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Review

Whole-genome sequencing links cases dispersed in time, place, and person while supporting healthcare worker management in an outbreak of Panton–Valentine leucocidin meticillin-resistant *Staphylococcus aureus*; and a review of literature

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SUMMARY

This is a report on an outbreak of Panton–Valentine leucocidin-producing meticillin-resistant *Staphylococcus aureus* (PVL-MRSA) in an intensive care unit (ICU) during the COVID-19 pandemic that affected seven patients and a member of staff. Six patients were infected over a period of ten months on ICU by the same strain of PVL-MRSA, and a historic case identified outside of the ICU. All cases were linked to a healthcare worker (HCW) who was colonized with the organism. Failed topical decolonization therapy, without systemic antibiotic therapy, resulted in ongoing transmission and one preventable acquisition of PVL-MRSA. The outbreak identifies the support that may be needed for HCWs implicated in outbreaks. It also demonstrates the role of whole-genome sequencing in identifying dispersed and historic cases related to the outbreak, which in turn aids decision-making in outbreak management and HCW support. This report also includes a review of literature of PVL-MRSA-associated outbreaks in healthcare and highlights the need for review of current national guidance in the management of HCWs' decolonization regimen and return-to-work recommendations in such outbreaks.

Introduction

Panton–Valentine leucocidin-producing meticillin-resistant *Staphylococcus aureus* (PVL-MRSA) is mostly associated with pyogenic skin and soft-tissue infections (SSTIs) [1]. However, it

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may be associated with life-threatening illness such as necrotizing pneumonia and necrotizing fasciitis [2]. PVL is a pore-forming toxin that causes lysis of neutrophils. There are two components, LukS-PV and LukF-PV, which are secreted separately and bind within the neutrophil cell membrane to form a pore which in turn causes cell lysis [3].

PVL-MRSA strains commonly cause community-associated MRSA (CA-MRSA) infections. There are no UK-wide data on PVL prevalence, but one single-site cross-sectional study estimates that PVL is more commonly associated with meticillin-susceptible *Staphylococcus aureus* (MSSA) than with MRSA at 9% and 0.8%, respectively [4]. Despite PVL association with severe necrotizing infections, it has not been found to have a higher associated mortality than those strains without PVL expression [5].

Numerous healthcare outbreaks of MRSA as well as some outbreaks of MSSA carrying the PVL-MRSA gene have already been reported. This report includes a review of literature of PVL-MRSA-associated healthcare outbreaks and our experience in managing such an outbreak in the intensive care unit (ICU) in a large secondary care hospital. The objective of this report is to emphasize challenges surrounding management of staff with chronic carriage of MRSA and to highlight the utility of techniques such as whole-genome sequencing (WGS) in managing such outbreaks.

Case presentation

The first hospital-acquired case of PVL-MRSA was identified in a patient on a 12-bedded ICU through routine MRSA swabbing from the nose and groin, after having had several weekly negative screening tests for MRSA. This had not been tested for PVL toxin in real-time. A look-back exercise for other hospital-acquired cases of MRSA with similar antibiogram, at that time, had not shown any other cases on the unit. This was an isolated case at that time; the organism had no impact on the patient's course and hence no further investigation was undertaken. However, 124 days later a second patient was identified as having acquired MRSA, more significantly, from their blood cultures and multiple skin swabs including the tracheostomy wound site (Figure 1). The aggressive nature of this patient's illness led to the samples (including the first patient's) being tested locally for PVL (Rotor Gene 5 plex; Qiagen, Hilden, Germany) and sent for typing at the Antimicrobial Resistance and Healthcare-Associated Infection Unit (AMRHAI) of the UK Health Security Agency (UKHSA) by whole-genome sequencing (WGS) [6]. Raw sequence (on Nextseq500/1000 Illumina platforms using Nextera XT libraries preparation) reads are available at European Bioinformatics Institute — EBI (ENA accession number PRJEB65285).

At this time, several infection control actions were instituted. Weekly hand hygiene audits in ICU and the bare-below-the-elbows policy were emphasized and monitored. All bed spaces had terminal cleaning with a chlorine-releasing disinfectant (sodium dichloroisocyanurate: NaDCC) which included cleaning of all surfaces and equipment.

Environmental sampling of the ICU was undertaken from 158 sites. Moistened swabs (Transwab®; Medical Wire and Equipment, Corsham, UK) were used to collect environmental samples. Approximately 10 cm^2 surface area of environmental

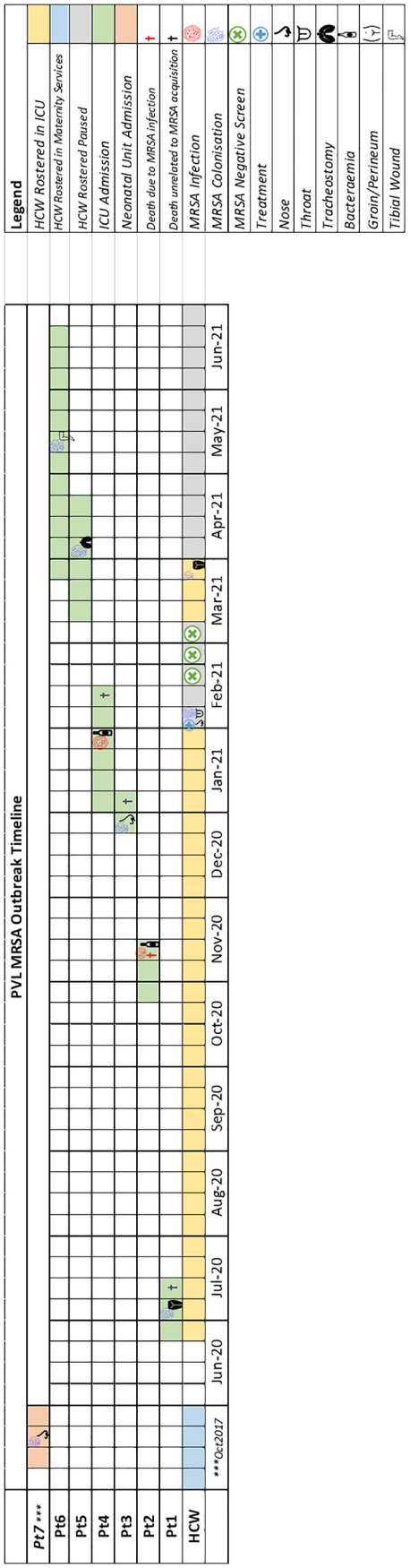

Figure 1. Timeline of healthcare worker (HCW) colonized with PVL-MRSA in relation to the seven patients (six from intensive care unit and one from neonatal unit) who acquired PVL-MRSA, site and type (colonization vs infection) of PVL-MRSA acquisition, and outcome for patient. Pt, patient; PVL-MRSA, Panton–Valentine leucocidin-producing meticillin-resistant *Staphylococcus aureus*; ICU, intensive care unit.

surfaces/equipment or personal protective equipment (PPE) was sampled whenever feasible. These were inoculated direct on to MRSA selective chromogenic agar (Colorex™; EO Laboratories Ltd, Bonnybridge, UK). Presumptive isolates were tested by matrix-assisted laser desorption—ionization time-of-flight mass spectrometry. Site of environmental sampling included screening of all bed spaces and any shared equipment in the ICU, including static equipment such as point-of-care testing machines as well as mobile equipment such as ultrasound scanners. Within this environment, all high-touch areas were screened as well as staff PPE, which included single-use gowns and aprons while they were in use. A similar process as described above was used to test gowns and aprons, i.e. moistened swabs were used to swab gowns and aprons, with areas that were likely to be contaminated being sampled. Several rounds of environmental screening failed to detect any MRSA in the unit.

All patients admitted to ICU were screened, as part of hospital policy, for MRSA on admission; and weekly thereafter. This process was audited and strengthened by way of reminders to ICU staff by members of the infection prevention and control (IPC) team.

Four weeks after the second case, a third patient was identified as having acquired MRSA on ICU in a nose swab, having previously had one set of negative screening swabs on admission, which was about a week prior to MRSA acquisition on the unit. The isolate tested positive for PVL toxin by in-house polymerase chain reaction (PCR) and was found to be carrying the toxin gene. It was sent for further typing to the reference laboratory.

While awaiting results of typing of all three isolates sent, an outbreak meeting was convened. It had already been noted that the samples had identical antibiograms. The MRSA had tested resistant to flucloxacillin, ciprofloxacin, gentamicin, erythromycin, and clindamycin by disc susceptibility testing; as well as testing positive for PVL toxin gene by PCR.

At the first outbreak meeting it was agreed to commence active surveillance for PVL-MRSA in the hospital. This included testing for PVL toxin and typing by WGS any MRSA isolate that was prospectively isolated from a case of hospital-acquired infection/colonization. Surveillance also included review of all previously isolated PVL-MRSA isolates from the hospital to determine whether they were hospital acquired and epidemiologically linked to the current outbreak and a look-back exercise to review all hospital-acquired cases of MRSA over a one-year period.

It was also agreed that routine enhanced cleaning with a chlorine-releasing disinfectant was to continue in all areas of the ICU. Patient screening for MRSA — as was already in place including admission screen and then weekly screen thereafter of nose/groin and any areas of broken skin or around device sites — was continued and audited. Weekly hand hygiene audits, some of which were independently assessed by the IPC team, were also continued. It was noted that all three patients had been in one of two bed spaces but had never been in the unit at the same time. A terminal clean, in view of MRSA isolation, had taken place between patients. Importantly at this outbreak meeting it was agreed that staff should be screened for MRSA carriage and a list of staff working with these patients was compiled. The outbreak team decided that the members of staff to be screened would include all members of staff who had been working on intensive therapy unit (ITU) (doctors, nurses, as well as allied health workers such as physiotherapists and dieticians) during the time period when the three cases on ITU were detected. This was to ensure that all potential staff who could have transmitted the MRSA were captured; while transient staff (such as visiting teams), who are unlikely to have had contact with all the cases over the extended time-period of the outbreak, were excluded. A detailed information leaflet on how to self-collect screening samples was provided to staff. Nose, throat, perineum and any wound, ulcer, or other area of broken skin/skin lesion were requested to be sampled. All staff from whom screening samples were requested complied with submitting samples.

Shortly after this meeting, WGS analyses using SnapperDB, a single nucleotide polymorphism (SNP)-based clustering methodology for isolate nomenclature called SNP address, showed that all three isolates were closely related genetically and belonged to the 5 SNP cluster 2.130.616.683.739.2815.#. with a range of 1—5 SNP between genome sequences, suggesting a transmission event [7]. This confirmed that this was an outbreak with likely transmission of same strain between patients despite being spread out over several months (between the first and second case) with gaps of potentially no transmission in between. Gene profiling confirmed the presence of *luk*F/S-PV and detected *tst* gene encoding the staphylococcal Toxic Shock Syndrome Toxin [8]. WGS confirmed the resistance to aminoglycoside (*aac*(6′)-*aph*(2″)), macrolide and lincosamide (*erm*C), and fluoroquinolone (chromosomal mutation grlA:S80S and gyrA:S84L). In addition, mechanisms of resistance to trimethoprim *drf*A and dfrB:F99Y were detected in the outbreak strain sequences.

Six days following this first outbreak meeting, and within two weeks of the third case, a fourth patient on ICU had MRSA identified in their blood culture as well as their tracheostomy site. WGS typing later confirmed the isolate as belonging to the outbreak.

In total, 145 members of staff were screened, including all 26 doctors on the unit, 15 physiotherapists, five dieticians, and 95 nurses/healthcare assistants. Of these, three screening swabs tested positive for MRSA. Two of these identified in the first round had antibiograms very different from the patient samples and were found to be PVL negative and later reported to be unrelated to outbreak strain by WGS. These members of staff were offered and completed topical decolonization therapy (with Mupirocin nasal ointment 2% and Octenisan Body Wash for five days) and no further follow-up was felt to be necessary. A third staff member's screening swab later detected an antibiogram identical to the outbreak strain and had tested PVL positive. While WGS results were awaited, and, based on the antibiogram and PVL testing, it was felt prudent to commence the healthcare worker (HCW) on topical decolonization therapy (as above) as well as exclusion from clinical-facing work until three negative swabs, each spaced one week apart, had returned. In addition, advice and an information leaflet was provided to the HCW concerning laundry of clothing at higher temperatures, avoiding sharing linen and other personal equipment, and other IPC precautions to prevent further transmission, as has been detailed in the UKHSA guidance document on managing HCW's colonized with PVL-MRSA [9]. Upon discussion and explanation of the situation to the HCW by the occupational health team, it was agreed that the HCW would be taken off work with full pay while undergoing decolonization therapy. The process of requiring

negative swabs to return to work was explained, as was the significance of this organism to convince them of the need for isolation from clinical work. Considering the contribution this HCW had made during the COVID-19 pandemic it was of vital importance that they were supported fully, and the team ensured that counselling was available.

Analysis of the entire SNP address collection available at UKSHA identified one further isolate — from a baby on the neonatal ward in the hospital, collected three years previously with similar SNP address, 2.130.616.683.739.#.#. within 10 SNP of the current outbreak strain. Review of working shifts revealed that the HCW had worked in the neonatal unit around the time of detection of the case of MRSA acquisition on the unit. Availability of WGS data and rapid confirmation of SNP-based relatedness results using SnapperDB enabled us to unequivocally establish that the member of staff, colonized with PVL-positive MRSA, represented the likely source of transmission as they had cared for each patient affected on intensive care unit, with the genetically similar PVL-producing MRSA as well as having the strain identified from their own screening swabs, with a possibility of having acquired it from the first case in the neonatal unit.

The HCW had returned three negative swabs three weeks apart and no more cases had been identified. An in-depth search for related cases in the community contacts by the local health protection team revealed that no members of the HCW's community contacts were found to be colonized with PVL-MRSA. With a sparse amount of evidence surrounding the long-term follow-up and management of staff colonized with PVL-MRSA or healthcare-acquired MRSA being available, a plan was agreed by the outbreak team to undertake surveillance screening at one, three, and six months following the initial three negative screens [7].

Unfortunately, within a week after the HCW had returned to work following the initial set of three negative swabs, another two cases of PVL-MRSA were identified on ICU: one from their tracheostomy site swab and the other from a surgical wound swab. At the same time the HCW's one-month surveillance swab came back positive for PVL-MRSA. WGS typing confirmed the genetic link with the outbreak strain, indicating unsuccessful topical decolonization therapy or the possibility of reacquisition of PVL-MRSA from an unidentified source. The genetic variability between the two HCW isolates pointed to carriage with multiple variants of the outbreak strain as previously described in another MRSA outbreak in the UK [10]. A phylogenetic tree (Figure 2) confirmed the existence of a single cluster, well separated from the local background bacterial population and from other national isolates belonging to the CC22 PVL-MRSA *tst*+ clade. Topology of the tree located the two isolates of the HCW on two distinct branches (bootstrap values >95%) of the outbreak clade. It also positioned the neonatal unit case on an ancestral branch in line with the evolutionary process (bootstrap values >95%).

It was therefore probable that the HCW was chronically colonized with the organism and that possible sources of chronic carriage with intermittent shedding needed to be investigated. A history of possible recurrent postnasal drip was then reported by the HCW; an ENT referral was then arranged.

It was agreed, following discussions with ENT team and the HCW concerned, that although no specific ENT pathology was identifiable, the HCW should receive a treatment course of systemic antibiotics to eliminate the carriage and intermittent shedding. The HCW was offered a 10-day course of per-oral doxycycline and rifampicin. Screening was performed three times at 48 h intervals post antibiotic treatment and then at one, three, and six months post treatment. The HCW was redeployed to a non-clinical role following discussions with hospital human resources department. After an 18-month follow-up, no further cases were detected on the ICU and the outbreak was closed.

Discussion

In this outbreak, a total of seven patients, including one patient from more than three years before identification of this outbreak in a different unit and a member of staff, were impacted by PVL-MRSA. The two patients with bacteraemia required systemic treatment for the infection, one of whom died as a result of systemic infection with this organism. In the other five cases, PVL-MRSA acquisition did not directly contribute to their clinical course [11].

The availability of WGS has greatly changed how outbreak epidemiology can be investigated and allows for greater certainty in describing genetic relatedness between different isolates of *Staphylococcus aureus* [11,12]. This outbreak demonstrates the utility of WGS and provides further evidence that it is currently an indispensable tool in laboratory practice in identification and management of such outbreaks [13—15]. In this outbreak, WGS was helpful to prove beyond all doubt that the outbreak was associated with the HCW by linking cases that were beyond a single setting of the ITU. Whereas outbreak investigations based on epidemiological data alone — and without tools such as WGS — may establish links in time, place, and person, they may miss cases that appear unrelated to a current outbreak that may have implications for outbreak management and its control. With reducing costs and faster turnaround times, literature is fast accumulating to show that there is a potential cost benefit to using WGS surveillance in hospital outbreaks, allowing rapid evidence-based support for decision-making related to IPC and staff management [16,17].

The decisions around HCW management were not taken lightly and followed an in-depth discussion involving the HCW's line manager, IPC team, human resources, occupational health, local health protection team, the UKHSA national PVL expert and the hospital's medical director. Hospital staff that were to be screened, including staff in ICU, were already reticent about staff screening being performed in case 'blame' should be assigned to anyone. Working with the hospital's communications team, a detailed information leaflet was produced to help staff understand what PVL was, why they were being screened, and what would happen if they were found to be carrying this organism. Clinical leads were identified within ICU and IPC teams to support staff that had any questions relating to the screening process.

Current UKHSA guidance suggests that:

> A HCW with a proven PVL-SA infection should not work until the acute infection has resolved and 48 hours of a five day decolonization regimen has been completed. Follow-up screens following topical decolonization are advised as for MRSA guidelines (three screens one week apart). Unlike hospital acquired MRSA, staff who are found to have PVL-SA are likely to have acquired the infection in the community, and hence re-colonization may occur from a close contact. Therefore, even if screens have been negative, staff

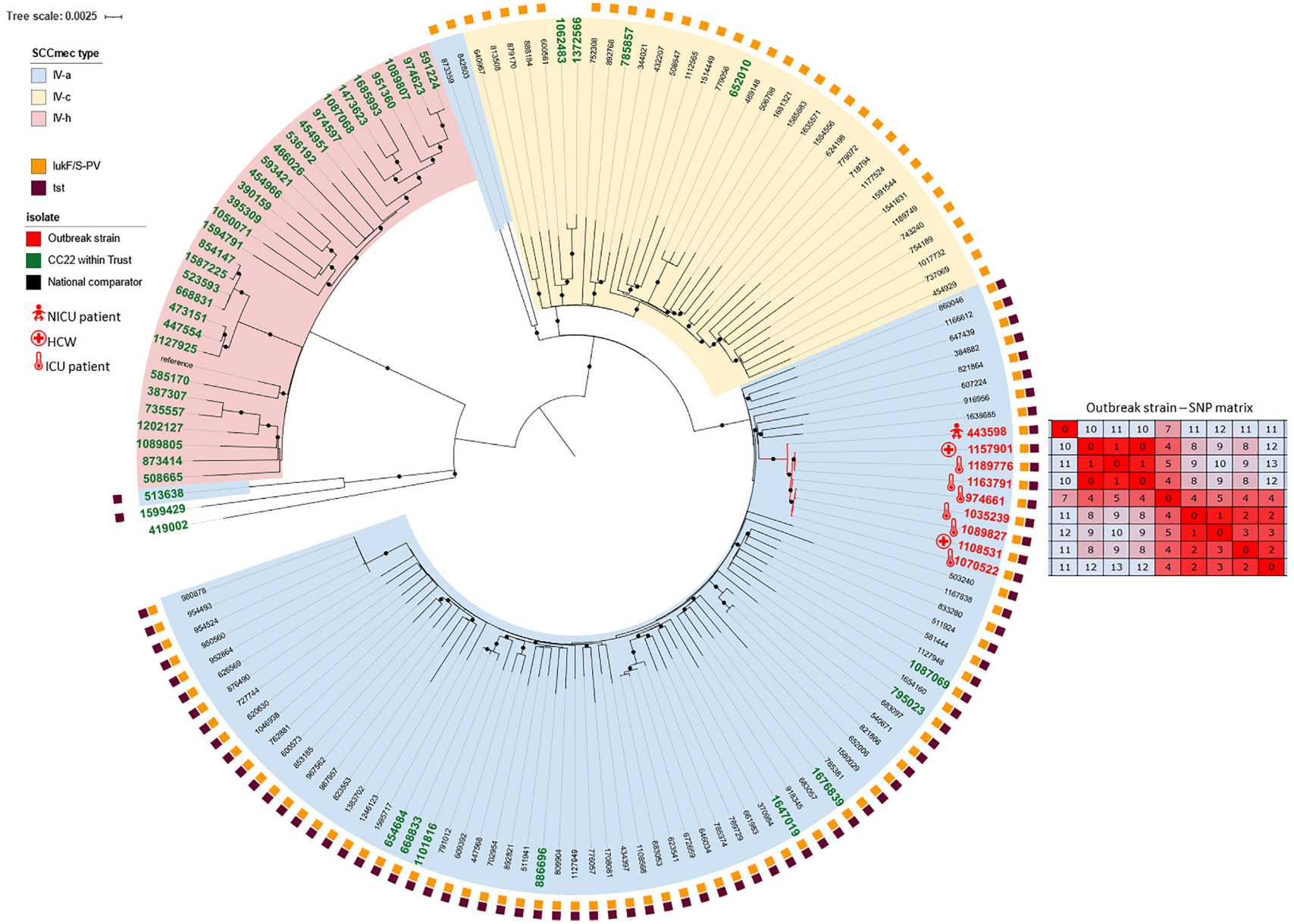

Figure 2. Phylogenetic analysis of CC22 PVL-MRSA tst+. Phylogeny was inferred by maximum likelihood analysis using raxML [36] GTRCAT model with 100 bootstraps from 8231 core genome single nucleotide polymorphism (SNP) alignment. Core genome SNP were called by using PHEnix pipeline and recombinant positions were excluded using gubbins [37,38]. The phylogenetic tree was drawn using itol [39]. The tree included the eight outbreak isolates, 49 local comparators (any isolates referred by the hospital for whole-genome sequencing (WGS) typing belonging to the multi-locus sequence typing clonal complex 22 irrespective of mec, PVL, and tst status) and 92 national comparators (a random selection of CC22 PVL-MRSA *tst*+/− referred to UKHSA for WGS typing). The scale represents approximately 20 SNPs. SNP distances were calculated using snp-dists [40]. Sequence reads generated in this study have been deposited in the ENA repository under the BioProject accession (pending).

should understand that they should stop working if a further skin lesion develops. If, despite two courses of decolonization treatment, a staff member remains a carrier, they should be able to continue work providing they are not implicated in hospital transmission of PVL-SA infection and they cease working as soon as a possibly infected skin lesion develops.

As is evident in our outbreak, the presence of skin lesions alone does not directly relate to risk of onward transmission. Other than some postnasal drip, the HCW in this outbreak had no other pathology such as eczema, psoriasis, or chronic respiratory disease to support chronic carriage. Several rounds of environmental testing and cleaning (not just as part of this outbreak — data not included here) had failed to detect MRSA in the hospital environment. This made it less likely that the HCW was re-acquiring MRSA from the hospital environment. No other members of the HCW's close family or more extended family were detected to be colonized with MRSA. The HCW had not been in close contact with any animals nor had any pets. All other members of staff screened had tested negative for MRSA colonization with the outbreak strain and the outbreak ceased when there was no longer any patient contact with the index HCW. These factors support the hypothesis that the HCW was likely to be chronically colonized rather than the possibility of the HCW reacquiring it from the hospital environment or close community contacts.

Staffing pressures are an ever-present fact in the current day-to-day running of the NHS; and during the COVID-19 pandemic, the hospital management team were extremely concerned about this, especially so during the peak of the pandemic waves. It is likely that if staffing was at required levels, such incidents would be less frequent. As has been reported by Scheithauer *et al.*, increased workload, time pressure, and emotional fatigue have a negative impact on IPC practices [18]. This is also the possible explanation of how transmission could have occurred in an ICU setting during the pandemic when staff were required to wear face masks with or without other PPE with all patient contact; where staffing pressures due to the demands of the pandemic, additional time required for PPE, and emotional fatigue are all likely to have impacted on IPC practices. In the current state of the NHS this is something that will only become more prevalent unless the staffing crisis is addressed.

Three of the six patients who acquired MRSA on the unit tested positive in their tracheostomy sites and another in a recent surgical site on a limb, suggesting that during wound care there may have been lapses in aseptic technique. Of these, two developed infection and one succumbed to PVL-MRSA bacteraemia (Figure 1). It is possible with combined work pressures due to staffing levels and intensity of work during the pandemic in an ICU that the HCW either had insufficient opportunity for ideal hand hygiene, especially while performing high-risk transmission tasks such as wound care, or that they were 'super-shedding' from skin during these times and that these events may not have been prevented, despite full PPE, unless fully decolonized. Many studies have reported that mask wearing, as was mandatory in ITU during the COVID-19 pandemic, did not increase the frequency of face or mucosal touching behaviour, hence is less likely to be directly associated with transmission events [19—21].

The fact that a strain identical to the outbreak stain was isolated three years prior, in a different part of the hospital, and that there was a long gap (124 days between cases 1 and 2 on ICU) between patient acquisition despite HCW being at work during these times, supports the possibility of chronic carriage and probable intermittent super-shedding periods. This raises several questions that need further research — are particular strains of MRSA or PVL-MRSA more associated with persistent carriage? Are some strains more likely to pose difficulties with eradication? Is enhanced dissemination in the environment dependent on bacterial genotypic or phenotypic traits?

Apart from the staffing issue already mentioned, this outbreak highlights the need for continued surveillance by IPC teams, even during time of the pandemic, and robust laboratory support to identify and manage such outbreaks and resources to be available for such teams to be able to undertake such actions.

The human side must be considered in this scenario; and we found the aspect often overlooked is, 'how to approach the issue holistically?' We focus on containing the organism and management scenarios for this, however this outbreak highlighted to us the need to consistently implement practices around management of HCW's at the centre of it. HCW's are prone to mental health problems, especially so during a pandemic [22]. The removal of the implicated HCW from their support network at work, supporting them through feelings of guilt, and the required role change indicates the difficulty in taking such decisions outside of current guidance [23]. Availability of results from WGS helped the outbreak management team as well as the HCW in such decisions.

There are differing approaches surrounding the topical decolonization/systemic antimicrobial treatment and exclusion from work of staff who are identified to have chronic carriage of PVL-MRSA in an outbreak situation (Table I). Of the 15 MRSA PVL outbreaks in healthcare that we could find reported in literature (Table I), four out of eight reports where the screening information was available undertook long-term screening beyond three negative swabs. In five out of nine outbreak reports, exclusion from work was until three negative screens were obtained or HCW was asymptomatic, where this information was available in the report. In all these reports topical decolonization only was reported to have been used unless evidence of active infection was present; except for the report by Haill *et al.* who used routine systemic antibiotics along with topical agents in the management of MRSA transmission events in their hospital [24].

Based on this experience, locally IPC policy has moved towards a prolonged period of screening for HCW colonized with PVL-MRSA with early systemic treatment to ensure clearance before return to work to minimize the negative impact on patients and implicated HCW.

In conclusion, WGS is a valuable tool in outbreak investigations and surveillance for early detection of healthcare outbreaks and to make rapid and unequivocal inferences on mode of transmission that link remote cases (in time, place, and person). This is critical in providing accurate information to staff and supporting implicated HCWs. More work needs to be done on how HCWs implicated in outbreaks can be supported, especially by occupational health departments, during outbreak investigations and to manage the negative consequences an outbreak may have on them. Funding needs to be focused on ensuring adequate staffing levels, IPC resources for surveillance, and the maintenance of laboratory services even during

Table I
Outbreak reports of PVL-MRSA in healthcare settings involving at least one healthcare worker [22]

Setting	MRSA type	No. of people (staff) in whom carriage was detected	No. of symptomatic cases (mortality)	Screening regimen for HCW	HCW management	Period of exclusion of HCW post treatment	Other issues	Reference
Neonatal intensive care	PVL-MRSA ST30	3 (2)	4	Weekly ×3 then, monthly ×3 (nose and throat)	Topical decolonization plus chlorhexidine gargles	Until three negative screens (collected weekly)	Two household contacts also carriers; weekly screening of all babies	Ali *et al.* [22]
Multiple hospitals and multiple sites + community: outpatients, emergency department, gynaecology and neonatal intensive care unit	PVL-MRSA ST8-IVa (H1+2). PVL-MRSA ST5-IVc	Cluster in two distinct hospitals: 10. In a third hospital cluster: 18 (1)	Not reported	Not reported	Not reported	Not reported		McManus *et al.* [23]
Hospital ward and community	PVL-MRSA ST30-IVc	17 (9)	12 (2)	Nasal, throat and perineum swab 48 h post treatment/ decolonization until negative. Follow-up screening at 1, 4, 12 months	Topical decolonization/ systemic treatment in active infection	Until free of symptoms of SSTI, negative screening ≥48 h post decolonization/ treatment	All household contacts screened (two carriers) — if positive or symptoms of recurrent SSTI or SSTI requiring admission. Then simultaneous decolonization therapy as home decontamination.	Orendi *et al.*. [24]
Coronary care unit and ITU	PVL-MRSA T019	6 (2)	0	Weekly nose, axilla, and groin swabs	Topical decolonization and chlorhexidine gargles	Until three consecutive weeks of negative screens	Three members of staff identified with unrelated PVL-MRSA. Household contacts that required decolonization via Public Health England.	Papastergiou and Tsiouli [25]

Neonatal ITU	PVL-MRSA ST22	17 (1)	6 (2)	Surveillance not discussed	Topical decolonization 5 days	Not discussed	Source of outbreak never identified, parents, patients and staff colonized — all 'successfully decolonized'	Pinto *et al.* [26]
Maternity unit and community	PVL-MRSA CC398	36 (1)	17 (0)	Swabs on days 7, 14, 21 after treatment and then at 6 months (as per Danish health authority guidance)	Topical decolonization	Three days from being identified as likely source while undergoing decolonization therapy		Møller *et al.* [27]
University hospital ward	PVL-MRSA ST8-IVa	7 (1)	7 (0)	No data	HCW became infected and had active systemic treatment of disease (osteomyelitis, pulmonary septic emboli and renal abscess)	Not applicable: active infection requiring treatment	Every patient isolated had active infection, cause for HCW infection never identified	Kobayashi *et al.* [28]
Hospital and community	PVL-MRSA ST22 and ST80	52 (21) [outbreak 1]; 8 (3) [outbreak 2]	14 (0) [outbreak 1]; 2 (0) [outbreak2]	Not discussed — 'undertaken with public health authorities'	Not discussed — 'undertaken with public health authorities'	Not discussed — 'undertaken with public health authorities'	Two separate outbreaks within hospitals; the first involved related hospitals	Linde *et al.* [29]
Burns unit	PVL-MRSA	30 (10)	10 (0)	Weekly nose, throat, and groin swabs	Topical decolonization for 10 days, if failure then 5 days treatment with linezolid and rifampicin with further topical decolonization	Until three consecutive weeks of negative screens		Teare *et al.* [30]
General medical ward	PVL-MRSA ST8	10 (6)	10 (0)	Not discussed	Systemic treatment as actively infected, varying regimens	Not discussed		Nagao *et al.* [31]
Neonatal intensive care unit	PVL-MRSA ST8	9 (3)	8 (1)	Not discussed	All systemic treatment	Not discussed		McAdams *et al.* [32]

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Table I (*continued*)

Setting	MRSA type	No. of people (staff) in whom carriage was detected	No. of symptomatic cases (mortality)	Screening regimen for HCW	HCW management	Period of exclusion of HCW post treatment	Other issues	Reference
Obstetrics and neonatal department	PVL-MRSA ST8	8 (3)	3 (0)	Daily for three days, three days after having completed decolonization then repeat screening at 10 days, 1, 3, 6 and 12 months	Topical decolonization with nasal ointment, gargling treatments and body and hair wash for 5 days	Until they had three negative swabs (presumed in a row although not explicitly stated)	Uncertain as to the origin of the outbreak, was it a patient or HCW? Final case in a patient was identified post HCW decolonization and no other cases identified after this isolated extra case	Kossow *et al.* [33]
Special care baby unit	PVL-MRSA ST2371	27 (1)	14 (0)	Not discussed	Topical decolonization	Unspecified time but they were removed from clinical duty until successful decolonization had taken place		Harris *et al.* [10]
Neonatal intensive care unit	PVL-MRSA ST772	10 (2)	0 (0)	Multiple screens, positive for a second occasion on their third screen, not expanded on further than this	Topical decolonization for five days of nasal ointment and body and hair wash	Not discussed	Suspected index case required decolonization twice and relative found to be colonized and had to undergo decolonization	Brennan *et al.* [34]
Neonatal intensive care unit	PVL-MRSA ST59	16 (1)	2 (0)	Screened for 2 consecutive weeks, 1 week post decolonization therapy	Topical decolonization for five days of nasal ointment and body and hair wash	Inferred for the period of decolonization but not stated	Suspected that this was a community introduced case by a patient 6 months prior to this outbreak. HCW acquired MRSA from a patient	Cheng *et al.* [35]

PVL-MRSA, Panton–Valentine leucocidin-producing meticillin-resistant *Staphylococcus aureus*; HCW, healthcare worker; ST, sequence type; ITU, intensive therapy unit; SSTI, skin/soft-tissue infection.

acute healthcare crisis situations such as during pandemics. Finally, prolonged surveillance screening and early systemic treatment needs consideration in managing HCW colonization irrespective of the presence or absence of skin lesions. These aspects of current UKHSA guidance on the management of staff colonized with PVL-MRSA require review.

Ethical approval
Informed consent was not gained from patients or members of staff involved in this outbreak. All patients were treated according to clinical judgement and infection control practices in order to treat them and control the outbreak according to local guidelines. Patients did not undergo randomization or intervention for the purpose of this report. Data has been analysed and presented fully anonymized. This publication constitutes a report of routine outbreak control procedures and does not constitute primary research. Ethical approvals were therefore not considered to be necessary.

Conflict of interest statement
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