Journal of Hospital Infection 139 (2023) 192–200

Available online at www.sciencedirect.com

Journal of Hospital Infection

journal homepage: www.elsevier.com/locate/jhin

Impact of a new hospital with close to 100% single-occupancy rooms on environmental contamination and incidence of vancomycin-resistant *Enterococcus faecium* colonization or infection: a genomic surveillance study

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ARTICLE INFO

Article history:
Received 12 May 2023
Accepted 29 June 2023
Available online 12 July 2023

Keywords:
Vancomycin-resistant enterococci
Genomics
Environment
Infection
Single occupancy
Colonization

SUMMARY

Background: Vancomycin-resistant *Enterococcus faecium* (VRE) is a leading cause of nosocomial infection, driven by its ability to spread between patients and persist in the hospital environment.

Aim: To investigate the impact of a long-established cardiothoracic hospital moving to new premises with close to 100% single-occupancy rooms on the rates of environmental contamination and infection or colonization by VRE.

Methods: Prospective environmental surveillance for VRE was conducted at five time-points between April and November 2019, once in the original building, and four times in the new building. Incidence rate ratios (IRRs) of VRE infection/colonization were determined for the one-year period before and after the hospital move, and compared to a nearby hospital.

Findings: In the original location, the first environmental screen found 29% VRE positivity. The following four screens in the new location showed a significant reduction in positivity (1–6%; $P<0.0001$). The VRE infection/colonization rates were halved in the new location (IRR: 0.56; 95% confidence interval: 0.38–0.84), compared to the original location, contrasting with an increase in a nearby hospital (1.62; 1.17–2.27) over the same time-period. Genomic analysis of the environmental isolates was consistent with reduced transmission in the new hospital.

Conclusion: The use of single-occupancy rooms was associated with reduced environmental contamination with VRE, and lower transmission and isolation of VRE from clinical samples. The cost-effectiveness of single-occupancy room hospitals in reducing

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https://doi.org/10.1016/j.jhin.2023.06.025

healthcare-associated infections should be reassessed in the context of operational costs of emerging pandemic and increasing antimicrobial resistance threats.

Introduction

Enterococcus faecium is a leading cause of nosocomial infection in immunocompromised and critically ill patients [1]. Its success as an opportunistic pathogen followed the emergence and worldwide dissemination of a hospital-adapted clade that is resistant to numerous antibiotics, including vancomycin, limiting treatment options, and is associated with an estimated 200,000 deaths per annum globally [2,3]. Reflecting its clinical impact and limited treatment options, the World Health Organization listed vancomycin-resistant *E. faecium* (VRE) as one of the high-priority pathogens for which new antimicrobials are urgently needed [4].

Underpinning its success is its ability to persist in hospital environments, which is a particular concern for immunocompromised patients, or those undergoing long hospital stays [5]. Levels of VRE contamination in the environment can vary greatly depending on setting and local prevalence, reaching almost 50% in hyperendemic settings [6]. Admission to a room previously occupied by a VRE-colonized patient has been shown to be an independent predictor of VRE acquisition [7]. Many items can become contaminated with VRE, including beds, baths, and keyboards, and spread of epidemic clones has been associated with contamination of communal toilets and shared medical devices such as mobile computer units or infusion pumps [6,8]. Molecular typing using traditional and genomic methods shows that VRE recovered from the near-patient environment is a surrogate for carriage strains, and may represent a viable surveillance strategy obviating the need for rectal screening to ascertain levels of patient colonization [6,9].

Alarmingly, rates of clinically significant VRE are rising globally as its control presents multiple operational challenges [10]. Enhanced hospital cleaning strategies have been shown to be effective at reducing rates of VRE infection consistent with the crucial role the environmental reservoir plays in nosocomial transmission. Effective interventions include enhanced terminal cleaning with hydrogen peroxide vapour fogging or bleach and ultraviolet (UV) light, and intensive routine and terminal cleaning programmes [11—14]. Control has also been achieved with bundles of interventions including VRE screening and isolation/single room contact precautions [15]. Institutions and units that instigate contact isolation of patients with VRE in single rooms experience lower rates compared to those that do not [16,17]. However, isolation may be impossible even in high-risk patient populations because demand may outstrip availability of single rooms, which are often prioritized for organisms of higher infection control consequence. In the absence of these intensive control methods, VRE can establish endemicity underpinned by multi-clonal direct or indirect patient-to-patient spread [6,18].

Evidence of the impact of single occupancy rooms in reducing hospital-associated colonization or infection rates with multidrug-resistant organisms is conflicting, being stronger for higher-dependency than for lower-acuity settings [19—21]. One study looked at the impact of remodelling an intensive care unit (ICU) from open-plan to single occupancy rooms, and found a 47% reduction in meticillin-resistant *Staphylococcus aureus* (MRSA) incidence, and a 43% reduction in *Clostridioides difficile* incidence, but found too few VRE for comparison [22]. To our knowledge, only two studies have investigated the effects of a move to a new building with 100% single rooms on incidence of VRE. A time-series analysis conducted in Canada investigated rates of VRE in patients before and after a hospital move to a new building, and found a decrease in both colonization (IRR: 0.25) and infection (IRR: 0.30) [23]. A study in the Netherlands performed environmental colony counts and swabbing for highly resistant micro-organisms (HRMOs) before and after a hospital move, following up over three years. That study found no change in total colony counts, but rather a reduction in swabs positive for HRMOs, from 3.3% to 0.1%, though too few VREs were found to make a comparison [24].

Our study has investigated the impact of a long-established cardiothoracic hospital moving to new premises with close to 100% single-occupancy rooms on the rates of environmental contamination and infection or colonization by VRE, and the genomic relatedness between environmental and clinical VRE isolates.

Methods

Study setting

Royal Papworth Hospital (RPH) is a 300-bed regional specialist cardiothoracic hospital serving the East of England, providing heart and lung transplantation, and an extracorporeal membrane oxygenation service. RPH moved to new premises, which, with the exception of one ward, consists almost entirely of single-occupancy rooms in April 2019, one of the first of its kind for the National Health Service (NHS) in England. The patient move was completed in stages within a one-week period. The new hospital was designed to reduce nosocomial transmission of opportunistic pathogens following concerns of *Mycobacterium abscessus* transmission among cystic fibrosis patients, despite the conventional infection control practices in place at the previous site [25]. The new building included a mechanical ventilation system providing 15 air changes per hour in cystic fibrosis patient areas (enhanced ventilation), or six air changes per hour in other clinical areas. By contrast, the original building dated from 1918 and had undergone multiple rounds of renovation and extension work, consisted mainly of traditional open-plan Nightingale-style multi-occupancy bays, and relied on natural ventilation through windows and doors. The environmental surveillance of this study concentrated on the critical care unit (CCU) and the cardiothoracic surgical ward, where patients are more prone to VRE infections.

In the original building, the CCU consisted of 27 beds in an open-plan ward consisting of four bays, and six single rooms (18%), with one sink to three beds. Each bed was individually nursed and had its own computer workstation. The surgical

ward had 44 beds in multi-bed bays with sinks at each bay and shared bathroom and toilet facilities in the corridors, and six single rooms (12%). In the new building, the CCU consists of 46 individual rooms separated by glass walls and doors, grouped into four sections. In addition, it houses six enhanced ventilation rooms with anterooms. All rooms have permanent computer workstations. The surgical ward consists of 42 beds, all of which are in single-occupancy rooms with private toilet and shower facilities. In both units, most of the hospital beds, furniture and computers were new, but some equipment, including hospital beds, was transferred from the old site, following decontamination with Actichlor.

Infection control procedures

No significant changes in infection control procedures (cleaning, handwashing regimens, VRE screening) or antimicrobial stewardship policies occurred between the two locations, with the exception that six-monthly hydrogen peroxide vapour cleans in the original CCU were discontinued on moving to the new hospital. There were no changes in nurse-to-patient ratios. Routine daily and terminal cleans were performed using Actichlor (1:1000 ppm chlorine). VRE screening using rectal swabs was limited to: (i) admission screening for patients transferred from other critical care facilities; (ii) admission screening for patients admitted for ventricular assist device insertion, then repeated weekly. In the original hospital, due to the limited availability of single rooms which were prioritized for other multidrug-resistant organisms such as MRSA or carbapenemase-producing organisms, and infective diarrhoeal or respiratory viral illnesses, patients positive for VRE were not isolated, though enteric precautions were observed.

Environmental screening

The hospitals were screened for VRE in the environment on five separate time-points between April and October 2019. The original hospital was screened one week prior to the patients moving to the new hospital. The new hospital was screened: one day before opening to patients, one week after completion of patient transfer from the original hospital, and repeated one month and six months later. A planned one-year follow-up screen could not be completed due to restrictions following the onset of the COVID-19 pandemic. On each occasion, 100 swabs were taken, divided evenly between the surgical ward and the critical care unit.

Environmental sampling was adapted from a previously described method, including pooling up to three high-frequency touch areas [6]. Flocked swabs (FLOQSwabs; Copan, Brescia, Italy), pre-moistened in SRK® (detergent-neutralizing) transport solution, were used to sample a standardized area of $\sim$10 cm^2, first in one direction, then again perpendicular to the first direction. In the surgical wards, one swab ('bed space') was used for the bed rail, bedside table, and bedside locker if present. Toilets in communal bathrooms were swabbed on the toilet handle followed by the toilet seat. In addition, showers were swabbed if present in the communal bathrooms. In the surgical ward of the new hospital, each bed space had a private toilet, and each of these was screened with a second swab as above. Other areas screened were sluices (macerator and sink) and portable workstations (mouse and keyboard). In the CCU, two swabs were used for each bed space. The first for the bed area (bed rail, bedside table, bedside locker), and the second for the bedside computer (mouse and keyboard). As before, sluices and portable workstations were also screened. Wherever possible, bed spaces currently occupied by patients were prioritized.

Each swab was placed in 10 mL Enterococcosel Broth (BD, Oxford, UK) containing 6 mg/L vancomycin to select for vancomycin-resistant enterococcus, then incubated in air for up to 72 h at 37 °C. Controls were performed using vancomycin-resistant and vancomycin-susceptible enterococci. For any broths that turned black (indicating growth of enterococcus), 100 μL was sub-cultured on to a Brilliance VRE agar plate (Oxoid, Basingstoke, UK) and incubated overnight in air at 37 °C. If purple (presumptive *E. faecium*) or blue (presumptive *E. faecalis*) growth was observed, a single colony was selected and sub-cultured on to Columbia blood agar (Oxoid) for overnight incubation at 37 °C, then stored at −80 °C in a microbank vial containing glycerol (Pro-lab Diagnostics, Wirral, UK). DNA was extracted using the QIAcube (Qiagen, Hilden, Germany). DNA libraries were prepared and sequenced on an Illumina HiSeq2000 with 150 bp paired-end runs.

Data were collected on the number of hospital admissions and VRE cases for one year before and after the hospital move from electronic hospital data systems.

Clinical isolates

From February 2019 to February 2020, VRE and vancomycin-susceptible (VSE) cultures isolated from VRE screening or clinical infection samples obtained as part of routine clinical care were collected from the diagnostic laboratory. *E. faecium* was identified to species level using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (Bruker Daltonics, Coventry, UK) and antimicrobial susceptibility testing was performed using disc diffusion testing and interpreted according to European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines. These isolates were stored and sequenced as described above.

Statistical analysis

Data on total numbers of VRE clinical infections/VRE carriage in the hospital was collected for one year pre- and post-move, deduplicated for each of the two time-periods, along with number of occupied bed-days. Institutional VRE rates expressed as the number of VRE-positive patients per 10,000 bed-days in a month, for a year before and after the move, were compared using regression analysis. Incidence rate ratios (IRR) were calculated with 95% confidence intervals (CI) comparing the two periods. A similar analysis was performed for a neighbouring teaching hospital, Cambridge University Hospitals NHS Foundation Trust (CUH), which has a 25% single-occupancy room capacity, to control for regional trends. The difference in proportion of positive environmental swabs between different time-points was analysed using a two-sample *Z*-test. The difference in the number of environmental samples genetically related to other environmental samples before and after the move was analysed using Fisher's exact test. All analyses were performed using Stata/IC, version 14.2 (StataCorp, College Station, TX, USA).

Contextual collections

A total of 2077 *E. faecium* genomes were analysed in this study: 40 environmental plus 53 clinical from RPH; deduplicated subset of 1134 *E. faecium* isolates from a One Health study from a variety of sources (livestock and meat, wastewater treatment plants, and bloodstream infections) in the UK in 2014–15; and 847 isolates from a UK haematology study, performed in 2015 in a neighbouring hospital where multiple *E. faecium* isolates were sequenced per patient, and was thus deduplicated to keep only one isolate per subtype in each patient (see definition of *E. faecium* subtype in Methods) [6,26].

Genomics and phylogenetic analyses

Draft assemblies were generated using an automated de-novo assembly pipeline based on Spades v3.10.0 and annotated using Prokka v1.11 [27–29]. Multi-locus sequence typing (MLST) was determined from de-novo assemblies using MLST Check (https://github.com/sanger-pathogens/mlst_check) with novel alleles and sequence types (STs) deposited in the pubMLST website (https://pubmlst.org/efaecium/). Presence of *van* genes in all RPH isolates was confirmed using ARIBA v2.14.6 using the DNA sequences of the *vanA* operon downloaded from CARD (GenBank accession: M97297.1) [30,31]. Eight genomes with a total assembly length of >3.3 Mb (i.e. clear outliers) were excluded from further analysis based on potential contamination. Reads were mapped to the *E. faecium* Aus0004 strain (CP003351) reference genome using Snippy v4.6.0 (https://github.com/tseemann/snippy). Whole-genome alignments were created by keeping a version of the reference genome with only substitution variants (i.e. single nucleotide polymorphisms (SNPs) but not indels) replaced. The *E. faecium* core genome was computed using Panaroo v1.2.3 with strict stringency mode, but using an independent and diverse strain collection of 1432 isolates obtained from livestock ($N = 256$), wastewater treatment plants ($N = 383$), and bloodstream infections ($N = 782$) in the UK [26,32]. A core-genome alignment was created by keeping the core-genome regions (total length: 1,634,019 bp) from the reference whole-genome alignment (length: 2,955,294 bp). This core-genome was used to create a maximum likelihood tree using IQ-TREE v1.6.10 with the extended model selection followed by tree inference (-m MFP) and 1000 ultrafast bootstraps (-bb 1000). When this tree was annotated with the clade assignation of contextual isolates, this helped identify the split between clades B and A, and clade A1. A whole-genome alignment of clade A1 isolates only was used for further analyses. Recombination events were detected using Gubbins v1.4.10, using a clade B isolate as an outgroup and an IQ-TREE phylogenetic tree as the starting tree [33]. The clade A1 whole-genome alignment was manipulated to mask recombination regions detected by Gubbins and annotated MGEs. IQ-TREE was used to produce the final clade A1 phylogenetic tree from this alignment. Pairwise SNP distances were calculated from this alignment to avoid counting SNPs at MGE or recombinogenic regions. The final IQ-TREE phylogenetic tree and pairwise SNP distances were used to define monophyletic clades (hereafter referred to as 'sub-types') using a phylogenetic clustering approach (https://github.com/francesccoll/phylogenetic_clustering), with a minimum bootstrap support of 70% and a maximum SNP distance of 20 SNPs as previously done [6]. Trees were plotted using ggTree v3.0.2 [34].

Ethics

The study was conducted under ethical approval from the National Research Ethics Service (reference no. 12/EE/0439) and the Cambridge University Hospitals NHS Foundation Trust (CUH) Research and Development Department (reference no. A092685).

Results

Environmental screening

The results of the environmental screening swabs are summarized in Table I. In total, 40 environmental swabs were positive for vancomycin-resistant *E. faecium*, the majority of which (28/40, 70%) were from the single screen in the old hospital. Of the repeated screens in the new building, none of the positive locations were the same between separate screens. There was a significant reduction in positivity between the first two time-points from 28.9% pre-move to 1.0% post-move ($P < 0.001$). There was no significant difference in positivity between time-points in the new location (time-points 2 to 3, $P = 0.576$; time-points 3 to 4, $P = 0.320$; time-points 4 to 5, $P = 0.651$).

Table I
Proportion and location of environmental swabs positive for VRE for each screening time-point

Location	Time of screening	Swabs VRE positive	CCU	Surgical ward
Original hospital	One-week pre-move	28/97 (28.9%)	5 bed space pairs (bed area and computer) 2 bed areas 4 computers	6 bed areas 1 side room pair (bed and toilet) 1 sluice (macerator and sink) 2 communal bathrooms
New hospital	One-day pre-move	1/100 (1.0%)		1 macerator
New hospital	One-week post-move	6/102 (5.9%)	1 bed space pair (bed area and computer) 1 bed area 1 macerator	1 bed area 1 portable workstation
New hospital	One-month post-move	3/100 (3.0%)		1 bed area 2 toilets
New hospital	Six months post-move	2/100 (2.0%)		1 bed space pair (bed and toilet)

VRE, vancomycin-resistant *Enterococcus faecium*; CCU, critical care unit.

VRE rates of infection/carriage

Prior to the move, the rate of VRE infection/carriage was 10.9 cases per 10,000 bed-days (95% CI: 8.2–13.7). During the year following the move, the rate of VRE infection/carriage was nearly halved, to 6.2 cases per 10,000 bed-days (95% CI: 3.8–8.5), IRR 0.56 (95% CI: 0.38–0.84; $P = 0.005$). To determine whether the drop in VRE rates was unique to RPH or represented a regional trend, data was also collected for neighbouring Cambridge University Hospitals NHS Foundation Trust (CUH). During the year following RPH's move, the rate of VRE infection/carriage at CUH increased with IRR 1.62 (95% CI: 1.17–2.27; $P<0.005$) (Figure 1).

Isolate relatedness

The environmental ($N = 40$) and clinical ($N = 53$) *E. faecium* isolates from RPH sequenced in this study were combined with two independent collections to assign their clade and delineate transmitting clones in the context of a wider collection. A total of 1134 genomes from a one-health study in the UK and 847 isolates from an UK haematology study were included [6,26] (Supplementary Table S2). A core-genome phylogeny of both RPH and contextual isolates ($N = 2069$) confirmed that all RPH isolates belonged to the hospital-adapted clade A1. Most were positive for *vanA* (84%) and ST80 was the commonest sequence type (66%). Full details are given in Supplementary Table S1. Next a phylogenetic tree of all clade A1 isolates ($N = 1700$) was built, after masking regions of recombination and mobile genetic elements, and a clustering approach was applied to define subtypes as previously described [6]. This enabled quantification of the diversity of subtypes in this population, which amounted to 732 different subtypes (208 clusters and 524 singletons), of which 42 were represented among RPH isolates (Figure 2).

Pairwise SNP distances among RPH isolates only (i.e. environmental isolates and the clinical isolates dated from two months pre-to 11 months post-move) were computed and a genetic relatedness cut-off of $\leq$6 SNPs was applied to capture recent transmission and define transmission clusters, as previously proposed [6]. Eight clusters with at least one environmental sample were found, containing two to 12 related isolates (Table II, Figure 2). In addition to genetic links, most clusters (six out of eight) were epidemiologically related (Figure 3), whereas no epidemiological relationships could be found for the remaining two clusters.

Cluster 3

Cluster 3 (Figure 3) involved eight isolates, found in both wards of the original and in the new hospital. V051 and V052 came from a bed space and toilet, respectively, in a single side room in the original surgical ward. V155 originated from a macerator that had been transferred from the original hospital to the new surgical ward. V044 was isolated from a bed space of the original CCU, EFM0055 came from a patient in the same ward. V284 was isolated from a bed space in the new CCU two weeks later. V232 and V235 both came from the new surgical ward, from a workstation located in the corridor, and a bed space respectively.

Cluster 5

Cluster 5 involved several isolates from the original and new surgical wards. Six environmental samples and one patient

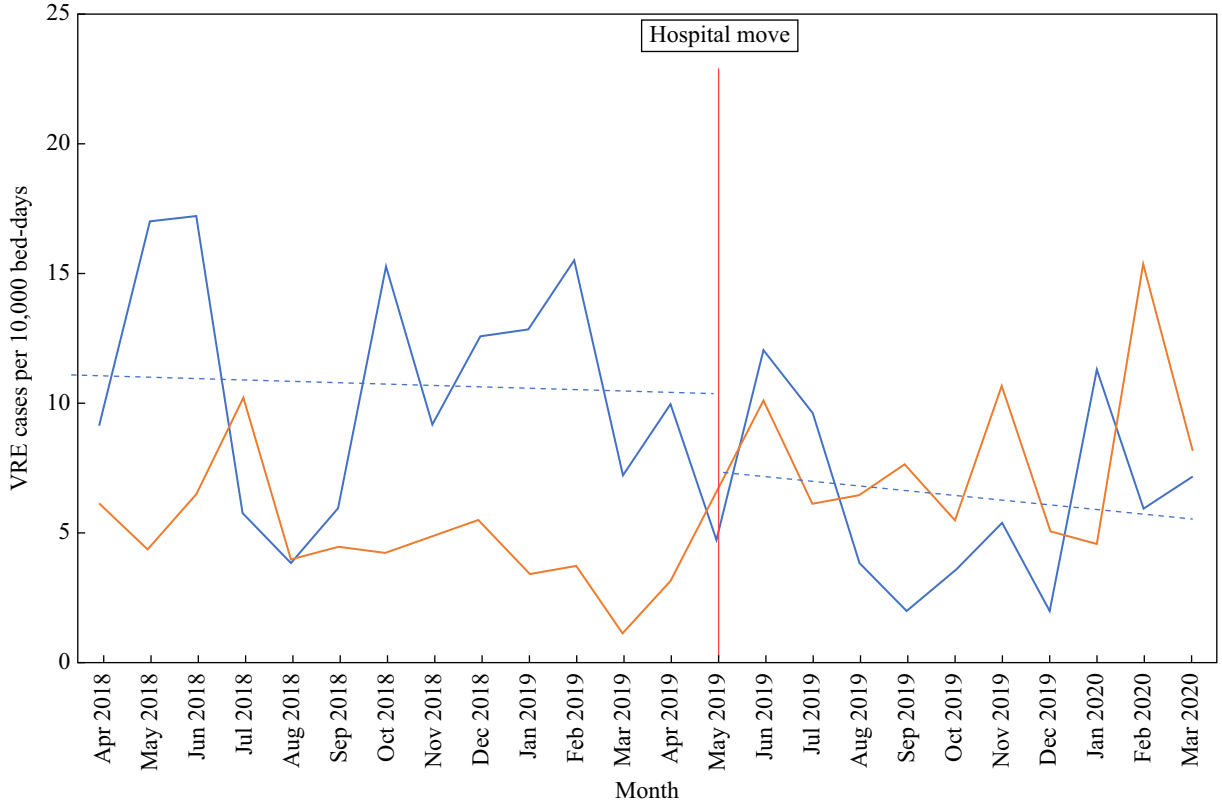

Figure 1. Rate of vancomycin-resistant *Enterococcus faecium* (VRE) carriage or infection per 10,000 bed-days, one year pre- and post-move at Royal Papworth Hospital (blue), compared with Cambridge University Hospitals (orange) during the same time-period.

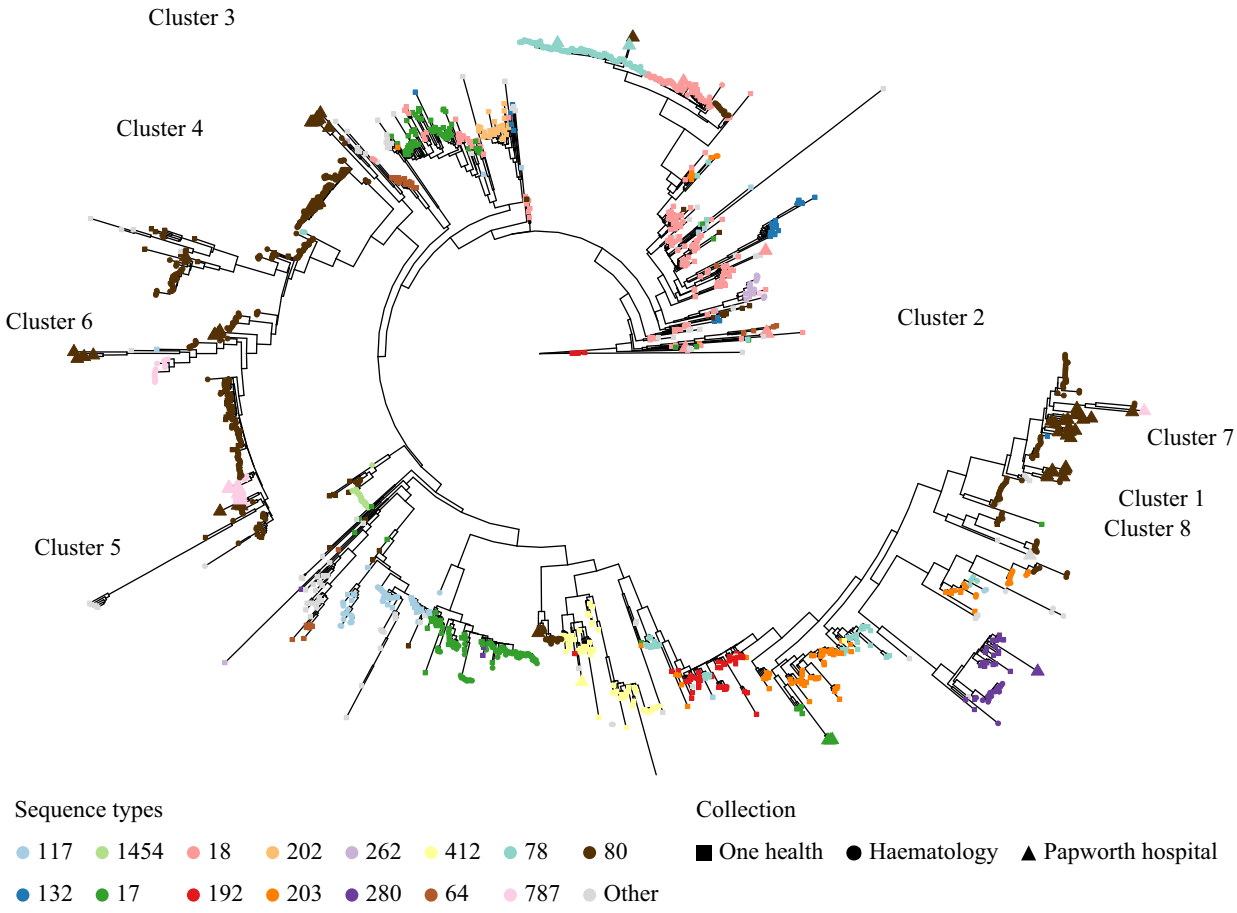

Figure 2. Phylogenetic tree highlighting related clusters in the context of a wider local collection of farm, wastewater and hospital isolates. Phylogeny of 1700 clade A1 *E. faecium* isolates including 88 (47 clinical and 40 environmental) from Royal Papworth Hospital (RPH) and 1612 contextual from recent collections (850 from one-health and 762 from clinical study in neighbouring hospital). Subtypes containing RPH isolates are highlighted with light blue. The tips of the tree are colour-coded by sequence types; only the most common ones (found in >10 isolates) are coloured, while the rest are labelled as 'other' and shown in grey. The shape of tips denotes the origin of the collection isolates. The phylogenetic positions of the nine epidemiological clusters involving RPH isolates (summarized in Table II) are also indicated.

sample came from the original surgical ward one week before the move, and two were found in the new CCU one month after the move. In addition, a further macerator was positive in the new CCU, which had been transferred from the previous location, along with three isolates from a single patient in CCU.

This study then examined the degree of genetic relatedness among environmental isolates before and after the move as a surrogate for the extent of transmission. We assumed that a higher degree of genetic relatedness among environmental isolates — as shown by isolates being genetically linked (≤6 SNPs) to other environmental isolates in the same hospital or a lower number of unique subtypes identified — would indicate a higher degree of transmission. It was found that environmental isolates in the original hospital were more often related (25/28, 89%) to other environmental isolates in the same hospital than those in the new hospital (8/12, 67%), although this was not statistically significant ($P = 0.168$, Fisher's exact test). Accordingly, the degree of diversity (number of unique subtypes) among environmental isolates was lower in the original hospital (eight unique subtypes among 28 isolates) compared to the new one (seven unique subtypes among 12 isolates). Overall, these results point to a reduced transmission in the new hospital.

Discussion

In this natural experiment, we investigated the impact of a hospital move to new premises with close to 100% single-occupancy rooms on rates of VRE, using environmental, epidemiological and genomic approaches. An immediate and marked reduction in levels of VRE contamination was detected in the environment of the CCU and the cardiothoracic ward from 29% to <6%, which was sustained for six months of study follow-up. In addition, the rate of VRE carriage/infection almost halved in the year following the move, from 10.9 to 6.2 cases per 10,000 bed-days, by contrast with a neighbouring hospital where rates increased during the same time-period. Analysis of whole-genome sequencing data revealed that there was some carryover of clones between the two locations but that this was consistent with reduced transmission in the new hospital as evidenced by a higher diversity of VRE subtypes. Together, these results are consistent with the importance of the built environment in reducing contamination and transmission of VRE, in particular the creation of segregated bed spaces, en-suite facilities, and the installation of a new ventilation system. These reductions could be explained by

Table II
Clusters of genetically related isolates

Cluster	No. of SNPs apart	Isolates	Location	Time related to hospital move
1	0–1	V064, V065, V095	Original surgical ward	One week prior
2	1–4	V285	New CCU	One week post
		V360	New surgical ward	One month post
3	1–5	V051, V052	Original surgical ward	One week prior
		V044, EFM055	Original CCU	One week prior
		V155	New surgical ward	One day prior
		V284	New CCU	One week post
		V232, V235	New surgical ward	One week post
4	1–3	V016, V031, V033, V038, V040, V043, EFM0075	Original CCU	One week prior
		V296	New CCU	One week post
5	0–5	V061, V062, V066, V076, V083, V084	Original surgical ward	One week prior
		V268, EFM0084	New CCU	One week post
		V356, V393	New surgical ward	One month post
6	2–6	V011, V012, V019, V020, V032	Original CCU	One week prior
7	1–3	V003, V004, EFM0033	Original CCU	One week prior
8	2	V001	Original CCU	One week prior
		EFM0017	Original CCU	Two months prior

SNP, single nucleotide polymorphism; CCU, critical care unit.

fewer opportunities for patient-to-patient direct contact, or indirect contact via contaminated communal environment such as shared toilets. There is still an opportunity for transfer of VRE via contaminated healthcare worker hands, via contaminated shared equipment, or from inadequate decontamination of the room from a previously colonized prior occupant; therefore single-occupancy rooms are not a substitute for infection control procedures such as disinfection and handwashing.

Hospitals with single-occupancy rooms have been mandated in the USA for many years, and are accepted as the norm in many European countries. England has been slow to adopt this, although the COVID-19 pandemic has reignited the public debate and re-emphasized their potential advantages in terms of infection control and operational capacity including patient-flow, in addition to accepted benefits for patient privacy and dignity [35]. Single-occupancy rooms represent a 'horizontal' infection control intervention that has the potential to impact not only VRE and other multidrug-resistant pathogens, but also respiratory and gastrointestinal viral spread in hospitals.

Our study has several limitations. We had originally planned to perform another environmental screen one year after the

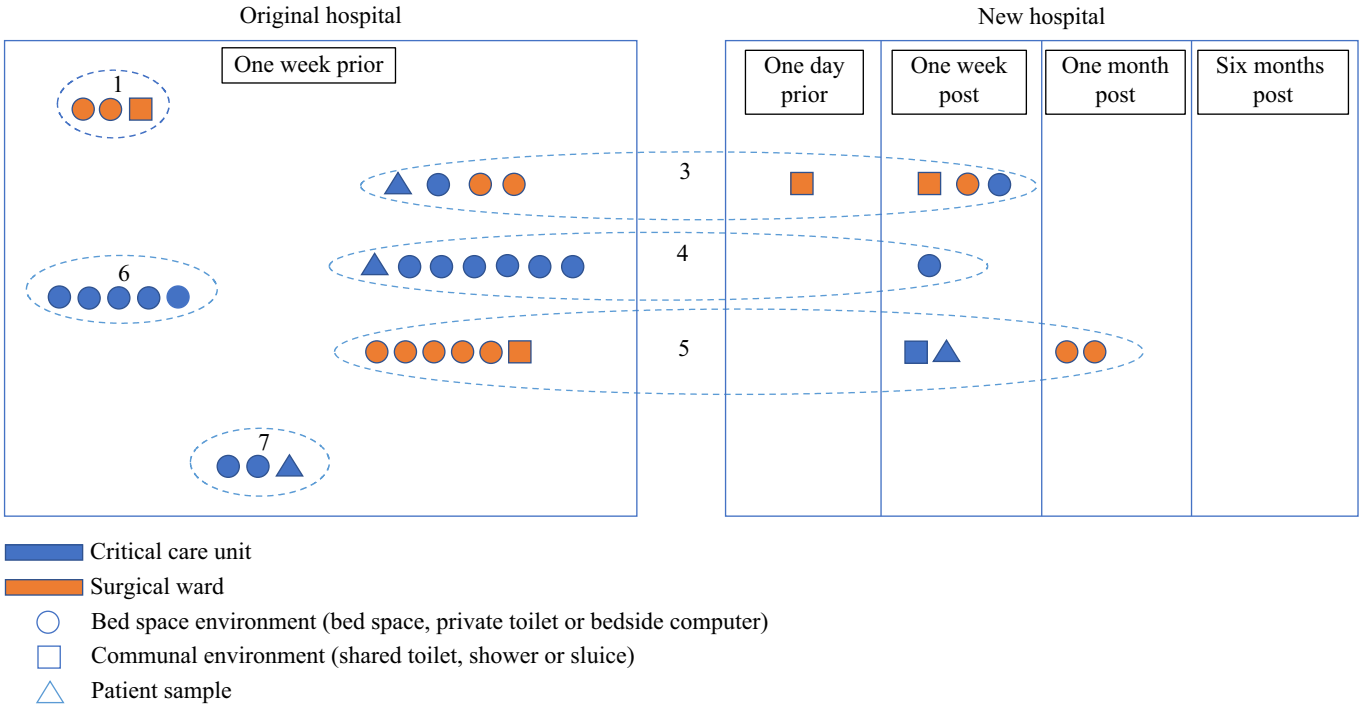

Figure 3. Location and timing of six clusters of genetically and epidemiologically related environmental and patient samples.

move, but this could not be completed due to the onset of the SARS-CoV-2 pandemic. Not every bed space was swabbed in the two wards, prioritizing bed spaces occupied by patients. Therefore, it is possible that total positivity was underestimated. VRE carriage screening was only undertaken in a limited number of patients, so the true VRE incidence in hospital was likely underestimated. In addition, we were unable to differentiate colonization from infection. Instead of carriage, environmental contamination was used, which has been shown to be a good surrogate. Adherence to infection control procedures was not formally assessed, although hospital audit data showed no notable differences in adherence to cleaning or handwashing standards. The study was conducted in a highly specialized population, which may limit the generalizability of the conclusions. Nevertheless, the reduction in clinical VRE rates was comparable to that noted in a recent study in a general hospital population in Canada [23]. Strengths of this study include the combined epidemiological, environmental and genomic analyses all converging to the same conclusion, and the use of control data from a nearby teaching hospital, which experienced a rise in VRE rates over the same time-period.

In conclusion, this hospital move created a unique opportunity to investigate the effect of improved building controls on VRE environmental contamination levels and associated patient VRE carriage and transmission. We have shown that the move to the new building with close to 100% single-occupancy rooms was associated with a reduction in environmental contamination. This information should be of particular importance for units serving vulnerable patients such as critically ill or immunocompromised populations that are susceptible to VRE infections. More broadly, the cost-effectiveness of single-occupancy room hospitals in reducing healthcare-associated infections should be reassessed in the context of operational costs of emerging pandemic and antimicrobial resistance threats.

Acknowledgements

The authors would like to thank A. Akram and C. Churcher for their help in sample collection.

Author contributions
B.B., T.G., and S.J.P. designed the study, which was supervised and managed by TG. B.B. and T.G. were responsible for the environmental screening. B.B. performed the laboratory work. B.B. and K.R. collected patient data. F.C., K.R., and B.B. did the epidemiological and bioinformatic analyses. O.A., R.M.K., S.P., and R.A.F. provided access to the wards, supported the study, and provided data. All authors had access to all the data in the study. B.B., T.G., and F.C. wrote the first draft of the article, which was revised and approved by all authors.

Conflict of interest statement
None declared.

Funding sources
This publication presents independent research supported by the Health Innovation Challenge Fund (WT098600, HICF-T5-342), a parallel funding partnership between the Department of Health and Wellcome Trust. The views expressed in this publication are those of the author(s) and not necessarily those of the Department of Health or Wellcome Trust. F.C. reports funding from the Wellcome Trust (LSHTM/Wellcome Institutional Strategic Support Fund Fellowship [204928/Z/16/Z]. K.R. was supported by an ESCMID Research Grant (ref. 15996).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhin.2023.06.025.

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