going review of IPC strategies and guidelines targeted at minimizing
438 MRSA/MSSA TEs[7,24].
439
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Conflict of interest statement

Declarations of interest: HH has been in receipt of research funding from Astellas and Pfizer in recent years and has received a consultancy fee from Pfizer in the last three years.

All other authors have no conflicts of interest to declare.

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Figure Legends

Figure 1. Clonal complexes represented by best-fit UPGMA trees generated by investigating the similarity between core-genome MLST profiles of 183 MSSA isolates sequenced. Trees were generated using the categorical differences algorithm and the UPGMA method using the BioNumerics suite of bioinformatics software. Isolates exhibiting ≤24 allelic variations clustered in related isolate groups (RIGs) consisting of isolates from patients (patient volunteer participants and clinical isolates), HCWs and environmental sources. RIGs are indicated by grey shading and annotated by numerals 1-59. The node colours represent isolates from different sources as indicated by the legend. The total network length (TNL) comprising the number of allelic differences within each CC is shown beneath each CC, with the average (Av) number of allelic differences and standard deviation (Sd). The associated n × n matrices generated for each CC group was calculated using

BioNumerics and are provided in Table SIII. RIGs 1-59 isolates are detailed in Table SI along with study isolates unrelated to all other isolates, which for convenience were assigned to RIG-0 (Table SI).

Figure 2. Recovery timeline for 183 MSSA isolates segregated into related isolate groups (RIGs) by cgMLST analysis. Isolates within each RIG exhibited ≤24 allelic variations and were deemed very closely relayed based on previously suggested relatedness thresholds[17, 18]. A green bar indicates the timeline for recovery of the related isolates that comprise each RIG with blue lines indicating the time point an isolate(s) was recovered. RIGs are numbered 1-59 to the side of the figure as follows: RIGs containing isolates associated with potential TEs involving at least two isolates from a HCW, a patient or clinical sample (i.e. patient infection) are indicated by numerals in white font on a red background. RIGs including one isolate recovered from one of these sources with environmental isolates and RIGs containing environmental isolates only are indicated by numerals in black font on a white background. Isolates recovered at individual time points are labelled using coloured font indicating different wards as indicated by the legend. Multiple isolates recovered from the same ward or different wards on the same date are enclosed within a circle. Isolates recovered from HCWs, patients, clinical samples, air and other environmental sites are indicated beginning with a capital H, P, A, C and E, respectively.

Table I. Genotypic and phenotypic details for recurrent meticillin-susceptible *Staphylococcus aureus* (MSSA) isolates recovered from 21 healthcare workers during multiple sampling phases

Panel (a) Persistent carriage of closely related MSSA strains over two sampling phases by 10 HCWs									
Isolate	**Study phase**	**Sample date**	**CC**	**ST**	**RIG[1]**	**Antimicrobial resistance**	**SCC**	**Ward**	**cgMLST allelic variation**
HO0016.1	I	24/05/2017	45	972	47	Ap	NA	A	13
HN0016.2	II	22/11/2017	45	972	47	Ap, Cd	NA	A	
HN0044.1	I	12/06/2017	5	6	10	Ap	NA	A	0
HN0044.2	III	18/08/2018	5	6	10	Ap, Cd	NA	A	
HN0094.1	I	19/07/2017	45	508	50	Ap	NA	B	6
HN0094.2	II	29/11/2017	45	508	50	Ap	NA	B	
HN0184.1	I	31/08/2017	5	6	9	Susceptible	NA	G	5
HN0184.2	II	11/04/2018	5	6	9	Susceptible	NA	G	
HN0206.1	I	09/07/2017	15	5033	16	Ap	NA	F	0
HN0206.2	II	01/12/2018	15	5033	16	Ap, Cd	NA	F	
HN0220.1	I	13/09/2017	45	45	43	Ap	NA	G	3
HN0220.2	II	14/05/2018	45	45	43	Ap	NA	E	
HN0224.1	I	13/09/2017	30	30	39	Ap, Cd	NA	I	10
HN0224.2	II	07/02/2018	30	30	39	Ap, Cd	NA	I	
HN0282.1	I	04/10/2017	30	30	31	Ap, Cd	NA	I	3
HN0282.2	II	15/12/2017	30	30	31	Ap, Cd	NA	A	
HN0076.1	I	12/07/2017	30	30	33	Ap, Cd	NA	D	10
HN0076.2	II	15/11/2017	30	30	33	Ap, Cd	NA	B	

HN0318.1	II	12/12/2017	22	22	22	Ap, Cd	NA	A	3
HN0318.2	III	18/08/2018	22	22	22	Ap	NA	A	

Panel (b) Loss and Gain of different MSSA strains over two sampling phases by 11 HCWs

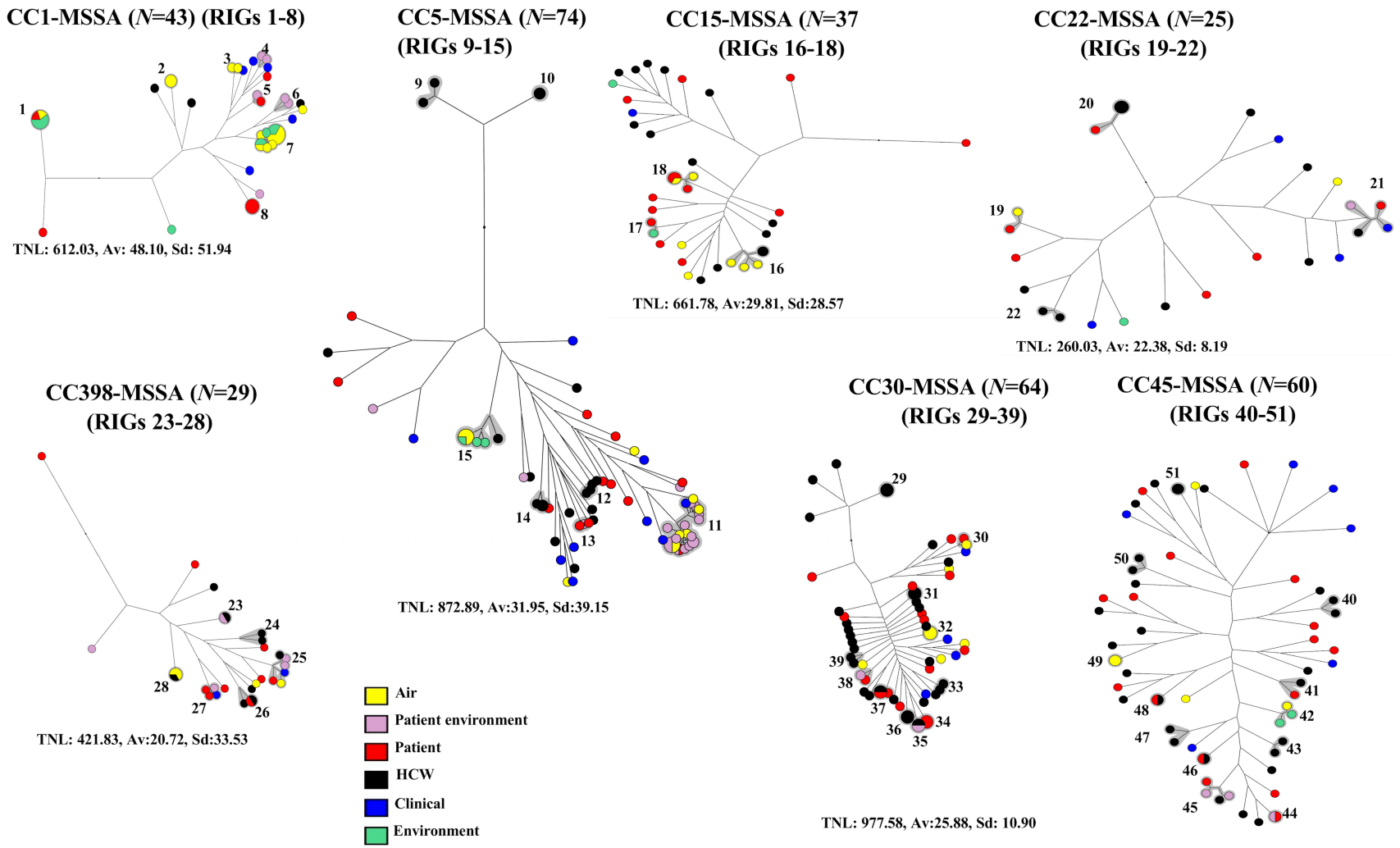
Isolate	Study phase	Sample date	CC	ST	RIG[1]	Antimicrobial resistance	SCC	Ward	cgMLST allelic variation
HN0020.1	I	25/05/2017	25	25	0	Ap, Er	NA	A	1484
HO0020.2	III	18/08/2018	5	5	0	Ap, Cd	NA	A	
HO0030.1	I	31/05/2017	15	582	0	Ap	NA	D	1302
HO0030.2	III	18/12/2018	1	1	0	Fd	NA	D	
HN0072.1	I	12/07/2017	30	34	0	Ap	NA	D	1720
HN0072.2	III	20/09/2018	97	97	0	Susceptible	NA	D	
HO0088.1	I	18/07/2017	2250	2250	0	Fd	NA	B	1327
HN0088.2	II	07/12/2017	72	72	56	Ap	NA	B	
HN0142.1	I	10/08/2017	30	30	0	Ap, Cd	NA	H	1708
HN0142.2	II	02/11/2017	96	96	0	Ap, Cd	NA	H	
HN0202.1	I	07/09/2017	320	320	0	Susceptible	NA	F	1284
HN0202.2	II	01/11/2017	15	582	0	Ap	NA	D	
HO0398.1	II	28/02/2018	8	8	0	Susceptible	NA	I	1504
HO0398.2e	III	19/03/2019	5	5	15	Ap, Fd	*ccrAB4, ,fusC*	I	
HO0110.2	II	12/12/2017	15	15	0	Ap, Er	NA	B	1719
HN0110.3	III	13/09/2018	30	39	0	Ap, Cd	NA	B	
HN0138.1	I	10/08/2017	15	582	0	Susceptible	NA	F	

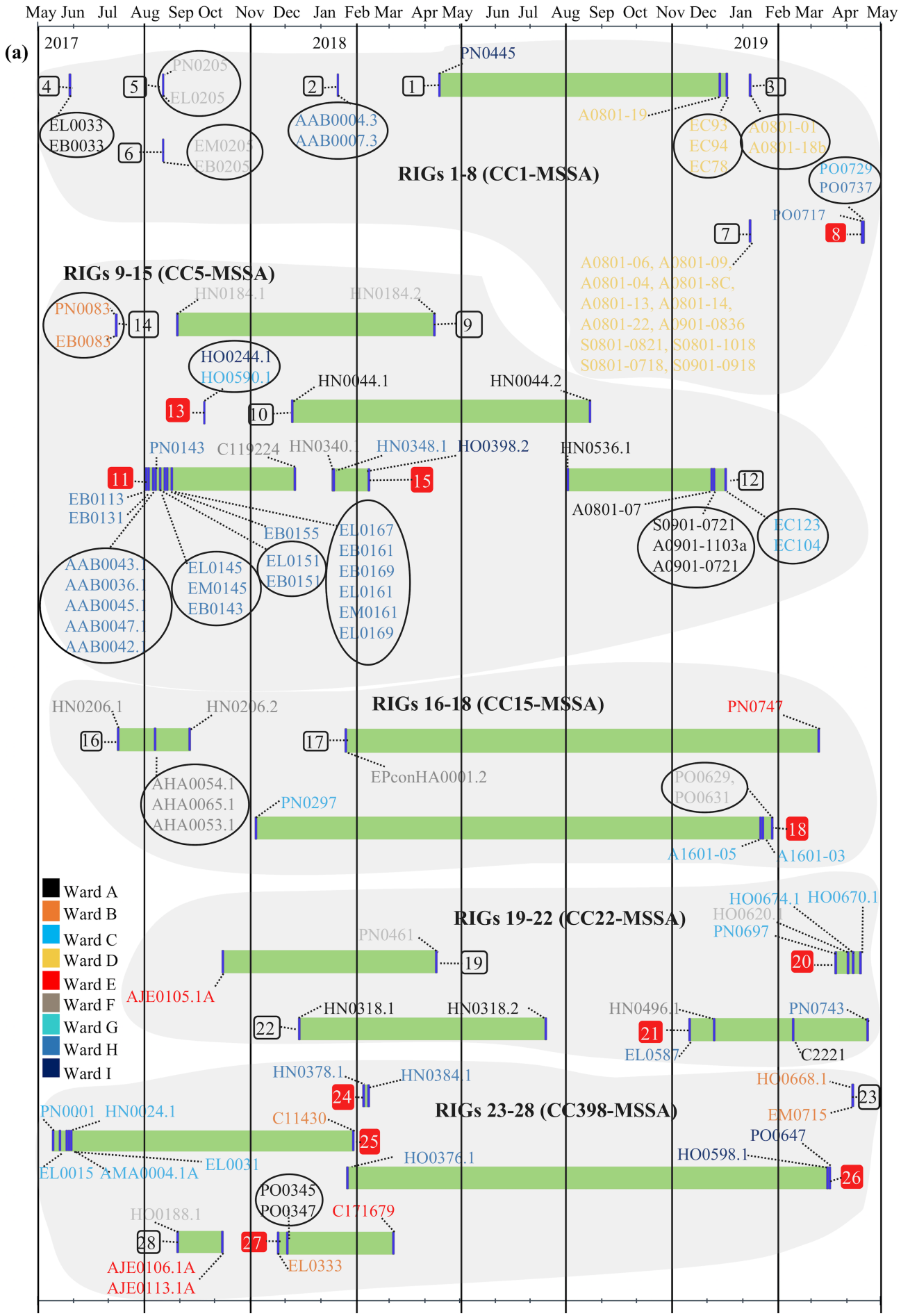
HN0138.2	II	18/10/2017	15	582	0	Susceptible	NA	C	217
HN0260.1	II	10/03/2017	45	5036	0	Ap	NA	E	63
HN0260.3	III	26/03/2019	45	5036	40	Ap, Cd	NA	E	
HN0048.2	II	09/11/2017	188	188	0	Susceptible	NA	A	1714
HN0048.3	III	18/08/2018	30	39	0	Ap, Rif, Mp, Cd	NA	A	

Of the 121/326 (37.1%) HCWs colonised with MSSA, 21/121 (17.3%) HCWs yielded MSSA from nasal and/or oral carriage during two sampling phases. Isolates were placed into RIGs by core genome (cg) MLST analysis using BioNumerics version 8 (Applied Maths, Sint-Martens-Latem, Belgium) (Figure 1). Briefly, isolates of the same CC group were selected for comparison by cgMLST. The similarity between cgMLST profiles was investigated using the categorical differences algorithm and the UPGMA method in BioNumerics to generate a UPGMA tree which was circularised, and a best fit figure was generated. All isolates that exhibited ≤24 allelic variations between them were shaded in grey in Figure 1 and the nodes are differentiated by colours representing each source type.

In panel (a), 10/21 of the HCWs harboured closely related MSSA strains (≤24 cgMLST allelic variations) during two sampling phases indicating persistent carriage. The remaining 11 HCWs (panel b) harboured unrelated MSSA strains (exhibiting ≥24 cgMLST) during different sampling phases indicating loss and gain of different MSSA clones between sampling phases. Genotypic information including multilocus-sequence typing clonal complexes (CCS) and sequence types (STs) as well as any presence of staphylococcal chromosome cassette elements were extracted from WGS data using BioNumerics (Applied Maths) and SCC*mec* finder[19].

[1]Isolates were categorised into related groups of isolates (RIGs) if they exhibited ≤24 cgMLST allelic differences to all other isolates within a RIG. Unrelated isolates were categorised into RIG-0 (see Table S1 for full list of RIGs 1-59 and associated isolates). Abbreviations: ampicillin (Ap), cadimium acetate (Cd), chloramphenicol (Chl), ciprofloxacin (Cp), Daptomycin (Da), erythromycin (Er), Ethidium bromide (Eb), fusidic acid (Fd), gentamicin (Gn), kanamycin (kn), mupirocin (Mp), neomycin (Nm), phenyl mercuric acetate (PMA), rifampicin (Rf), spectinomycin (Sp), streptomycin (St), sulphonamide (Su), tetracycline (Te), tobramycin (Tb) and trimethoprim (Tmp).


CC1-MSSA (N=43) (RIGs 1-8)
1
2
3
4
5
6
7
8
TNL: 612.03, Av: 48.10, Sd: 51.94
CC5-MSSA (N=74)
(RIGs 9-15)
9
10
15
14
12
13
11
TNL: 872.89, Av:31.95, Sd:39.15
CC15-MSSA (N=37
(RIGs 16-18)
18
17
16
TNL: 661.78, Av:29.81, Sd:28.57
CC22-MSSA (N=25)
(RIGs 19-22)
20
21
19
22
TNL: 260.03, Av: 22.38, Sd: 8.19
CC398-MSSA (N=29)
(RIGs 23-28)
23
24
25
28
27
26
TNL: 421.83, Av:20.72, Sd:33.53
Air
Patient environment
Patient
HCW
Clinical
Environment
CC30-MSSA (N=64)
(RIGs 29-39)
29
30
31
32
39
38
33
37
34
36
35
TNL: 977.58, Av:25.88, Sd: 10.90
CC45-MSSA (N=60)
(RIGs 40-51)
51
50
40
49
41
48
42
47
43
46
45
44
TNL: 1306.37, Av:37.52, Sd:29.05


(a)
May Jun Jul Aug Sep Oct Nov Dec Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec Jan Feb Mar Apr May
2017
2018
2019
RIGs 1-8 (CC1-MSSA)
RIGs 9-15 (CC5-MSSA)
RIGs 16-18 (CC15-MSSA)
RIGs 19-22 (CC22-MSSA)
RIGs 23-28 (CC398-MSSA)
PN0445
PN0205
EL0205
EL0033
EB0033
EM0205
EB0205
AAB0004.3
AAB0007.3
A0801-19
EC93
EC94
EC78
A0801-01
A0801-18b
PO0729
PO0737
PO0717
A0801-06, A0801-09,
A0801-04, A0801-8C,
A0801-13, A0801-14,
A0801-22, A0901-0836
S0801-0821, S0801-1018
S0801-0718, S0901-0918
PN0083
EB0083
HN0184.1
HN0184.2
HO0244.1
HO0590.1
HN0044.1
HN0044.2
PN0143
C119224
HN0340.
HN0348.1
HO0398.2
HN0536.1
EB0113
EB0131
EB0155
EL0151
EB0151
EL0167
EB0161
EB0169
EL0161
EM0161
EL0169
AAB0043.1
AAB0036.1
AAB0045.1
AAB0047.1
AAB0042.1
EL0145
EM0145
EB0143
A0801-07
S0901-0721
A0901-1103a
A0901-0721
EC123
EC104
HN0206.1
HN0206.2
PN0747
EPconHA0001.2
AHA0054.1
AHA0065.1
AHA0053.1
PO0629,
PO0631
PN0297
A1601-05
A1601-03
Ward A
Ward B
Ward C
Ward D
Ward E
Ward F
Ward G
Ward H
Ward I
HO0674.1
HO0670.1
HO0620.1
PN0697
PN0461
AJE0105.1A
HN0318.1
HN0318.2
HN0496.1
PN0743
EL0587
C2221
HN0378.1
HN0384.1
HO0668.1
EM0715
PN0001
HN0024.1
C11430
PO0647
HO0598.1
EL0015
AMA0004.1A
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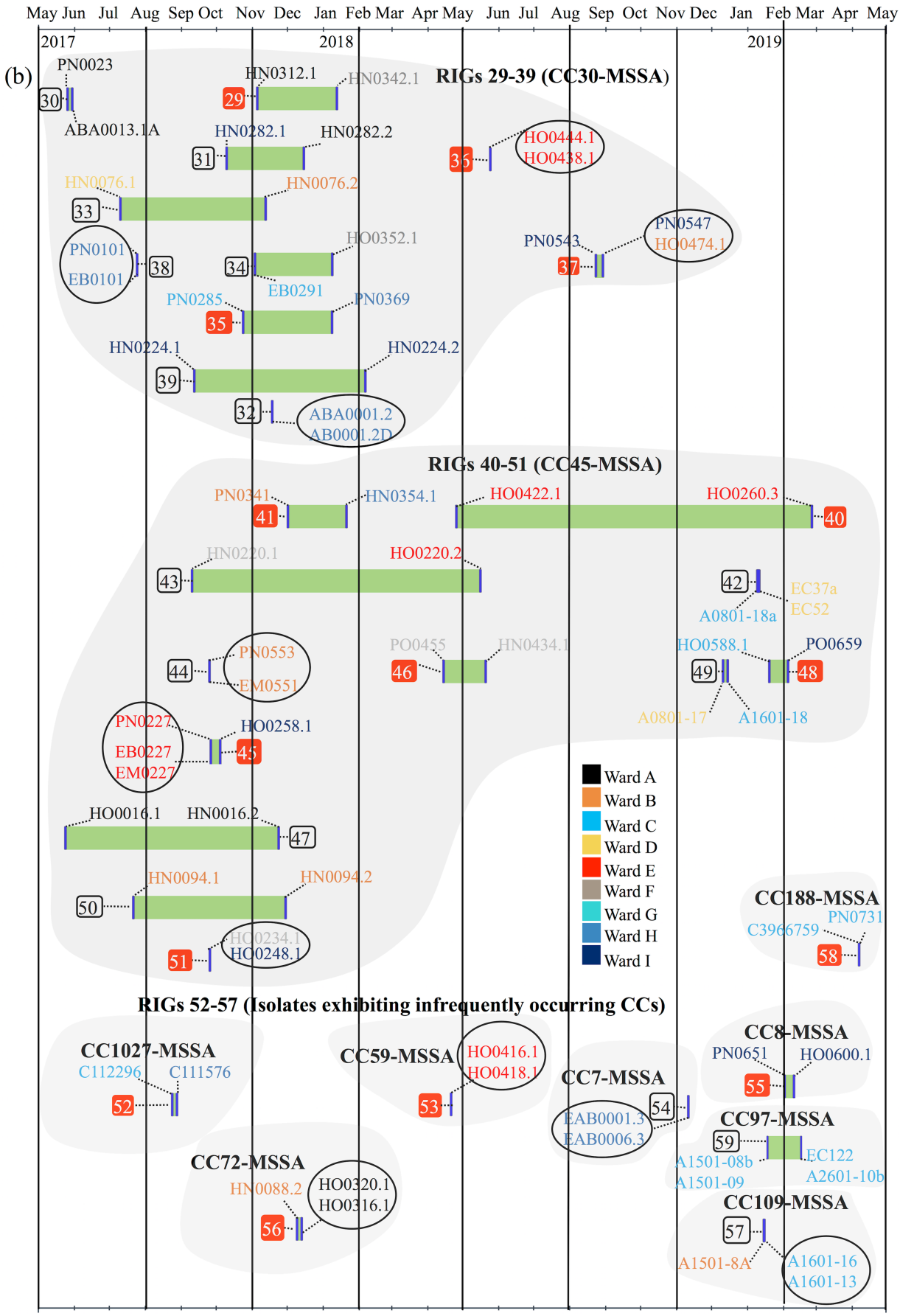
PO0345
PO0347
C171679
HO0188.1
AJE0106.1A
AJE0113.1A
EL0333


(b)
May Jun Jul Aug Sep Oct Nov Dec Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec Jan Feb Mar Apr May
2017
2018
2019
RIGs 29-39 (CC30-MSSA)
PN0023
30
ABA0013.1A
HN0312.1
29
HN0342.1
HN0282.1
31
HN0282.2
HO0444.1
HO0438.1
35
HN0076.1
33
HN0076.2
PN0101
EB0101
38
HO0352.1
34
EB0291
PN0543
37
PN0547
HO0474.1
PN0285
35
PN0369
HN0224.1
39
HN0224.2
32
ABA0001.2
AB0001.2D
RIGs 40-51 (CC45-MSSA)
PN0341
41
HN0354.1
HO0422.1
HO0260.3
40
HN0220.1
43
HO0220.2
42
EC37a
EC52
A0801-18a
PN0553
EM0551
44
PO0455
46
HN0434.1
HO0588.1
PO0659
49
48
A0801-17
A1601-18
PN0227
EB0227
EM0227
HO0258.1
45
HO0016.1
HN0016.2
47
HN0094.1
50
HN0094.2
HO0234.1
HO0248.1
51
Ward A
Ward B
Ward C
Ward D
Ward E
Ward F
Ward G
Ward H
Ward I
CC188-MSSA
PN0731
C3966759
58
RIGs 52-57 (Isolates exhibiting infrequently occurring CCs)
CC1027-MSSA
C112296
C111576
52
CC59-MSSA
HO0416.1
HO0418.1
53
CC7-MSSA
54
EAB0001.3
EAB0006.3
CC8-MSSA
PN0651
HO0600.1
55
CC97-MSSA
59
EC122
A1501-08b
A1501-09
A2601-10b
CC72-MSSA
HN0088.2
HO0320.1
HO0316.1
56
CC109-MSSA
57
A1501-8A
A1601-16
A1601-13

Isolate	Source	Study phase	Sample date	CC	ST	RIG[1]	Antimicrobial resistance	SCC	Ward
CC1 (*N*=45) MSSA isolates with 30/45 isolates associated with RIGs 1-8									
PN0445	Patient	II	13/04/2018	CC1	ST1	1	Ap, Er,	NA	I
A0801-19	Air	III	08/01/2019	CC1	ST1	1	Ap, Er	NA	D
EC93	Environment	III	15/01/2019	CC1	ST1	1	Ap, Er, Su	NA	D
EC94	Environment	III	15/01/2019	CC1	ST1	1	Ap, Er	NA	D
EC78	Environment	III	15/01/2019	CC1	ST1	1	Ap, Er, Su	NA	D
AAB0004.3	Air	III	14/11/2019	CC1	ST1	2	Ap, Er	NA	H
AAB0007.3	Air	III	14/11/2019	CC1	ST1	2	Ap, Er, Cd	NA	H
A0801-01	Air	III	08/01/2019	CC1	ST1	3	Ap, Fd, Cd	*ccrAB1* & *fusC*	D
A0801-18b	Air	III	08/01/2019	CC1	ST1	3	Ap, Fd, Cd	*ccrAB1* & *fusC*	D
EL0033	Patient environment	I	30/05/2017	CC1	ST1	4	Ap, Fd	*ccrAB1* & *fusC*	A
EB0033	Patient environment	I	30/05/2017	CC1	ST1	4	Er, Fd	*ccrAB1* & *fusC*	A
EL0205	Patient environment	I	14/09/2017	CC1	ST1	5	Fd	*ccrAB1* & *fusC*	G
PN0205	Patient	I	14/09/2017	CC1	ST1	5	Fd	*ccrAB1* & *fusC*	G
EM0205	Patient environment	I	14/09/2017	CC1	ST1	6	Fd	*ccrAB1* & *fusC*	G
EB0205	Patient environment	I	14/09/2017	CC1	ST1	6	Fd	*ccrAB1* & *fusC*	G
A0801-06	Air	III	08/01/2019	CC1	ST1	7	Ap, Fd, Cd	*ccrAB1* & *fusC*	D
S0801-0821	Environment	III	08/01/2019	CC1	ST1	7	Ap, Fd, Cd	*ccrAB1* & *fusC*	D
A0801-09	Air	III	08/01/2019	CC1	ST1	7	Ap, Er	*ccrAB1* & *fusC*	D
S0801-1018	Environment	III	08/01/2019	CC1	ST1	7	Ap, Fd, Cd	*ccrAB1* & *fusC*	D
S0801-0718	Environment	III	08/01/2019	CC1	ST1	7	Ap, Fd, Cd	*ccrAB1* & *fusC*	D
A0801-04	Air	III	08/01/2019	CC1	ST1	7	Ap, Fd, Cd	*ccrAB1* & *fusC*	D
A0801-8C	Air	III	08/01/2019	CC1	ST1	7	Ap, Fd, Cd	*ccrAB1* & *fusC*	D
A0801-13	Air	III	08/01/2019	CC1	ST1	7	Ap, Fd, Cd	*ccrAB1* & *fusC*	D

S0901-0918	Environment	III	09/01/2019	CC1	ST1	7	Ap, Fd, Cd	*ccrAB1 & fusC*	D
A0801-14	Air	III	08/01/2019	CC1	ST1	7	Ap, Fd, Cd	*ccrAB1 & fusC*	D
A0801-22	Air	III	08/01/2019	CC1	ST1	7	Ap, Fd, Cd	*ccrAB1 & fusC*	D
A0901-0836	Air	III	09/01/2019	CC1	ST1	7	Ap, Fd, Cd	*ccrAB1 & fusC*	D
PO0717	Patient	III	03/04/2019	CC1	ST1	8	Fd	NA	H
PO0729	Patient	III	08/04/2019	CC1	ST1	8	Fd	NA	H
PO0737	Patient	III	08/04/2019	CC1	ST1	8	Fd	NA	C
CC5 (*N*=75) MSSA isolates with 39/75 isolates associated with RIGs 9-15									
HN0184.1[2]	HCW	I	31/08/2017	CC5	ST6	9	Susceptible	NA	G
HN0184.2[2]	HCW	I	11/04/2018	CC5	ST6	9	Susceptible	NA	G
HN0044.1[2]	HCW	I	12/06/2017	CC5	ST6	10	Ap	NA	A
HN0044.2[2]	HCW	III	18/08/2018	CC5	ST6	10	Ap, Cd	NA	A
EB0113	Patient environment	I	02/08/2017	CC5	ST5	11	Susceptible	NA	H
EB0131	Patient environment	I	03/08/2017	CC5	ST5	11	Susceptible	NA	H
AAB0043.1	Air	I	10/08/2017	CC5	ST5	11	Susceptible	NA	H
AAB0036.1B	Air	I	10/08/2017	CC5	ST5	11	Susceptible	NA	H
AAB0045.1	Air	I	10/08/2017	CC5	ST5	11	Susceptible	NA	H
AAB0047.1A	Air	I	10/08/2017	CC5	ST5	11	Susceptible	NA	H
AAB0042.1B	Air	I	10/08/2017	CC5	ST5	11	Susceptible	NA	H
EL0145	Patient environment	I	15/08/2017	CC5	ST5	11	Susceptible	NA	H
EM0145	Patient environment	I	15/08/2017	CC5	ST5	11	Susceptible	NA	H
EB0143	Patient environment	I	15/08/2017	CC5	ST5	11	Susceptible	NA	H

PN0143	Patient	I	15/08/2017	CC5	ST5	11	Susceptible	NA	H
EL0151	Patient environment	I	17/08/2017	CC5	ST5	11	Er	NA	H
EB0151	Patient environment	I	17/08/2017	CC5	ST5	11	Susceptible	NA	H
EB0155	Patient environment	I	18/08/2017	CC5	ST5	11	Er	NA	H
EB0161	Patient environment	I	23/08/2017	CC5	ST5	11	Susceptible	NA	H
EL0161	Patient environment	I	23/08/2017	CC5	ST5	11	Susceptible	NA	H
EM0161	Patient environment	I	23/08/2017	CC5	ST5	11	Er	NA	H
EL0167	Patient environment	I	23/08/2017	CC5	ST5	11	Susceptible	NA	H
EB0169	Patient environment	I	23/08/2017	CC5	ST5	11	Susceptible	NA	H
EL0169	Patient environment	I	23/08/2017	CC5	ST5	11	Susceptible	NA	H
C119224	Clinical	I	11/12/2017	CC5	ST5	11	Er	NA	F
HO0536.1	HCW	III	01/08/2018	CC5	ST5	12	Ap, Er	NA	D
A0801-07	Air	III	08/01/2019	CC5	ST5	12	Ap, Er, Cd	NA	D
S0901.0721	Environment	III	09/01/2019	CC5	ST5	12	Ap, Er, Cd,	NA	D
A0901-1103a	Air	III	09/01/2019	CC5	ST5	12	Ap, Cd	NA	D
A0901-0721	Air	III	09/01/2019	CC5	ST5	12	Ap, Er, Cd	NA	D
EC123	Environment	III	16/01/2019	CC5	ST5	12	Ap, Er, Cd	NA	C
EC104	Environment	III	16/01/2019	CC5	ST5	12	Ap, Er, Cd	NA	C
HO0244.1	HCW	I	21/09/2017	CC5	ST5	13	Ap	NA	I
HO0590.1	HCW	I	21/09/2017	CC5	ST5	13	Susceptible	NA	C
EB0083	Patient environment	I	12/07/2017	CC5	ST5	14	Susceptible	NA	B

PN0083	Patient	I	12/07/2017	CC5	ST5	14	Susceptible	NA	B
HN0340.1	HCW	II	11/01/2018	CC5	ST3130	15	Ap, Er, Fd	*ccrAB4, dinG, fusC*	F
HN0348.1	HCW	II	12/01/2018	CC5	ST3130	15	Ap, Er, Fd, Cd	*ccrAB4, dinG, fusC*	H
HO0398.2e	HCW	III	19/03/2019	CC5	ST5	15	Ap, Fd	*ccrAB4, dinG, fusC*	I
CC15 (*N*=39) MSSA isolates with 12/39 isolates associated with RIGs 16-18									
HN0206.1[2]	HCW	I	09/07/2017	CC15	ST5033	16	Ap	NA	F
AHA0054.1	Air	I	10/08/2017	CC15	ST5033	16	Ap	NA	F
AHA0065.1	Air	I	10/08/2017	CC15	ST5033	16	Ap	NA	F
AHA0053.1A	Air	I	10/08/2017	CC15	ST5033	16	Ap	NA	F
HN0206.2[2]	HCW	III	01/12/2018	CC15	ST5033	16	Ap, Cd	NA	F
PconHA0001.2	Environment	II	24/01/2018	CC15	ST15	17	Ap, Te, Tb, Cd	NA	F
PN0747	Patient	III	10/04/2019	CC15	ST15	17	Ap, TMP, Cd	NA	E
PN0297	Patient	II	02/11/2017	CC15	ST15	18	Ap, Er, Cd	NA	C
A1601-05	Air	III	15/01/2019	CC15	ST15	18	Ap	NA	C
A1601-03	Air	III	16/01/2019	CC15	ST15	18	Ap, Cd	NA	C
PO0629	Patient	III	24/01/2019	CC15	ST15	18	Ap, Cd	NA	G
PO0631B.2	Patient	III	24/01/2019	CC15	ST15	18	Susceptible	NA	G
CC22 (*N*=26) MSSA isolates with 12/26 isolates associated with RIGs 19-22									
AJE0105.1A	Air	I	12/10/2017	CC22	ST22	19	Ap, Cd	Na	E
PN0461	Patient	II	17/04/2018	CC22	ST22	19	Ap, Da, Cd,	NA	G
PN0697	Patient	III	22/03/2019	CC22	ST737	20	Ap	NA	C
HO0620.1	HCW	III	04/04/2019	CC22	ST737	20	Susceptible	NA	G
HO0674.1	HCW	III	10/04/2019	CC22	ST737	20	Ap, Da, Cd,	NA	C

HO0670.1	HCW	III	16/04/2019	CC22	ST737	20	Ap	NA	C
EL0587	Patient environment	III	11/02/2018	CC22	ST22	21	Ap, Er, Fd, Cd	NA	H
HN0496.1	HCW	III	18/10/2018	CC22	ST22	21	Ap, Er, Fd, Cp, Cd	NA	F
C2221	Clinical	III	14/01/2019	CC22	ST22	21	Ap, Fd, Cp, Cd	NA	A
PN0743	Patient	III	08/04/2019	CC22	ST22	21	Ap, Er, Fd, Cp, Cd	NA	H
HN0318.1[2]	HCW	II	12/12/2017	CC22	ST22	22	Ap, Cd	NA	A
HN0318.2[2]	HCW	III	18/08/2018	CC22	ST22	22	Ap	NA	A
CC398 (*N*=29) MSSA isolates with 20/29 isolates associated with RIGs 23-28									
HO0668.1	HCW	III	10/04/2019	CC398	ST398	23	Ap, Er	NA	B
EM0715	Patient environment	III	04/08/2019	CC398	ST398	23	Ap, Er	NA	B
HN0378.1	HCW	III	08/02/2018	CC398	ST398	24	Ap, Er	NA	H
HN0384.1	HCW	III	15/02/2018	CC398	ST398	24	Ap, Er	NA	H
PN0001	Patient	I	08/05/2017	CC398	ST398	25	Ap, Er	NA	C
EL0015	Patient environment	I	16/05/2017	CC398	ST398	25	Er	NA	C
AMA0004.1A	Air	I	22/05/2017	CC398	ST398	25	Er	NA	C
HN0024.1	HCW	I	23/05/2017	CC398	ST398	25	Er	NA	C
EL0031	Patient environment	I	24/05/2017	CC398	ST398	25	Er	NA	C
C11430	Clinical	III	31/01/2018	CC398	ST398	25	Susceptible	NA	B
HO0376.1	HCW	III	26/01/2018	CC398	ST398	26	Ap, Er	NA	H
HO0598.1	HCW	III	20/02/2019	CC398	ST398	26	Ap, Er	NA	I
PO0647	Patient	III	22/02/2019	CC398	ST398	26	Ap, Er	NA	I
EL0333	Patient environment	II	30/11/2017	CC398	ST398	27	Er	NA	B

PO0345	Patient	III	05/12/2017	CC398	ST398	27	Er	NA	A
PO0347	Patient	III	05/12/2017	CC398	ST398	27	Er	NA	A
C171679	Clinical	I	05/03/2018	CC398	ST398	27	Er	NA	E
HN0188.1	HCW	I	31/08/2017	CC398	ST398	28	Ap, Er	NA	G
AJE0106.1A	Air	I	12/10/2017	CC398	ST398	28	Ap, Er	NA	E
AJE0113.1A	Air	I	12/10/2017	CC398	ST398	28	Ap, Er	NA	E
CC30 (*N*=64) MSSA isolates with 23/64 isolates associated with RIGs 29-39									
HO0312.1	HCW	III	22/02/2017	CC30	ST39	29	Ap, Er, Te, Cd	NA	A
HN0342.1	HCW	III	11/01/2018	CC30	ST39	29	Ap, Cd	NA	F
PN0023	Patient	I	24/05/2017	CC30	ST34	30	Ap, Ln	NA	A
ABA0013.1A	Air	I	31/05/2017	CC30	ST34	30	Ap, Cd	NA	A
HN0282.1[2]	HCW	I	04/10/2017	CC30	ST30	31	Ap, Cd	NA	I
HN0282.2[2]	HCW	II	15/12/2017	CC30	ST30	31	Ap, Cd	NA	A
ABA0001.2	Air	II	21/11/2017	CC30	ST30	32	Ap, Er, Cp, Cd	NA	H
AB0001.2D	Air	II	21/11/2017	CC30	ST30	32	Ap, Er, Sp, Cd	NA	H
HN0076.1[2]	HCW	I	12/07/2017	CC30	ST30	33	Ap, Cd	NA	D
HN0076.2[2]	HCW	II	15/11/2017	CC30	ST30	33	Ap, Cd	NA	B
EB0291	Patient environment	II	02/11/2017	CC30	ST30	34	Kn, Ne, Tb, Ap, Er, Fd, Cp, Sp, Cd	NA	C
HO0352.1	HCW	II	17/01/2018	CC30	ST30	34	Cd	NA	F
PN0285	Patient	II	25/10/2017	CC30	ST30	35	Ap, Cd	NA	C
PN0369	Patient	II	12/01/2018	CC30	ST30	35	Ap, Er, Cd	NA	H
HO0444.1	HCW	III	23/05/2018	CC30	ST30	36	Ap	NA	E
HO0438.1	HCW	III	23/05/2018	CC30	ST30	36	Ap	NA	E

PN0543	Patient	III	31/08/2018	CC30	ST30	37	Ap, Cd	NA	A
PN0547	Patient	III	04/09/2018	CC30	ST30	37	Ap, Er	NA	A
HO0474.1	HCW	III	04/09/2018	CC30	ST30	37	Ap, Cd	NA	B
PN0101	Patient	I	26/07/2017	CC30	ST5043	38	Ap, Cd	NA	H
EB0101	Patient environment	I	26/07/2017	CC30	ST5043	38	Ap, Cd	NA	H
HN0224.1[2]	HCW	I	13/09/2017	CC30	ST30	39	Ap, Cd	NA	I
HN0224.2[2]	HCW	II	07/02/2018	CC30	ST30	39	Ap, Cd	NA	I
CC45 (*N*=62) MSSA isolates with 27/62 isolates associated with RIGs 40-51									
HN0422.1	HCW	II	27/04/2018	CC45	ST5036	40	Ap, Cd	NA	E
HN0260.3	HCW	III	26/03/2019	CC45	ST5036	40	Ap, Cd	NA	E
PN0341	Patient	III	01/12/2017	CC45	ST45	41	Ap	NA	B
HN0354.1	HCW	III	17/01/2018	CC45	ST45	41	Susceptible	NA	H
A0801-18a	Air	III	08/01/2019	CC45	ST45	42	Ap, Cd	NA	C
EC37a	Environment	III	09/01/2019	CC45	ST45	42	Ap, Cd	NA	D
EC52	Environment	III	09/01/2019	CC45	ST45	42	Ap, Cd	NA	D
HN0220.1[2]	HCW	I	13/09/2017	CC45	ST45	43	Ap	NA	G
HN0220.2[2]	HCW	I	14/05/2018	CC45	ST45	43	Ap	NA	E
EM0551	Patient environment	III	13/09/2018	CC45	ST5036	44	Ap, Er	*ccrC1, arsR, cadR, copA*	B
PN0553	Patient	III	13/09/2018	CC45	ST5036	44	Ap, Er	*ccrC1, arsR, cadR, copA*	B
PN0227	Patient	I	27/09/2017	CC45	ST5031	45	Ap	NA	E
EB0227	Patient environment	I	27/09/2017	CC45	ST5031	45	Ap	NA	E
EM0227	Patient environment	I	27/09/2017	CC45	ST5031	45	Ap	NA	E

HO0258.1	HCW	I	03/10/2017	CC45	ST5031	45	Ap	NA	I
PO0455	Patient	II	13/04/2018	CC45	ST45	46	Susceptible	NA	G
HN0434.1	HCW	III	18/05/2018	CC45	ST45	46	Ap, Er, Sp	NA	G
HO0016.1[2]	HCW	I	24/05/2017	CC45	ST972	47	Ap	NA	A
HN0016.2[2]	HCW	2	22/11/2017	CC45	ST972	47	Ap, Cd	NA	A
HO0588.1	HCW	III	18/02/2019	CC45	ST45	48	Ap, Cd	NA	C
PO0659	Patient	III	08/03/2019	CC45	ST45	48	Ap, Su, Cd	NA	I
A0801-17	Air	III	08/01/2019	CC45	ST45	49	Ap	NA	D
A1601-18	Air	III	16/01/2019	CC45	ST45	49	Ap	NA	C
HN0094.1[2]	HCW	I	19/07/2017	CC45	ST508	50	Ap	NA	B
HN0094.2[2]	HCW	II	29/11/2017	CC45	ST508	50	Ap	NA	B
HO0234.1	HCW	I	21/09/2017	CC45	ST45	51	Ap	NA	G
HO0248.1	HCW	I	21/09/2017	CC45	ST45	51	Ap	NA	I
CC1027 (*N*=3) with 2/3 isolates associated with RIG-52									
C112296	Clinical	I	22/08/2017	CC1027	ST1027	52	Ap	NA	C
C111576	Clinical	I	29/08/2017	CC1027	ST1027	52	Ap	NA	H
CC59 (*N*=3) with 2/3 isolates associated with RIG-53									
HO0416.1	HCW	III	27/04/2018	CC59	ST59	53	Ap, Er, Sp	NA	E
HO0418.1	HCW	III	27/04/2018	CC59	ST59	53	Ap	NA	E
CC7 (*N*=6) with 2/7 isolates associated with RIG-54									
EAB0006.3	Environment	III	14/11/2018	CC7	ST7	54	Ap, Cd	NA	H
EAB0001.3	Environment	III	14/11/2018	CC7	ST7	54	Ap, Er	NA	H
CC8 (*N*=15) with 2/15 isolates associated with RIG-55									

PN0651	Patient	III	12/03/2019	CC8	ST8	55	Ap, Er, Fd, Cd	NA	I
HN0600.1	HCW	III	01/03/2019	CC8	ST8	55	Susceptible	NA	I
CC72 (*N*=4) with 3/4 isolates associated with RIG-56									
HN0088.2	HCW	II	07/12/2017	CC72	ST72	56	Ap	NA	B
HO0320.1	HCW	III	12/12/2017	CC72	ST72	56	Ap	NA	A
HO0316.1	HCW	III	12/12/2017	CC72	ST72	56	Ap	NA	A
CC109 (*N*=5) with 3/5 isolates associated with RIG-57									
A1501-8A	Air	III	15/01/2019	CC109	ST109	57	Ap, Er	NA	D
A1601-16	Air	III	16/01/2019	CC109	ST109	57	Ap, Er, Cd	NA	C
A1601-13	Air	III	16/01/2019	CC109	ST109	57	Ap, Er, Cd, Sp	NA	C
CC97 (*N*=4) with 4/9 isolates associated with RIG-58									
EC122	Environment	III	16/01/2019	CC97	ST97	58	Ap, Er, Su, Cd	NA	C
A1501-08b	Air	III	15/01/2019	CC97	ST97	58	Ap, Er, Cd	NA	C
A1601-10b	Air	III	16/02/2019	CC97	ST97	58	Ap, Er, Cd	NA	C
A1501-09	Air	III	15/01/2019	CC97	ST97	58	Ap, Er, Cd	NA	C
CC188 (*N*=2) with 2/8 isolates associated with RIG-59									
C3966759	Clinical	III	08/04/2019	CC188	ST188	0	Kn, Nm, Ap, Te, Cd	NA	C
PN0731	Patient	III	08/04/2019	CC188	ST188	0	Kn, Nm, Ap, Te, Cd	NA	C
Isolates (*N*=223) not included in any of the above RIGs (unrelated to any other isolate recovered in the study are listed in RIG-0									
ALA0084.1	Air	I	07/09/2017	CC1	ST2383	0	Er, Sp	NA	G
AJE0109.1	Air	I	12/10/2017	CC1	ST1	0	Ap, Te	NA	E
PO0033	Patient	I	30/05/2017	CC1	ST1	0	Ap, Fd	NA	A
C76440	Clinical	III	05/06/2018	CC1	ST1	0	Ap, Fd, Mp, Eb	NA	H

PN0359	Patient	II	08/12/2017	CC1	ST1	0	AP	NA	B
C110604	Clinical	III	23/08/2018	CC1	ST1	0	Ap, Er, Fd, Cd, Eb	NA	I
C80618	Clinical	III	20/06/2018	CC1	ST1	0	Ap, fd	NA	H
EB0397	Patient environment	II	15/02/2018	CC1	ST1	0	Ap, Fd,	NA	H
C12568	Clinical	III	21/02/2018	CC1	ST1	0	Ap, Fd,	NA	E
HO0470.1	HCW	III	30/08/2018	CC1	ST1	0	Ap, Cd	NA	A
EAB0004.3	Environment	III	13/11/2018	CC1	ST1	0	Ap, Er, Cd	NA	H
PN0457	Patient	II	13/04/2018	CC1	ST1	0	Fd	NA	G
HO0030.2	HCW	III	18/12/2018	CC1	ST1	0	Fd	NA	D
C8996	Clinical	II	28/01/2019	CC1	ST1	0	Fd	NA	B
HN0574.1	HCW	III	15/01/2019	CC1	ST1	0	Susceptible	NA	C
AJE0103.1	Air	I	12/10/2017	CC1027	ST1027	0	AP	NA	E
C166108	Clinical	I	29/11/2017	CC109	ST109	0	Ap, Er	NA	G
C160277	Clinical	I	19/11/2017	CC109	ST109	0	Ap, Er	NA	H
HO0012.2	HCW	II	01/11/2017	CC12	ST12	0	Ap, Cd	NA	C
HN0570.1	HCW	III	15/01/2019	CC12	ST12	0	Susceptible	NA	C
PO0063	Patient	I	06/07/2017	CC15	ST15	0	Ap	NA	B
HO0252.1	HCW	I	01/10/2017	CC15	ST1160	0	Ap	NA	E
PN0063	Patient	I	06/07/2017	CC15	ST15	0	Ap	NA	B
PN0041	Patient	I	07/06/2017	CC15	ST5041	0	Susceptible	NA	A
HO0030.1	HCW	I	31/05/2017	CC15	ST582	0	Ap	NA	D
PO0107	Patient	I	10/05/2017	CC15	ST5034	0	Ap	NA	B
HN0138.1	HCW	I	10/08/2017	CC15	ST582	0	Susceptible	NA	F
HN0600.1a	HCW	III	26/02/2019	CC15	ST582	0	Susceptible	NA	I

HN0330.1	HCW	II	05/12/2017	CC15	ST15	0	Ap, Cd	NA	A
HN0586.1	HCW	III	31/01/2019	CC15	ST582	0	Susceptible	NA	C
HN0534.1	HCW	III	01/08/2018	CC15	ST15	0	Te	NA	D
PO0409	Patient	II	23/02/2018	CC15	ST15	0	Ap	NA	H
HN0518.1	HCW	III	12/05/2018	CC15	ST582	0	Susceptible	NA	H
HN0138.2	HCW	II	18/10/2017	CC15	ST582	0	Susceptible	NA	C
PN0621	Patient	III	16/01/2019	CC15	ST15	0	Susceptible	NA	C
HO0110.3	HCW	III	12/09/2018	CC15	ST15	0	Ap, Cd	NA	B
A0901-0850	Air	III	09/01/2019	CC15	ST15	0	Susceptible	NA	D
HO0110.2	HCW	II	12/12/2017	CC15	ST15	0	Ap, Er	NA	B
PN0449	Patient	II	13/04/2018	CC15	ST582	0	Susceptible	NA	G
HN0202.2	HCW	II	01/11/2017	CC15	ST582	0	Ap	NA	D
A0901-1151	Air	III	09/01/2019	CC15	ST15	0	Ap, Cd	NA	D
PN0499	Patient	II	24/05/2018	CC15	ST15	0	Susceptible	NA	G
C32837	Clinical	I	07/02/2018	CC15	ST582	0	Ap	NA	A
HN0418.1	HCW	III	27/04/2018	CC15	ST15	0	Ap	NA	E
EC75	Environment	III	15/01/2019	CC15	ST582	0	Susceptible	NA	D
PO0329	Patient	II	22/11/2017	CC15	ST15	0	Ap, Mp, Tb, Cd	NA	B
PN0475	Patient	II	27/04/2018	CC15	ST15	0	Ap	NA	E
EM0669	Patient environment	III	14/03/2019	CC188	ST188	0	Ap, Cd	NA	C
PN0343.2	Patient	II	05/12/2017	CC188	ST188	0	Ap, Cd	NA	A
PN0471	Patient	II	23/04/2018	CC188	ST188	0	Ap	NA	G
EB0117	Patient environment	I	02/08/2017	CC188	ST188	0	Ap	NA	H
HO0430.1	HCW	II	18/05/2018	CC188	ST188	0	Ap	NA	G

HN0048.2	HCW	III	09/11/2017	CC188	ST188	0	Susceptible	NA	A
PN0119	Patient	I	02/08/2017	CC20	ST20	0	Te	NA	H
EL0059	Patient environment	I	05/07/2017	CC20	ST20	0	Susceptible	NA	B
HO0452.1	HCW	III	24/05/2018	CC20	ST20	0	Ap	NA	E
AMA0002.1B	Air	I	22/05/2017	CC22	ST22	0	Er, Ln, Cp	NA	C
PN0033	Patient	I	30/05/2017	CC22	ST22	0	Er, Fd	NA	A
HN0144.1	HCW	I	15/08/2017	CC22	ST22	0	Ap, Cd	NA	F
C24146	Clinical	III	05/03/2019	CC22	ST22	0	Gn, Kn, Tb, Ap, Su, TMP	NA	A
HN0338.2	HCW	II	18/10/2018	CC22	ST22	0	Ap, Er, Fd, Cp, Cd	NA	F
C131087	Clinical	III	17/10/2018	CC22	ST22	0	Ap, Er, Fd, Cp	NA	I
HN0410.1	HCW	II	27/03/2018	CC22	ST22	0	Ap, Cd	NA	G
EC89	Environment	III	09/01/2019	CC22	ST22	0	Ap, Fd, Cd	NA	D
HO0368.1	HCW	II	06/02/2018	CC22	ST22	0	Gn, Kn, Ap, Cp, Tb, Cd,	NA	H
PO0157	Patient	I	18/08/2017	CC22	ST22	0	Ap, Er, Sp	NA	H
HN0278.1	HCW	I	04/10/2017	CC22	ST22	0	Ap, Cd	NA	I
C434873	Clinical	III	08/04/2019	CC22	ST22	0	Ap, Er, Da	NA	H
PN0707	Patient	III	09/04/2019	CC22	ST22	0	Ap	NA	H
A1501.13b	Air	III	15/01/2019	CC22	ST22	0	Ap, Er, Fd, Cp, Sp, Cd	NA	C
HN0132.1	HCW	I	10/08/2017	CC2233	ST2233	0	Ap, Cp	NA	H
HO0088.1	HCW	I	18/07/2017	CC2250	ST2250	0	Fd	NA	B
HO0468.1	HCW	III	30/08/2018	CC2250	ST2250	0	Ap, Cd	NA	A
HO0100.1	HCW	I	26/07/2017	CC2250	ST2250	0	Kn, Nm, Ap, Te, Cd	NA	H
HN0020.1	HCW	I	25/05/2017	CC25	ST25	0	Ap, Er	NA	A

PN0035	Patient	I	30/05/2017	CC30	ST30	0	Ap, Cd	NA	A
HO0168.1	HCW	I	23/08/2017	CC30	ST30	0	Ap, Cd	NA	G
PN0129	Patient	I	03/08/2017	CC30	ST30	0	Ap, Cd, Eb	NA	H
AJE0108.1	Air	I	12/10/2017	CC30	ST34	0	Ap, Cd	NA	E
PN0057	Patient	I	04/07/2017	CC30	ST30	0	Ap, Cd	NA	D
PN0223	Patient	I	27/09/2017	CC30	ST30	0	Ap, Cd	NA	E
HN0142.1	HCW	I	10/08/2017	CC30	ST30	0	Ap, Cd	NA	H
PO0023	Patient	I	24/05/2017	CC30	ST34	0	Ap, Cd	NA	A
HN0072.1	HCW	I	12/07/2017	CC30	ST34	0	Ap	NA	D
HN0034.1	HCW	I	31/05/2017	CC30	ST30	0	Ap	NA	A
HN0128.1	HCW	I	09/08/2017	CC30	ST34	0	Ap, Cd	NA	F
HN0284.1	HCW	I	04/10/2017	CC30	ST30	0	Ap, Cd	NA	I
HO0084.1	HCW	I	18/07/2017	CC30	ST30	0	Ap, Cd	NA	B
PN0131	Patient	I	03/08/2017	CC30	ST34	0	Ap, Cd	NA	H
HO0284.1	HCW	I	04/10/2017	CC30	ST30	0	Ap, Cd	NA	I
HN0118.1	HCW	I	09/08/2017	CC30	ST30	0	Ap, Cd	NA	F
C104218	Clinical	I	29/08/2017	CC30	ST30	0	Ap, Er, Da, Sp, Cd	NA	B
HN0542.1	HCW	III	10/01/2019	CC30	ST30	0	Susceptible	NA	D
HN0110.3	HCW	III	12/12/2017	CC30	ST39	0	Ap, Cd	NA	B
HO0134.2	HCW	II	12/12/2017	CC30	ST30	0	Ap, Cd	NA	B
HN0412.1	HCW	III	29/03/2018	CC30	ST30	0	Ap, Cd	NA	I
HN0274.2	HCW	II	04/10/2017	CC30	ST30	0	Ap, Cd	NA	I
HO0490.1	HCW	III	21/09/2018	CC30	ST30	0	Susceptible	NA	B

PN0487	Patient	II	16/05/2018	CC30	ST30	0	Ap	NA	E
HO0462.1	HCW	III	18/08/2018	CC30	ST30	0	Ap, Cd	NA	A
AAB0049.1	Air	I	10/08/2017	CC30	ST30	0	Ap, Er, Sp, Cd	NA	H
C171546	Clinical	I	11/12/2017	CC30	ST2889	0	Ap, Cd	NA	B
HO0464.1	HCW	III	27/08/2018	CC30	ST30	0	Ap, Cd	NA	A
C19346	Clinical	III	12/02/2019	CC30	ST2896	0	Ap, Cd	NA	C
A1501-13a	Air	III	15/01/2019	CC30	ST30	0	Ap, Er, Sp, Cd	NA	C
A0801-05	Air	III	08/01/2019	CC30	ST30	0	Ap, Cd	NA	D
C19650	Clinical	III	12/02/2019	CC30	ST30	0	Ap, Er	NA	B
HN0660.1	HCW	III	16/04/2019	CC30	ST30	0	Ap, Cd	NA	H
PO0269	Patient	III	19/10/2017	CC30	ST30	0	Ap, Cd	NA	C
PO0375	Patient	III	17/01/2018	CC30	ST30	0	Cd	NA	F
PN0419	Patient	II	16/03/2018	CC30	ST34	0	Ap, Cd	NA	G
HO0440.1	HCW	III	23/05/2018	CC30	ST39	0	Ap	NA	E
HO0072.1	HCW	I	12/07/2017	CC30	ST34	0	Ap	NA	D
PN0423	Patient	II	27/03/2018	CC30	ST30	0	Ap, Er, Sp, Cd	NA	I
HN0478.1	HCW	III	20/09/2018	CC30	ST30	0	Ap, Cd	NA	B
HN0048.3	HCW	III	18/08/2018	CC30	ST39	0	Ap, Rif, Mp, Cd	NA	A
HN0202.1	HCW	I	07/09/2017	CC320	ST320	0	Susceptible	NA	F
EL0027	Patient environment	I	24/05/2017	CC398	ST398	0	Susceptible	NA	A
PN0417	Patient	II	16/03/2018	CC398	ST398	0	Ap, Er	NA	G
PN0523	Patient	III	18/08/2018	CC398	ST398	0	Ap, Er, Cd	NA	A
PN0519	Patient	III	18/08/2018	CC398	ST398	0	Susceptible	NA	A

PN0623	Patient	III	22/01/2019	CC398	ST398	0	Susceptible	NA	C
HN0386.1	HCW	II	15/02/2018	CC398	ST398	0	Ap	NA	H
A0801-10	Air	III	08/01/2019	CC398	ST398	0	Ap, Er, Cd	NA	D
HO0392.1	HCW	III	28/02/2018	CC398	ST398	0	Ap	NA	I
PN0483	Patient	II	02/05/2018	CC398	ST398	0	Er	NA	E
PN0085	Patient	I	12/07/2017	CC45	ST45	0	Ap	NA	B
HO0150.1	HCW	I	17/08/2017	CC45	ST3634	0	Er, Sp	NA	H
HN0186.1	HCW	I	31/08/2017	CC45	ST508	0	Ap	NA	G
PN0089	Patient	I	19/07/2017	CC45	ST45	0	Ap	NA	B
PN0173	Patient	I	30/08/2017	CC45	ST54	0	Ap	NA	G
PN0065	Patient	I	06/07/2017	CC45	ST45	0	Er, Fd, Sp	NA	B
HN0232.1	HCW	I	21/09/2017	CC45	ST45	0	Ap	NA	G
PO0161	Patient	I	23/08/2017	CC45	ST45	0	Susceptible	NA	H
ABA0016.1B	Air	I	31/05/2017	CC45	ST45	0	Ap	NA	A
HN0280.1	HCW	I	04/10/2017	CC45	ST45	0	Ap	NA	I
HN0198.1	HCW	I	07/09/2017	CC45	ST45	0	Ap	NA	G
PN0429	Patient	II	28/03/2018	CC45	ST47	0	Ap	NA	G
HN0300.1	HCW	II	18/10/2017	CC45	ST45	0	Susceptible	NA	C
C11335	Clinical	III	13/08/2018	CC45	ST45	0	Susceptible	NA	I
HO0472.1	HCW	III	03/09/2018	CC45	STNA5	0	Ap, Cd	NA	A
C166368	Clinical	II	07/12/2017	CC45	ST45	0	Susceptible	NA	E
C12266	Clinical	III	01/02/2018	CC45	ST972	0	Ap	NA	A
PN0465	Patient	II	23/04/2018	CC45	ST45	0	Ap	NA	H
PN0413	Patient	II	14/03/2018	CC45	ST3182	0	Ap	NA	I

HN0260.1	HCW	II	03/10/2017	CC45	ST5036	0	Ap	NA	E
C75806	Clinical	I	06/06/2017	CC45	ST45	0	Ap	NA	H
C23693	Clinical	III	05/03/2019	CC45	ST45	0	Ap, Sp, Cd	NA	F
PN0507	Patient	II	25/05/2018	CC45	ST45	0	Susceptible	NA	G
A1601-10c	Air	III	16/01/2019	CC45	ST45	0	Ap, Cd	NA	C
HN0218.1	HCW	I	13/09/2017	CC45	ST45	0	Ap	NA	I
PN0245	Patient	I	04/10/2017	CC45	ST45	0	Susceptible	NA	E
HO0278.1	HCW	I	04/10/2017	CC45	ST5036	0	Ap, Cd	NA	I
PO0309	Patient	III	09/11/2017	CC45	ST45	0	Ap, Fd, Cd	NA	A
HO0286.1	HCW	I	04/10/2017	CC45	ST45	0	Ap	NA	I
C384610	Clinical	III	07/06/2018	CC45	ST45	0	Susceptible	NA	A
HO0366.1	HCW	III	06/02/2018	CC45	ST45	0	Ap	NA	F
HN0264.1	HCW	I	03/10/2017	CC45	ST45	0	Ap	NA	E
HN0380.1	HCW	III	08/02/2018	CC45	ST45	0	Ap, Er, Fd, Sp,	NA	H
AJE0094.1	Air	I	12/10/2017	CC45	ST45	0	Ap, Er	NA	E
HN0008.2	HCW	III	01/12/2017	CC45	ST45	0	Ap, Cd	NA	C
HO0024.1	HCW	I	23/05/2017	CC5	ST5	0	Er	NA	C
HN0200.1	HCW	I	07/09/2017	CC5	ST5	0	Ap	NA	F
HO0236.1	HCW	I	21/09/2017	CC5	ST5	0	Susceptible	NA	G
EL0063	Patient environment	I	06/07/2017	CC5	ST5029	0	Ap, Er, Cp, Tb	NA	B
HO0256.1	HCW	I	03/10/2017	CC5	ST1637	0	Ap, Cp	NA	E
PN0127	Patient	I	03/08/2017	CC5	ST5	0	Susceptible	NA	H
AMA0002.1A	Air	I	22/05/2017	CC5	ST5	0	Susceptible	NA	C
C106663	Clinical	I	29/08/2017	CC5	ST5	0	Ap, Cp, Tb, Cd	NA	C

PN0349	Patient	II	05/12/2017	CC5	ST5	0	Ap	NA	A
PN0431	Patient	II	28/03/2018	CC5	ST5	0	Te, Pma	NA	G
EM0705	Patient environment	III	09/04/2019	CC5	ST5	0	Ap, Er, Te, Cd	NA	G
EL0317	Patient environment	II	16/11/2017	CC5	ST5	0	Susceptible	NA	B
PN0685	Patient	III	04/04/2019	CC5	ST5	0	Ap, Cd	NA	G
C28660	Clinical	III	05/03/2019	CC5	ST5	0	Su	NA	C
C180327	Clinical	III	08/01/2019	CC5	ST5	0	Tb, Ap, Fd, Cd	NA	I
C9142	Clinical	III	01/02/2018	CC5	ST5	0	Ap, Er, Fd, Eb,	NA	E
PN0481	Patient	II	03/05/2018	CC5	ST5	0	Ap	NA	E
PN0567	Patient	III	27/09/2018	CC5	ST5	0	Cd	NA	B
C136448	Clinical	III	28/09/2018	CC5	ST5	0	Ap, Er, Fd, Cd	NA	B
C43913	Clinical	III	26/03/2018	CC5	ST5	0	Ap, Er, Fd	NA	E
HN0436.1	HCW	II	18/05/2018	CC5	ST5	0	Ap, Er, Sp, Eb	NA	E
HN0108.2	HCW	II	09/11/2017	CC5	ST5	0	Ap	NA	B
PN0645	Patient	III	01/02/2019	CC5	ST5	0	Ap, Cd	NA	I
HO0148.2	HCW	II	06/02/2018	CC5	ST5	0	Ap	NA	F
PN0459	Patient	II	17/04/2018	CC5	ST5	0	Nm, Tb, Ap, Er, Fd, Cp	NA	G
PO0451	Patient	II	13/04/2018	CC5	ST5	0	Ap	NA	G
EC79	Clinical	I	15/01/2019	CC5	ST5	0	Er, Sp	NA	D
HO0020.2	HCW	III	18/08/2018	CC5	ST5	0	Ap, Cd	NA	A
EL0113	Patient environment	I	02/08/2017	CC5	ST5	0	Susceptible	NA	H
ALA0094.1	Air	I	07/09/2017	CC5	ST5	0	Susceptible	NA	G
PN0733	Patient	III	08/04/2019	CC5	ST2304	0	Ap, Cd	NA	H

HO0520.1	HCW	III	12/05/2018	CC5	ST5	0	Ap, Fd	NA	H
HO0332.1	HCW	III	08/12/2017	CC5	ST5	0	Susceptible	NA	A
HN0166.1	HCW	I	23/08/2017	CC5	ST5	0	Ap	NA	F
AJE0102.1	Air	I	12/10/2017	CC5	ST5	0	Susceptible	NA	E
C117117	Clinical	I	09/01/2017	CC5	ST5	0	Ap, Cd, Fd	NA	G
AMA0005.1A	Air	I	22/05/2017	CC5030	ST5030	0	Susceptible	NA	C
C101093	Clinical	I	31/07/2017	CC59	ST59	0	Tb, Cp	NA	B
HN0164.1	HCW	I	23/08/2017	CC672	ST672	0	Kn, Nm, Ap, Er, Cp, Tmp	NA	F
HN0572.1	HCW	III	15/01/2019	CC672	ST672	0	Te	NA	C
HN0172.1	HCW	I	23/08/2017	CC7	ST789	0	Cp, Tmp	NA	G
C72785	Clinical	I	31/05/2017	CC7	ST7	0	Ap	NA	A
PN0433	Patient	III	29/03/2018	CC7	ST7	0	Susceptible	NA	G
HN0002.2	HCW	III	24/10/2017	CC7	ST7	0	Ap, Er	NA	C
HO0344.2	HCW	III	07/11/2018	CC72	ST72	0	Ap, Cd	NA	F
HO0034.1	HCW	I	31/05/2017	CC8	ST8	0	Ap, Cd	NA	A
PN0079	Patient	I	11/07/2017	CC8	ST8	0	Ap	NA	D
HN0104.1	HCW	I	26/07/2017	CC8	ST5042	0	Ap	NA	B
EB0649	Patient environment	III	01/02/2019	CC8	ST8	0	Su, Cd	NA	I
PN0317	Patient	II	16/11/2017	CC8	ST630	0	Ap, Fd, Cd	NA	B
HN0538.1	HCW	III	01/10/2018	CC8	ST8	0	Susceptible	NA	D
PN0395	Patient	III	15/02/2018	CC8	ST8	0	Ap	NA	H
PN0727	Patient	III	09/04/2019	CC8	ST8	0	Ap, Su, Cd	NA	H
PN0399	Patient	III	15/02/0218	CC8	ST8	0	Ap, Fd	NA	H

HO0398.1	HCW	III	28/02/2018	CC8	ST8	0	Susceptible	NA	I
HN0216.1	HCW	I	13/09/2017	CC8	ST8	0	Ap, Er	NA	I
HN0142.2	HCW	II	02/11/2017	CC96	ST96	0	Ap, Cd	NA	H
S1601-1010	Environment	III	16/01/2019	CC97	ST97	0	Ap, Er, Su, Cd	NA	C
C140338	Clinical	III	18/10/2018	CC97	ST97	0	Ap, Er, Sp, Cd	NA	C
HO0158.3	HCW	III	18/10/2018	CC97	ST97	0	Susceptible	NA	F
PO0313	Patient	II	16/11/2017	CC97	ST464	0	Ap, Cd	NA	A
HN0072.2	HCW	III	20/09/2018	CC97	ST97	0	Susceptible	NA	D

Table SI. Genotypic and phenotypic details for 406 meticillin-susceptible *Staphylococcus aureus* (MSSA) categorised into 59 related isolate groups (RIGs)[1] (*N*=183 isolates) (RIGs 1-59) and unrelated MSSA isolates listed in RIG-0 (*N*=223 isolates).

A total of 635 MSSA isolates were recovered during this study, of which 406 were selected for whole-genome sequencing (WGS). One isolate per HCW nasal or oral carriage, patient nasal or oral carriage and sampled environmental site per sampling phase was selected for WGS unless antimicrobial-susceptibility profiles from multiple isolates from the same participant/site were different. In total 183/406 MSSA isolates were associated with related isolate groups (RIGs).

[1]Isolates were categorised into RIGs if they exhibited ≤24 cgMLST allelic differences to all other isolates within a RIG. The remaining 223 MSSA isolates exhibited ≥24 cgMLST allelic differences and were therefore deemed unrelated and for convenience were listed in RIG-0. Genotypic information including multilocus-sequence typing clonal complexes (CCs) and sequence types (STs) as well as presence of staphylococcal chromosome cassette elements (SCCs) were extracted from WGS data using BioNumerics version 8 (Applied Maths, Sint-Martens-Latem, Belgium) and SCC*mec* finder (Kaya *et al*., 2017). RIGs 1-59 were identified following core genome (cg) MLST analysis using BioNumerics (see Figure 1). Briefly, isolates of the same CC group were selected for comparison by cgMLST. The similarity between cgMLST profiles was investigated using the categorical differences algorithm and the UPGMA method in BioNumerics to generate a UPGMA tree which was circularised, and a best fit figure was generated. All isolates that exhibited ≤ 24 allelic variations between them were shaded in grey in Figure 1 and the nodes are differentiated by colours representing each source type.

[2]Related isolates within RIGs recovered from the same HCW over multiple phases are indicated. Antimicrobial resistance phenotypes were determined by testing the susceptibility of isolates to a panel of 25 antimicrobial agents including amikacin, ampicillin (Ap), cadimium acetate (Cd), chloramphenicol (Chl), ciprofloxacin (Cp), clindamycin, Daptomycin (Da),

erythromycin (Er), Ethidium bromide (Eb), fusidic acid (Fd), gentamicin (Gn), kanamycin (kn), linezolid, mupirocin (Mp), neomycin (Nm), phenyl mercuric acetate (PMA), rifampicin (Rf), spectinomycin (Sp), streptomycin (St), sulphonamide (Su), tetracycline (Te), tobramycin (Tb), trimethoprim (Tmp) and vancomycin.

Table SII. Antimicrobial-resistance profiles exhibited by 635 MSSA study isolates

Antimicrobial-resistance profile	MDR MSSA (No. isolates)	Antimicrobial-resistance profile	Non-MDR MSSA (No. isolates)
Ap, Er, Sp, Cd	9	Ap	137
Ap, Te, Su, TMP, Cd	8	Ap, Cd	121
Ap, Er, Fd	7	Susceptible	87
Ap, Er, Fd, Cp, Cd	5	Ap, Er	48
Ap, Er, Fd, Cd	4	Ap, Er, Cd	27
Ap, Er, Fd, Cp	3	Ap, Fd, Cd	22
Ap, Er, Sp	3	Er	21
Ap, Er, Su, Cd	3	Fd	16
Ap, Er, Su	2	Ap, Fd	15
Ap, Er, Te, Cd	2	Ap, Sp, Cd	8
Ap, Fd, Mp, Su, Cd	2	Cd	5
Er, Fd, Sp	2	Ap, Cp	3
Kn, Nm, Ap, Er, Fd, Cp, Tmp, Cd	2	Cp, Tb	3
Kn, Nm, Ap, Te, Cd	2	Er, Sp	3
Ap, Da, Fd, Chl, Mp, TMP, Cd	1	Fd, Mp	3
Ap, Er, Cp, Tb	1	Ap, TMP, Cd	2
Ap, Er, Da	1	Ap, Tb, Cd	2
Ap, Er, Da, Sp, Cd	1	Er, Fd	2
Ap, Er, Fd, Cd, Eb	1	Fd, Te	2
Ap, Er, Fd, Cp, Sp, Cd	1	Su	2
Ap, Er, Fd, Eb	1	Su, Cd	2
Ap, Er, Fd, Sp	1	Ap, Cd, Eb	1
Ap, Er, Fd, Sp, Cd	1	Ap, Cd, Fd	1
Ap, Er, Mp	1	Ap, Da, Cd,	1
Ap, Er, Sp, Eb	1	Ap, Er, Cd, Eb	1
Ap, Er, Te, Cp	1	Ap, Ln	1
Ap, Fd, Cp, Cd	1	Ap, Te	1
Ap, Fd, Mp, Eb	1	Cp	1
Ap, Fd, Su, Cd	1	Cp, Tmp	1
Ap, Mp, Tb, Cd	1	Er, Cd	1
Ap, Rif, Mp, Cd	1	Kn	1
Ap, Te, Sp	1	Ln	1
Ap, Te, Tb, Cd	1	Tb, Cp	1
Da, Fd, Te, Cd	1	Te	1
Da, Fd, Tmp, Cd	1	Te, Pma	1
Er, Fd, Te	1	Ap, Cp, Tb, Cd	3
Er, Ln, Cp	1		
Fd, Cp, Su, Tmp	1		
Gn, Kn, Ap, Cp, Tb, Cd	1		

Gn, Kn, Tb, Ap, Su, TMP	1		
Kn, Ne, Tb, Ap, Er, Fd, Cp, Sp, cd	1		
Kn, Nm, Ap, Er, Cp, Tmp	1		
Kn, Nm, Tb, Ap, Er, Da, Te, Cp	1		
Nm, Tb, Ap, Er, Da, Fd	1		
Nm, Tb, Ap, Er, Fd, Cp	1		
Sp, Tb, Er, Mp, Eb	1		
Tb, Ap, Fd, Cd	1		
TOTAL	87	**TOTAL**	548

Antimicrobial-susceptibility profiling including meticillin-susceptibility confirmation using 30-μg cefoxitin disks (Oxoid, Basingstoke, UK) was undertaken as previously described using a panel of 23 antimicrobial agents and heavy metals by disk diffusion using the European Committee on Antimicrobial Susceptibility testing (EUCAST) methodology and interpretive criteria (Kaya *et al*., 2017; European centre for disease prevention and control (EARS-Net, 2019). Isolates were deemed multidrug resistant (MDR) if they exhibited resistance to three or more clinically used antibiotic classes (Rossney *et al*., 2007). Fusidic acid resistance was exhibited by 106 MSSA (16.7%) in 32/86 antimicrobial resistance profiles and mupirocin resistance was exhibited by 11 MSSA isolates (1.7%) in 8/86 antimicrobial resistance profiles. Abbreviations: ampicillin (Ap), cadimium acetate (Cd), chloramphenicol (Chl), ciprofloxacin (Cp), Daptomycin (Da), erythromycin (Er), Ethidium bromide (Eb), fusidic acid (Fd), gentamicin (Gn), kanamycin (Kn), mupirocin (Mp), neomycin (Nm), phenyl mercuric acetate (PMA), rifampicin (Rf), spectinomycin (Sp), streptomycin (St), sulphonamide (Su), tetracycline (Te), tobramycin (Tb) and trimethoprim (Tmp).

Table SIV. Available epidemiological information relating to 183 whole-genome sequenced meticillin-susceptible *Staphylococcus aureus* (MSSA) grouped into 59 related isolate groups (RIGs)[1] by core-genome multilocus sequence typing.

Isolate	Source	Sample date	RIG[1]	Ward	Epidemiological links/ associations
A0801-19	Air	08/01/2019	1	D	Four closely-related CC1/ST1-MSSA environmental isolates were recovered over a week in a surgical ward (Ward D). Approximately three months later a closely related patient isolate (PN0445) was recovered in a medical ward (Ward I) on a different floor. Shedding of CC1/ST1-MSSA by an unidentified colonized patient or HCW in ward D is probable.
EC93	Environment	15/01/2019	1	D	
EC94	Environment	15/01/2019	1	D	
EC78	Environment	15/01/2019	1	D	
PN0445	Patient	13/04/2018	1	I	
AAB0004.3	Air	14/11/2019	2	H	Detection of two closely related CC1/ST1 environmental isolates on the same day in a surgical ward (Ward H). Source likely to be a patient or HCW not included in the study.
AAB0007.3	Air	14/11/2019	2	H	
A0801-01	Air	08/01/2019	3	D	Detection of two closely related CC1/ST1 environmental isolates on the same day in a surgical ward (Ward D). Source likely to be a patient or HCW not included in the study.
A0801-18b	Air	08/01/2019	3	D	
EL0033	Patient environment	30/05/2017	4	A	Detection of two closely related CC1/ST1 environmental isolates on the same day from a patient NPE in a surgical ward (Ward A). The associated patient harbored two different MSSA strains including the CC22/ST22-MSSA isolate (PN0033) recovered from a nasal swab and a CC1/ST1-MSSA that exhibited a distant-relatedness (≥1200 allelic differences) to the two isolates recovered from the patients NPE. Source likely to be an unidentified patient or HCW.
EB0033	Patient environment	30/05/2017	4	A	
EL0205	Patient environment	14/09/2017	5	G	Detection of two closely related CC1/ST1 isolates on the same day from a patient and the patient's NPE in a medical ward (Ward G). Shedding of CC1/ST1 by colonized patient evident.
PN0205	Patient	14/09/2017	5	G	
EM0205	Patient environment	14/09/2017	6	G	Detection of two closely related CC1/ST1 environmental isolates from a patient's NPE on the same day in a medical ward (Ward G). The associated patient did yield a CC/ST1-MSSA isolate, however, it exhibited ≥ 24 cgMLST allelic differences to the two environmental isolates (i.e. 200 allelic differences) and was deemed unrelated. Shedding of CC1/ST1 by a colonized patient or HCW not included in the study is a likely source of the isolates.
EB0205	Patient environment	14/09/2017	6	G	
A0801-06	Air	08/01/2019	7	D	Recovery of 12 CC1-MSSA environmental isolates over two days in a surgical ward (Ward D) indicates probable shedding by a patient(s) or HCW(s) not included in the study.
S0801-0821	Environment	08/01/2019	7	D	

A0801-09	Air	08/01/2019	7	D	
S0801-1018	Environment	08/01/2019	7	D	
S0801-0718	Environment	08/01/2019	7	D	
A0801-04	Air	08/01/2019	7	D	
A0801-8C	Air	08/01/2019	7	D	
A0801-13	Air	08/01/2019	7	D	
S0901-0918	Environment	09/01/2019	7	D	
A0801-14	Air	08/01/2019	7	D	
A0801-22	Air	08/01/2019	7	D	
A0901-0836	Air	09/01/2019	7	D	
PO0717	Patient	03/04/2019	8	H	Closely related CC1-MSSA recovered from two patients five days apart in a surgical ward (Ward H) followed by a third isolate from another patient, five days after the first isolate in a surgical ward (Ward C). Transmission possibly by a patient or HCW not included in the study, or from the environment not sampled.
PO0729	Patient	08/04/2019	8	H	
PO0737	Patient	08/04/2019	8	C	
HN0184.1[2]	HCW	31/08/2017	9	G	Two closely related CC5/ST6 MSSA recovered from persistent HCW carrier during two separate sampling phases eight months apart on a medical ward (Ward G). No other MSSA isolates related to isolates recovered from this HCW were detected in the study.
HN0184.2[2]	HCW	11/04/2018	9	G	
HN0044.1[2]	HCW	12/06/2017	10	A	Two closely related CC5/ST6 MSSA recovered from persistent HCW carrier during two separate sampling phases 14 months apart on a surgical ward (Ward A). No other MSSA isolates related to isolates recovered from this HCW were detected in the study.
HN0044.2[2]	HCW	18/08/2018	10	A	
EB0113	Patient environment	02/08/2017	11	H	Evidence for a significant shedding of CC5-MSSA into the environment was detected in a surgical ward (Ward H) over a three week period with one patient isolate (PN0143), and a NPE isolate (EB0143) recovered from the same patient's bedframe on the same day. An additional 13 isolates were recovered from the NPEs of 13 other patients in the same ward. Unrelated MSSA exhibiting different CCs were recovered from 2/13 of these patients including a CC30/ST34-MSSA isolate (PN0131) and a CC45/ST45-MSSA isolate (PO0161). There were also five isolates recovered from air sampling in Ward H. A related patient infection isolate (C119224) was recovered from a medical ward (Ward F) located on a separate hospital floor four months later. This suggests a HCW(s) not included in the study was possibly responsible for spread of the CC5-MSSA, or an unidentified environmental source.
EB0131	Patient environment	03/08/2017	11	H	
AAB0043.1	Air	10/08/2017	11	H	
AAB0036.1B	Air	10/08/2017	11	H	
AAB0045.1	Air	10/08/2017	11	H	
AAB0047.1A	Air	10/08/2017	11	H	
AAB0042.1B	Air	10/08/2017	11	H	
EL0145	Patient environment	15/08/2017	11	H	

EM0145	Patient environment	15/08/2017	11	H	
EB0143	Patient environment	15/08/2017	11	H	
PN0143	Patient	15/08/2017	11	H	
EL0151	Patient environment	17/08/2017	11	H	
EB0151	Patient environment	17/08/2017	11	H	
EB0155	Patient environment	18/08/2017	11	H	
EB0161	Patient environment	23/08/2017	11	H	
EL0161	Patient environment	23/08/2017	11	H	
EM0161	Patient environment	23/08/2017	11	H	
EL0167	Patient environment	23/08/2017	11	H	
EB0169	Patient environment	23/08/2017	11	H	
EL0169	Patient environment	23/08/2017	11	H	
C119224[3]	Clinical	11/12/2017	11	F	
HO0536.1	HCW	01/08/2018	12	D	CC5-MSSA isolate HO0536.1 was recovered from a HCW in a surgical ward (Ward D) and was closely related to environmental isolates recovered from the same ward a week later and also from the environment in a surgical ward (Ward C) two weeks after the HCW isolate was recovered. These findings suggest shedding of CC5-MRSA into the environment of Wards D by HCW-0536. HCW-0536 or possibly another HCW that was not included in the study could also have been responsible for shedding of CC5-MRSA into the environment in Ward C.
A0801-07	Air	08/01/2019	12	D	
S0901.0721	Environment	09/01/2019	12	D	
A0901-1103a	Air	09/01/2019	12	D	
A0901-0721	Air	09/01/2019	12	D	
EC123	Environment	16/01/2019	12	C	
EC104	Environment	16/01/2019	12	C	
HO0244.1	HCW	21/09/2017	13	I	Closely related CC5-MSSA isolates recovered from two separate HCWs on separate wards on the same day. These two medical wards are on separate floors, but both would have high
HO0590.1	HCW	21/09/2017	13	C	

					turnover of staff with other wards. Suggests transmission of CC5-MSSA between the two wards possibly via HCWs, either directly or indirectly.
EB0083	Patient environment	12/07/2017	14	B	Shedding of CC5-MSSA by patient PN0083 into patient NPE in a medical ward (Ward B). Isolate EB0083 recovered from the patient's bedframe on the same day patient isolate PN0083 was recovered.
PN0083	Patient	12/07/2017	14	B	
HN0340.1	HCW	11/01/2018	15	F	CC5-MSSA HCW isolates HN0340.1 and HN0348.1 recovered one day apart in a medical ward (Ward F) and a surgical ward (Ward H) on a different floor. CC5-MSSA isolate HO0398.2e was recovered 14 months later in a medical ward (Ward I) on a different floor to either of the other two wards. Indicates isolate transmission between the three HCWs. There would be some staff crossover between these three wards but it is also possible the three HCWs were in contact in a hospital location outside the study locations.
HN0348.1	HCW	12/01/2018	15	H	
HO0398.2e	HCW	19/03/2019	15	I	
HN0206.1[2]	HCW	09/07/2017	16	F	One HCW (HCW-0206) was detected as a persistent-carrier of CC15/ST5033-MSSA in a medical ward (Ward F) over a 16 month period. The recovery of three environmental isolates in the same ward a month after the recovery of the first HCW isolate HN0206.1 suggests this HCW shed CC15/ST5033-MSSA into the ward environment.
AHA0054.1	Air	10/08/2017	16	F	
AHA0065.1	Air	10/08/2017	16	F	
AHA0053.1A	Air	10/08/2017	16	F	
HN0206.2[2]	HCW	01/12/2018	16	F	
EPconHA0001.2	Environment	24/01/2018	17	F	The recovery of CC15/ST5033-MSSA patient isolate PN0747 in a medical ward (Ward E) was preceded by a related environmental isolate (EPconHA0001.2) recovered 15 months earlier on a medical ward (Ward F) on a separate hospital floor. Some staff crossover between both wards. Shedding of CC15/ST5033-MSSA by an unknown persistent-carrier HCW may be responsible for shedding and transmission to the patient.
PN0747	Patient	10/04/2019	17	E	
PN0297	Patient	02/11/2017	18	C	The CC15/ST15 patient isolate PN0297 was recovered from a surgical ward (Ward C) followed approximately six weeks later by two related air isolates. Two further closely related patient isolates (PO0629 and PO0631B.2) were recovered approximately a year later on a medical ward (Ward G) on a different floor. There would also be a high overlap of staff on these two wards. Findings suggest an unknown HCW persistent carrier was likely responsible for shedding CC15/ST5033-MSSA into the environment and transmission to patients.
A1601-05	Air	15/01/2019	18	C	
A1601-03	Air	16/01/2019	18	C	
PO0629	Patient	24/01/2019	18	G	
PO0631B.2	Patient	24/01/2019	18	G	
AJE0105.1A	Air	12/10/2017	19	E	The CC22/ST22-MSSA patient isolate PN0461 was recovered on a medical ward (Ward G). This isolate was related to an air isolate (AJE0105.1A) recovered six months earlier in a different medical ward (Ward E) on a different hospital floor, but with a high staff overlap between these wards. A HCW(s) or patient not included in the study were likely responsible for shedding CC22/ST22-MSSA into the environment and for transmission to the patient.
PN0461	Patient	17/04/2018	19	G	
PN0697	Patient	22/03/2019	20	C	The CC22/ST737-MSSA patient isolate PN0697 recovered on a surgical ward (Ward C) in March 2019 was closely related to isolates (HO0674.1 and HO0670.1) recovered from two
HO0620.1	HCW	04/04/2019	20	G	

HO0674.1	HCW	10/04/2019	20	C	different HCWs on the same ward over a three week period after recovery of the patient isolate, and one HCW isolate (HO0620.1) recovered on a medical ward (Ward G). Both wards were on different hospital floors but would typically have a high cross over of staff between them. It is likely that the patient acquired their CC22/ST22-MSSA from one of these colonized HCWs, from another colonized HCW or patient not included in the study, or an unsampled environmental site. Transmission also between the three HCWs seems possible.
HO0670.1	HCW	16/04/2019	20	C	
EL0587	Patient environment	11/02/2018	21	H	A HCW (either HCW-0496 or another HCW not included in the study) harbouring a CC22/ST22-MSSA isolate on a medical ward (Ward F) was likely responsible for transmission of ST22-MSSA isolates including the shedding of an environmental isolate (EL0587) on a different surgical ward (Ward H). A closely related isolate (C2221) was recovered from a patient infection in a third surgical ward (Ward A) three months after the HCW isolate was recovered. A patient isolate (PN0742) was also recovered from the same surgical ward (Ward H) as the environmental isolate three months after the clinical isolate. All three wards are located on separate hospital floors but there would be a high crossover of HCW staff among these surgical wards.
HN0496.1	HCW	18/10/2018	21	F	
C2221[3]	Clinical	14/01/2019	21	A	
PN0743	Patient	08/04/2019	21	H	
HN0318.1[2]	HCW	12/12/2017	22	A	Closely related CC22/ST22-MSSA isolates recovered from a persistent HCW carrier during two separate sampling phases eight months apart on a surgical ward (Ward A) with a high turnover of staff.
HN0318.2[2]	HCW	18/08/2018	22	A	
HO0668.1	HCW	10/04/2019	23	B	One HCW was detected harbouring ST398-MSSA isolate (HO0668.1) on a medical ward (Ward B) in April 2019. A related environmental isolate (EM0715) was recovered four months later on the same ward. Indicates shedding into the environment, possibly by HCW-0688 or another HCW or patient not included in the study.
EM0715	Patient environment	04/08/2019	23	B	
HN0378.1	HCW	08/02/2018	24	H	Two closely related HCW ST398-MSSA isolates (HN0378.1 and HN0384.1) recovered from two separate HCWs a week apart on a surgical ward (Ward H). Indicates possible/probable transmission of ST398-MSSA between the two HCWs.
HN0384.1	HCW	15/02/2018	24	H	
PN0001	Patient	08/05/2017	25	C	The CC398/ST398 HCW isolate HN0024.1 was recovered from HCW-0024 on the 23rd May 2017 in a surgical ward (Ward C) two weeks after a related patient isolate (PN0001), six days after a related patient NPE isolate (EL0015), one day before a related air isolate and one day after another patient NPE isolate was recovered on the same ward. It is possible that HCW-0024 acquired the CC398/ST398 from patient PN0001, but it is also possible that HCW-0024 transmitted the CC398/ST398 to patient PN0001. The recovery of a related clinical isolate (C11430) from a patient infection in a medical ward (Ward B) eight months later suggests transmission by HCW-0024 or an unknown HCW.
EL0015	Patient environment	16/05/2017	25	C	
AMA0004.1A	Air	22/05/2017	25	C	
HN0024.1	HCW	23/05/2017	25	C	
EL0031	Patient environment	24/05/2017	25	C	
C11430[3]	Clinical	31/01/2018	25	B	
HO0376.1	HCW	26/01/2018	26	H	A CC398/ST398-MSSA isolate was recovered from HCW-376 on a surgical ward (Ward H) 13 months before a closely related isolates was recovered from HCW-0598 on a medical
HO0598.1	HCW	20/02/2019	26	I	

PO0647	Patient	22/02/2019	26	I	ward (Ward I), which is located on a different hospital floor to Ward H. Both wards would have crossover of staff. A third related isolate was recovered from patient isolate (PO0647) two days after the second HCW isolate in the same ward (Ward I). Transmission of CC398/ST398-MSSA between HCW-376 and HCW-0598 is evident. HCW-0598.1 likely source of patient CC398/ST398-MSSA.
EL0333	Patient environment	30/11/2017	27	B	Two closely related CC398/ST398-MSSA patient isolates (PO0345 and PO0347) were recovered from a surgical ward (Ward A) on the same day one week after an environmental isolate (EL0333) was recovered from a different patient's bedside locker in a medical ward (Ward B). A closely related patient infection isolate (C171679) was also recovered three months after the two patient isolates in a medical ward (Ward E). Ward E is on a different hospital floor to wards A and B. Wards A and B are in close proximity to each other on the same hospital floor. There would be high crossover of staff between all three wards. A colonized HCW not included in the study may have been responsible for transmission.
PO0345	Patient	05/12/2017	27	A	
PO0347	Patient	05/12/2017	27	A	
C171679[3]	Clinical	05/03/2018	27	E	
HN0188.1	HCW	31/08/2017	28	G	HCW-188 yielded an CC398/ST398-MSSA isolate (HN0188.1) on a medical ward (Ward G) in August 2017. Two closely related air isolates were recovered two months later in a different medical ward (Ward E). These two wards were located on separate hospital floors but there would be a lot of staff overlap between them. Environmental shedding by HCW-188 and/or a HCW not included in the study is likely.
AJE0106.1A	Air	12/10/2017	28	E	
AJE0113.1A	Air	12/10/2017	28	E	
HO0312.1	HCW	22/02/2017	29	A	Closely related CC30/ST39-MSSA isolates recovered from a two HCW carriers 11 months apart on two surgical wards (Wards A and F) located on separate floors but with a high turnover of staff.
HN0342.1	HCW	11/01/2018	29	F	
PN0023	Patient	24/05/2017	30	A	Likely shedding to the environment of CC30/ST39-MSSA by colonized patient.
ABA0013.1A	Air	31/05/2017	30	A	
HN0282.1[2]	HCW	04/10/2017	31	I	Closely related CC30/ST39-MSSA isolates recovered from a persistent HCW carrier during two separate sampling phases two months apart on a medical ward (Ward I) and a surgical ward (Ward A). Both wards are on separate hospital floors.
HN0282.2[2]	HCW	15/12/2017	31	A	
ABA0001.2	Air	21/11/2017	32	H	Shedding to the environment of CC30/ST30-MSSA by a colonized patient or HCW not included in the study.
AB0001.2D	Air	21/11/2017	32	H	
HN0076.1[2]	HCW	12/07/2017	33	D	Closely related CC30/ST30-MSSA isolates recovered from a persistent HCW carrier during two separate sampling phases four months apart on a surgical ward (Ward D) and a medical ward (Ward B). The two wards are in close proximity to each other on the same floor.
HN0076.2[2]	HCW	15/11/2017	33	B	
EB0291	Patient environment	02/11/2017	34	C	Likely shedding to the environment of CC30/ST30 by colonized HCW-0352 in a medical ward (Ward F) and/or colonized HCW or patient not included in the study into a surgical ward (Ward C). Wards C and F are located on separate hospital floors.
HO0352.1	HCW	17/01/2018	34	F	

PN0285	Patient	25/10/2017	35	C	Recovery of closely related CC30/ST30-MSSA patient isolates over two months apart on a surgical ward (Ward C) and a surgical ward (Ward H) located on a separate floor. Likely transmission by a colonized HCW(s) not included in the study.
PN0369	Patient	12/01/2018	35	H	
HO0444.1	HCW	23/05/2018	36	E	Closely related CC30/ST30-MSSA isolates recovered from two separate HCWs on the same day on a medical ward (Ward E). Transmission of CC302/ST30-MSSA between HCWs seems evident.
HO0438.1	HCW	23/05/2018	36	E	
PN0543	Patient	31/08/2018	37	A	Closely related CC30/ST30-MSSA isolates recovered from two separate patients on a surgical ward (Ward A) five days apart. A closely related isolate recovered from HCW-0474 on the same day as the second patient isolate in a medical ward (Ward B). Not possible to determine direction of transmission (i.e. patient to HCW or *vice versa*).
PN0547	Patient	04/09/2018	37	A	
HO0474.1	HCW	04/09/2018	37	B	
PN0101	Patient	26/07/2017	38	H	Shedding to the environment of CC30/ ST5043 by colonized patient.
EB0101	Patient environment	26/07/2017	38	H	
HN0224.1[2]	HCW	13/09/2017	39	I	Closely related CC30/ST30-MSSA isolates recovered from a persistent HCW carrier during two separate sampling phases over four months apart on a medical ward (Ward I).
HN0224.2[2]	HCW	07/02/2018	39	I	
HN0422.1	HCW	27/04/2018	40	E	Closely related CC45/ ST5036-MSSA isolates recovered from two separate HCWs almost eleven months apart on a medical ward (Ward E). Transmission between the HCWs seems evident.
HN0260.3	HCW	26/03/2019	40	E	
PN0341	Patient	01/12/2017	41	B	Closely related CC45/ST45 isolates recovered from a patient in a medical ward (Ward B) and 47 days later from a HCW in a surgical ward (Ward H). these two wards are in close proximity on the same floor. Not possible to determine direction of transmission (i.e. patient to HCW or vice versa).
HN0354.1	HCW	17/01/2018	41	H	
A0801-18a	Air	08/01/2019	42	C	Closely related CC45/ST45 environmental isolates recovered over two days in a surgical ward (Ward C) and a surgical ward (Ward D). The two wards were in close proximity to each other on the same floor. Shedding to the environment by a colonized HCW(s) not included in the study is likely.
EC37a	Environment	09/01/2019	42	D	
EC52	Environment	09/01/2019	42	D	
HN0220.1[2]	HCW	13/09/2017	43	G	Closely related CC45/ST45-MSSA isolates recovered from a persistent HCW carrier during two separate sampling phases eight months apart on two medical wards (Ward E and G), located on different floors.
HN0220.2[2]	HCW	14/05/2018	43	E	
EM0551	Patient environment	13/09/2018	44	B	Shedding to the environment of CC45/ST5036 by colonized patient.
PN0553	Patient	13/09/2018	44	B	
PN0227	Patient	27/09/2017	45	E	

EB0227	Patient environment	27/09/2017	45	E	The CC45/ST503-MSSA HCW isolate HO0258.1 was recovered in a medical ward (Ward I) and was closely related to three isolates from a medical ward (Ward E) on a different floor, recovered a week earlier from a patient (PN0227) and the same patient's NPE (bedframe and mattress). The direction of transmission is unclear. The patient is likely shedding into their near environment and may have been a source for the HCW. Alternatively, The HCW may have harboured the CC45-MSSA long before the recovery date and represents a possible source for the patient.
EM0227	Patient environment	27/09/2017	45	E	
HO0258.1	HCW	03/10/2017	45	I	
PO0455	Patient	13/04/2018	46	G	A CC45/ST45-MSSA patient isolate (PO0455) was recovered on a medical ward (Ward G) and a month later a HCW isolate (HN0434.1) was recovered from the same ward. The direction of transmission is uncertain.
HN0434.1	HCW	18/05/2018	46	G	
HO0016.1[2]	HCW	24/05/2017	47	A	Closely related CC45/ST972-MSSA recovered from a persistent HCW carrier during two separate sampling phases almost six months apart on a surgical ward (Ward A).
HN0016.2[2]	HCW	22/11/2017	47	A	
HO0588.1	HCW	18/02/2019	48	C	A HCW CC45/ST45-MSSA isolate (HO0588.1) was recovered in a surgical ward (Ward C) a month before a patient isolate (PO0659) was recovered from a medical ward (Ward I) located on a different floor. HCW-0588 is the likely possible source for the patient isolate.
PO0659	Patient	08/03/2019	48	I	
A0801-17	Air	08/01/2019	49	D	Two environmental CC45/ST45-MSSA isolates recovered a week apart on a surgical ward (Ward D) and a surgical ward (Ward C) on a different floor. Shedding of CC45/ST45-MSSA by a HCW not included in the study is likely.
A1601-18	Air	16/01/2019	49	C	
HN0094.1[2]	HCW	19/07/2017	50	B	Closely related CC45/ST508-MSSA recovered from a persistent HCW carrier during two separate sampling phases over four months apart on a medical ward (Ward B).
HN0094.2[2]	HCW	29/11/2017	50	B	
HO0234.1	HCW	21/09/2017	51	G	Closely related CC45/ST5-MSSA isolates recovered from two separate HCWs on the same day in a medical ward (Ward G) and another medical ward (Ward I). Both wards are in close proximity to each other on the same floor.
HO0248.1	HCW	21/09/2017	51	I	
C112296[3]	Clinical	22/08/2017	52	C	Closely related CC1027/ST1027-MSSA isolates recovered a week apart from separate patient infections in a surgical ward (Ward C) and a surgical ward (Ward H) located on a separate floor. A HCW or patient not included in the study was likely responsible for transmission, or an unsampled source.
C111576[3]	Clinical	29/08/2017	52	H	
HO0416.1	HCW	27/04/2018	53	E	Closely related CC595/ST59-MSSA isolates recovered from two separate HCWs on the same day in a medical ward (Ward E).
HO0418.1	HCW	27/04/2018	53	E	
EAB0006.3	Environment	14/11/2018	54	H	Two closely related CC7/ST7-MSSA environmental isolates recovered on the same day in a surgical ward (Ward H). A colonized patient or HCW not included in the study is the likely source.
EAB0001.3	Environment	14/11/2018	54	H	
PN0651	Patient	12/03/2019	55	I	Two closely CC8/ST8-MSSA isolates were recovered from a HCW followed 12 days later from a patient on a medical ward (Ward I). The HCW was a likely source of transmission to the patient.
HN0600.1	HCW	01/03/2019	55	I	

HN0088.2	HCW	07/12/2017	56	B	Three closely related CC72/ST72 isolates were recovered from three separate HCWs. The first isolate (HN0088.2) was recovered on a medical ward (Ward B) followed five days later by two isolates on a surgical ward (Ward A) located on a different floor. Transmission between the three HCWs is evident.
HO0320.1	HCW	12/12/2017	56	A	
HO0316.1	HCW	12/12/2017	56	A	
A1501-8A	Air	15/01/2019	57	D	Closely related CC109/ST109-MSSA environmental isolates were recovered over two days in a surgical ward (Ward D) and a surgical ward (Ward C) located on a separate floor. Shedding by a colonized HCW or patient not included in the study is the likely the source of the isolates.
A1601-16	Air	16/01/2019	57	C	
A1601-13	Air	16/01/2019	57	C	
EC122	Environment	16/01/2019	58	C	Four closely related CC97/ST97-MSSA environmental isolates were recovered in a surgical ward (Ward C) over a two day period indicating a possible colonized patient or HCW not included in the study shedding CC97/ST97-MSSA into the environment
A1501-08b	Air	15/01/2019	58	C	
A1601-10b	Air	16/01/2019	58	C	
A1501-09	Air	15/01/2019	58	C	
C3966759[3]	Clinical	08/04/2019	59	C	Closely related CC188/ST188-MSSA isolates recovered from a patient infection and a different patient's nasal sample on the same day. Transmission may have been from either patient or from an a HCW not included in the study
PN0731	Patient	08/04/2019	59	C	

[1]In total 183/406 sequenced MSSA isolates grouped into 59 related isolate groups (RIGs) by core-genome multilocus sequence typing (cgMLST). Isolates were categorised into RIGs if they exhibited ≤24 cgMLST allelic differences to all other isolates within a RIG. Isolates within each RIG were closely related based on previously proposed thresholds (≤24 cgMLST allelic differences) (Earls *et al*, 2018; Humphreys *et al* 2019). The remaining 223 MSSA isolates exhibited ≥24 cgMLST allelic differences and were therefore deemed unrelated. These 223 isolates were grouped in to RIG-0 for convenience. Genotypic information including multilocus-sequence typing clonal complexes (CCs) and sequence types (STs) were extracted from whole-genome sequencing data using BioNumerics version 8 (Applied Maths, Sint-Martens-Latem, Belgium). RIGs 1-59 were identified following cgMLST analysis using BioNumerics (see Figure 1 main text and Table SI). Briefly, isolates of the same CC group were selected for comparison by cgMLST. The similarity between cgMLST profiles was investigated using the categorical differences algorithm and the UPGMA method in BioNumerics to generate a UPGMA tree which was circularised, and a best fit figure was generated. [2]Related isolates within RIGs recovered from the same HCW over multiple phases. There may have been a high degree of movement between all of the study wards as well as mixing of HCWs and/or patients in other hospital environments such as café/canteens within the hospital that are outside the scope of this investigation. Movement of patients between wards is also another factor that likely contributed to transmission events in the study. [3]Eight clinical isolates recovered from patient infections (e.g. surgical sites) and involved in RIGs on the wards during the study period as part of routine hospital clinical activities. These differed from patient volunteer nasal or oral isolates recovered as part of the study.

Abbreviations: HCWs, healthcare workers; NPE, near-patient environment.

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