Infection Control & Hospital Epidemiology (2023), **44**, 31–39
doi:10.1017/ice.2022.57

SHEA

Original Article

Synergistic effects of length of stay and prior MDRO carriage on the colonization and co-colonization of methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus*, and carbapenemase-producing Enterobacterales across healthcare settings

Htet Lin Htun MPH[1], Pei-Yun Hon MSc[1], Rei Tan MBBS (Year 5)[2], Brenda Ang MPH[2,3,4] and Angela Chow PhD[1,4,5]

[1]Department of Clinical Epidemiology, Office of Clinical Epidemiology, Analytics and Knowledge (OCEAN), Tan Tock Seng Hospital, Singapore, [2]Yong Loo Lin School of Medicine, National University of Singapore, Singapore, [3]Department of Infectious Diseases, Tan Tock Seng Hospital, Singapore, [4]Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore and [5]Saw Swee Hock School of Public Health, National University of Singapore, Singapore

Abstract

Objective: To characterize the epidemiology of methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), and carbapenemase-producing Enterobacterales (CPE) co-colonization and to compare risk factors between healthcare facility types.

Design, setting, and participants: We conducted a 3-year cross-sectional study among patients admitted to an acute-care hospital (ACH) and its 6 closely affiliated intermediate- and long-term care facilities (ILTCFs) in Singapore in June and July of 2014–2016.

Methods: Specimens were concurrently collected from nares, axillae, and groins for MRSA detection, and from rectum or stool for VRE and CPE detection. Co-colonization was defined as having >1 positive culture of MRSA/VRE/CPE. Multinomial logistic regression was performed to determine predictors of co-colonization.

Results: Of 5,456 patients recruited, 176 (3.2%) were co-colonized, with higher prevalence among patients in ITCFs (53 of 1,255, 4.2%) and the ACH (120 of 3,044, 3.9%) than LTCFs (3 of 1,157, 0.3%). MRSA/VRE was the most common type of co-colonization (162 of 5,456, 3.0%). Independent risk factors for co-colonization included male sex (odds ratio [OR], 1.96; 95% confidence interval [CI], 1.37–2.80), prior antibiotic therapy of 1–3 days (OR, 10.39; 95% CI, 2.08–51.96), 4–7 days (OR, 4.89; 95% CI, 1.01–23.68), >7 days (OR, 11.72; 95% CI, 2.81–48.85), and having an open wound (OR, 2.34; 95% CI, 1.66–3.29). Additionally, we detected the synergistic interaction of length of stay >14 days and prior multidrug-resistant organism (MDRO) carriage on co-colonization. Having an emergency surgery was a significant predictor of co-colonization in ACH patients, and we detected a dose–response association between duration of antibiotic therapy and co-colonization in ILTCF patients.

Conclusions: We observed common and differential risk factors for MDRO co-colonization across healthcare settings. This study has identified at-risk groups that merit intensive interventions, particularly patients with prior MDRO carriage and longer length of stay.

(Received 13 December 2021; accepted 21 February 2022; electronically published 30 March 2022)

The increasing incidence of infections associated with multidrug-resistant organisms (MDROs) is one of the most pressing public health problems globally in the 21st century, and is of importance not only in acute-care hospitals (ACHs) but also in intermediate- and long-term care facilities (ILTCFs).[1] Infections caused by MDROs are estimated to increase clinical and economic adverse outcomes by 2-fold compared with similar infections caused by susceptible strains of the same organism.[2,3]

Author for correspondence: Angela Chow, E-mail: angela_chow@ttsh.com.sg
Cite this article: Htun HL, *et al.* (2023). Synergistic effects of length of stay and prior MDRO carriage on the colonization and co-colonization of methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus*, and carbapenemase-producing Enterobacterales across healthcare settings. *Infection Control & Hospital Epidemiology*, 44: 31–39, https://doi.org/10.1017/ice.2022.57

The healthcare environment has been identified as a major reservoir of multiple MDROs such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), and more recently carbapenemase-producing Enterobacterales (CPE).[4–9] MRSA infections have previously been successfully treated with vancomycin, a glycopeptide antibiotic, until the emergence of vancomycin-intermediate *Staphylococcus aureus* (VISA), followed by vancomycin-resistant *Staphylococcus aureus* (VRSA).[10] Since 1996, infections caused by VISA and heterogeneous VISA (hVISA) have been reported in tertiary-care hospitals in developed countries, including Singapore.[11–14] VRSA occurs when MRSA acquires a *vanA* gene through genetic conjugation with VRE from studying the specimens collected from patients co-colonized with MRSA/VRE.[15] In a study involving an interconnected healthcare network in

Singapore, the prevalence of *vanA* was very high (94% of total VRE isolates) across healthcare settings.[5] The prevalence of CPE has also been rising over the years, especially in ACHs.[7]

Many previous studies were conducted to explore the occurrence and risk factors of co-colonization, especially MRSA/VRE, in specific healthcare settings such as ACHs, LTCFs, or intensive care units. However, to date, information has been limited on the comparative epidemiology of co-colonization between patients from different healthcare settings. Thus, assessments of facility-specific determinants at which targeted interventions could be developed are lacking. Furthermore, sparse data are available for co-colonization rates of CPE in addition to MRSA/VRE.

We contemporaneously compared the epidemiology of MDROs co-colonization among patients from 7 different but interconnected healthcare facilities. We sought to identify common and differential risk factors between facility types that might serve to define at-risk groups for whom targeted infection prevention and control efforts could be implemented.

Methods

Study design, setting, and participants

We conducted a serial cross-sectional surveillance study over 6 weeks during June–July for 3 consecutive years from 2014 to 2016 in a 1,700-bed, adult, tertiary, acute-care hospital (ACH) in Singapore and its 3 closely affiliated intermediate-term care facilities (ITCFs): a 100-bed rehabilitation center, a 360-bed community hospital, and a 116-bed community hospital. This health system also includes 3 long-term care facilities (LTCFs): a 234-bed nursing home, a 164-bed chronic illness unit, and a 236-bed nursing home (open since 2015). Stratified sampling for patients admitted to the ACH with a ≥48-hour stay proportional to the bed census of the ward was performed, although we included all residents of the ITCFs and LTCFs who consented to participate in the study. The ITCFs, also known as community hospitals, provide medical, nursing, and rehabilitation care for patients who require a short period of continuing care, usually after discharge from an ACH. The LTCFs (or nursing homes) provide care for long-staying residents who require long-term assistance and nursing care with most of their activities of daily living.

Microbiological analysis

We concurrently collected the specimens including separate nasal, axillary, and groin swabs to investigate for MRSA, and we collected rectal swabs (or stool samples from participants who declined rectal swab) to screen for VRE and CPE, on the same day. Methodological details of laboratory investigations were reported in our previous publications,[4,5,7,16] with a brief description provided in the supplementary methods. Participants whose specimens did not yield any bacterial isolation were classified as non-colonized. We have previously reported the risk factors in single pathogen-specific studies.[4,5,7] In this study, we focused on the co-colonization of the pathogens and classified patients as co-colonized if they had >1 positive culture of MRSA, VRE, and/or CPE in their concurrent specimens. We classified patients as singly-colonized otherwise.

Data collection and quantitative variables

We collected several groups of study data. First, we collected demographics (age, sex, ethnicity) and comorbidities (cerebrovascular disease, congestive cardiac failure, connective tissue disease, chronic pulmonary disease, diabetes mellitus, myocardial infarction, peptic ulcer disease, peripheral vascular disease, chronic renal disease, and human immunodeficiency virus infection) to obtain the Charlson's comorbidity index (CCI) and categorized it into ≤5 and >5. We included the use of percutaneous devices and peripheral lines in the preceding 12 months. The variables of interest from the current admission included length of stay (LOS) at the time of specimen collection, healthcare facility type, and number of beds per room. We also ascertained prior admission to intensive care unit or any healthcare facilities in the preceding 12 months; prior MRSA, VRE and carbapenemase-resistant Enterobacterales (CRE) colonization in the 12 months preceding screening. Other patient data included prior antibiotic use in the preceding 12 months including aminoglycoside, carbapenem, cephalosporin, fluoroquinolone, penicillin and vancomycin; prior emergency surgery in preceding 12 months; any type of surgical treatment in the preceding 90 days; and presence of open wounds in the preceding 12 months, based on published literature.[17,18] Prior antibiotic use was further categorized into 0, 1–3, 4–7, and >7 days of therapy (DOT).

Data were collected electronically from the ACH and ILTCF electronic medical records (EMRs). In the ILTCFs where EMR data were unavailable, clinical data were collected manually from paper-based medical records by trained research assistants in a standardized fashion.

Statistical analysis

Characteristics of patients were described with frequencies and percentages for categorical variables, mean and standard deviation (SD), and median and interquartile range (IQR) for continuous and ordinal variables, respectively. The differences among the non-colonized group, the single colonization group, and the co-colonized groups were compared using the Pearson's χ^2 test or the Fisher's exact test for categorical variables. We used the one-way ANOVA test or Kruskal-Wallis test for continuous variables. Multinomial logistic regression was performed to estimate odds ratios (ORs) and calculate 95% confidence intervals (CIs). Significant variables from descriptive statistical analysis were used to build a multivariable model. Model 2 (full model) included the following variables: age >65 years, sex, year screened, CCI > 5, any percutaneous devices, peripheral line, LOS >14 days, admitted healthcare facility, number of beds per room, prior ICU admission, prior hospital/ILTCFs admission, prior carriage of MRSA/VRE/CRE, days of antibiotic therapy, prior emergency surgical care, surgical care in the past 90 days, and open wounds. Next, these variables were considered for inclusion in the subsequent multivariable model in backward stepwise selection, that is, model 3 (stepwise model). Although we adjusted for age, sex, and year in the stepwise model, other variables were retained only if $P < .05$. We further explored the interaction between prior carriage of MRSA/VRE/CRE and LOS >14 days in model 4 (final model) along with the variables included in model 3. Additionally, we performed a multinomial logistic regression stratified by healthcare facility (ACH vis-à-vis ILTCFs) using explanatory variables from model 4. All reported *P* values were 2-tailed with an α level of 0.05. All statistical analyses were performed using Stata version 13.1 software (StataCorp College Station, TX).

Ethics approval

The study was approved by the Domain Specific Research Board, National Healthcare Group (reference no. 2014/01139). Informed

https://doi.org/10.1017/ice.2022.57 Published online by Cambridge University Press

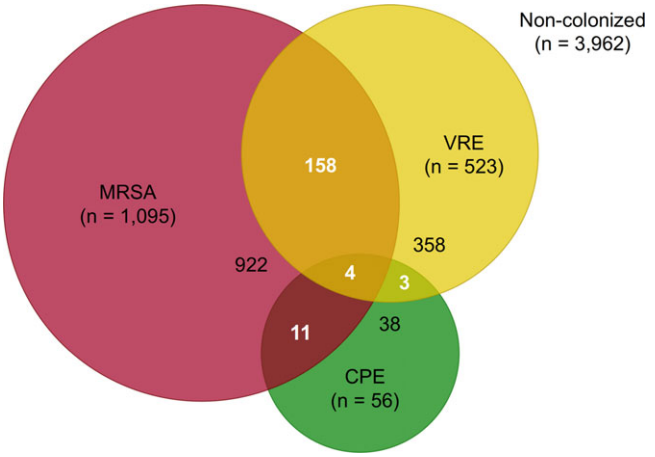

Fig. 1. Diagrammatic presentation of colonization status among study participants. Non-colonized (n = 3,962, 72.6%); singly-colonized with MRSA (n = 1,095, 20.1%), with VRE (n = 523, 9.6%), and with CPE (n = 56, 1.0%); and co-colonized with MRSA/VRE (n = 162, 3.0%), VRE/CPE (n = 7, 0.1%), MRSA/CPE (n = 15, 0.3%), and MRSA/VRE/CPE (n = 4, 0.1%). Note. CPE, carbapenemase-producing Enterobacterales; MRSA, methicillin-resistant *Staphylococcus aureus*; VRE, vancomycin-resistant enterococci.

consent was provided by all cognitively intact participants or the legally authorized representatives (LARs) of cognitively impaired participants. A waiver of informed consent was granted for cognitively impaired participants from the ILTCFs who had no LAR.

Results

Characteristics of patients

From 2014 to 2016, we recruited 5,456 patients, and 1,494 (27.4%) were colonized with 1 or more MRSA/VRE/CPE: 1,318 (24.2%) were singly-colonized versus 176 (3.2%) who were co-colonized. MRSA/VRE was the most common type of co-colonization among our study participants (n = 162, 3.0%). Period prevalence of CPE co-colonized with MRSA and/or VRE was very low (0.1%–0.3%) (Fig. 1). Single colonization was most common in ITCF patients (n = 458, 36.5%), whereas co-colonization was equally frequent among ACH patients (n = 120, 3.9%) and ITCF patients (n = 53, 4.2%) but was very infrequent in LTCF patients (n = 3, 0.3%; $P < .001$) (Supplementary Table 1 online).

Patients with the following factors were more likely to be co-colonized: older, male, or had a higher CCI, a percutaneous device, a peripheral line, prior admission to ACH or ILTCF, prior carriage of MRSA/VRE/CRE, prior and longer DOT of antibiotics, prior emergency surgery, surgery in the preceding 90 days, and/or an open wound. A longer LOS was observed more frequently both in singly and co-colonized patients compared to non-colonized patients (Table 1).

Risk factors for colonization

In the multinomial logistic regression analysis, the reference category was non-colonized patients. First, after adjusting for age, year of screening, healthcare facility and prior emergency surgery, the following risk factors were associated with single colonization: male sex (OR, 1.41; 95% CI, 1.22–1.62), prior use of a percutaneous device (OR, 1.42; 95% CI, 1.22–1.65), 2–4 beds per room (OR, 1.18; 95% CI, 0.81–1.73), 5–8 beds per room (OR, 1.73; 95% CI, 1.30–2.29), and >8 beds per room (OR, 1.67; 95% CI, 1.21–2.31), 1–3 DOT of antibiotics (OR, 1.17; 95% CI, 0.81–1.68), 4–7 DOT (OR, 1.53; 95% CI, 1.17–1.99), >7 DOT (OR, 1.82; 95% CI, 1.49–2.23), presence of open wounds (OR, 1.48; 95% CI, 1.26–1.75), LOS ≤14 days in the absence of prior MDRO carriage (OR, 2.22; 95% CI, 1.83–2.70), LOS ≤ 14 days in the presence of prior MDRO carriage (OR, 5.04; 95% CI, 3.91–6.49), and LOS>14 days in the presence of prior MDRO carriage (OR, 6.32; 95% CI, 4.98–8.02) (Table 2).

Next, after adjusting for age, year of screening, healthcare facility, percutaneous device and number of beds per room, odds of co-colonization increased as follows: male (OR, 1.96; 95% CI, 1.37–2.80), 1–3 DOT of antibiotics (OR, 10.39; 95% CI, 2.08–51.96), 4–7 DOT (OR, 4.89; 95% CI, 1.01–23.68), >7 DOT (OR, 11.72; 95% CI, 2.81–48.85), prior emergency surgery (OR, 1.41; 95% CI, 0.99–2.01), and open wound (OR, 2.34; 95% CI, 1.66–3.29). Interestingly, we observed an interaction between prior MDRO carriage and LOS of current admission on an additive scale. Compared to patients who had no prior MDRO carriage and an LOS ≤14 days, the odds ratio of co-colonization for patients with LOS>14 days but no carriage was 6.59 (95% CI, 2.87–15.10) and the odds ratio was 31.90 (95% CI, 14.01–72.64) for individuals with a history of MDRO carriage but LOS≤14 days, which increased to 50.07 (95% CI, 22.26–112.60) when the patients had both risk factors (Table 2).

Stratified multinomial logistic regression by healthcare facility further revealed a dose–response relationship of DOT of antibiotics on co-colonization in ILTCFs: 1–3 DOT (OR, 5.22; 95% CI, 0.31–86.89), 4–7 DOT (OR, 12.70; 95% CI, 1.38–116.58), >7 DOT (OR, 19.75; 95% CI, 2.64–147.65). Additionally, a prior emergency surgery was a significant risk factor for co-colonization in ACH patients, but this factor was associated with single colonization in ILTCFs. Number of beds per room remained a significant risk factor for single colonization in ACH but not in ILTCFs. Notably, joint association between prior MDRO carriage and LOS on single colonization continued to be significant both in the ACH and the ILTCFs; however, the additive interaction was evident for co-colonization among ACH patients only (Table 3).

Discussion

We identified healthcare setting-specific factors associated with MDRO co-colonization, and we also compared the epidemiology of MDRO co-colonization in an ACH with its closely affiliated 6 ILTCFs in a healthcare network over 3 years. We observed that both single and co-colonization were more prevalent in the ITCFs (36.5% and 4.2%) than in the ACH (19.6% and 3.9%) and LTCFs (22.8% and 0.3%). This prevalence is likely due to the high prevalence of MRSA among ITCF patients in our study population, as described previously.[4] Although co-colonization remained infrequent, it was largely contributed by MRSA/VRE (3.0%); other types of MDRO co-colonization occurred infrequently at 0.1%–0.3%. These rates were significantly lower than the prevalence reported in other studies from the United States,[19–23] although a similar prevalence was observed in 2 studies conducted in intensive care units and a rehabilitation hospital.[24–26] In contrast, a German acute-care hospital reported a lower prevalence than our finding.[27] A recent meta-analysis estimated that the pooled prevalence of MRSA/VRE co-colonization was 7% (95% CI, 5%–9%) despite the evidence of statistical heterogeneity and publication bias.[28] The variability of prevalence across studies can be explained by differences in study population, healthcare facility, use of surveillance or clinical specimens for identification, and definition of co-colonization.

https://doi.org/10.1017/ice.2022.57 Published online by Cambridge University Press

Table 1. Epidemiological and Clinical Characteristics of Patients by Status of MDRO Colonization

Characteristics	Non-colonized (n = 3,962)	Singly-colonized (n = 1,318)	Co-colonized (n = 176)	*P* Value
Demographics				
Age, median y (IQR)	73 (61–81)	74 (63–82)	76 (64.5–83)	.01[a]
Age >65 y	2,619 (66.1)	918 (69.7)	129 (73.3)	.01
Sex, male	2,013 (50.8)	797 (60.5)	124 (70.5)	<.001
Ethnicity				
Chinese	3,015 (76.1)	1,008 (76.5)	146 (83.0)	.33
Malay	525 (13.3)	184 (14.0)	15 (8.5)	
Indian	314 (7.9)	98 (7.4)	12 (6.8)	
Others	108 (2.7)	28 (2.1)	3 (1.7)	
Year screened				
2014	1,233 (31.1)	413 (31.3)	52 (29.6)	<.01
2015	1,297 (32.7)	475 (36.0)	75 (42.6)	
2016	1,432 (36.1)	430 (32.6)	49 (27.8)	
Comorbidities				
CCI, median (IQR)	3 (1–5)	3 (2–5)	4 (2–6)	<.001[a]
CCI > 5	762 (19.2)	307 (23.3)	54 (30.7)	<.001
HIV	30 (0.8)	13 (1.0)	0 (0.0)	.44
Cerebrovascular disease	1,434 (36.2)	533 (40.4)	75 (42.6)	<.01
Congestive cardiac failure	456 (11.5)	188 (14.3)	39 (22.2)	<.001
Connective tissue	59 (1.5)	14 (1.1)	3 (1.7)	.49
Diabetes mellitus	1,604 (40.5)	618 (46.9)	77 (43.8)	<.001
Myocardial infarction	679 (17.1)	300 (22.8)	40 (22.7)	<.001
Peptic ulcer disease	231 (5.8)	96 (7.3)	18 (10.2)	.02
Peripheral vascular disease	386 (9.7)	196 (14.9)	36 (20.5)	<.001
Chronic pulmonary disease	401 (10.1)	147 (11.2)	26 (14.8)	.10
Renal disease	907 (22.9)	400 (30.4)	64 (36.4)	<.001
Percutaneous devices				
Arterial line	531 (13.4)	204 (15.5)	43 (24.4)	<.001
Central venous line	276 (7.0)	121 (9.2)	26 (14.8)	<.001
Peripheral line	3,078 (77.7)	1,125 (85.4)	170 (96.6)	<.001
PICC	133 (3.4)	86 (6.5)	26 (14.8)	<.001
Dialysis line	191 (4.8)	107 (8.1)	16 (9.1)	<.001
Nasogastric tube	1,060 (26.8)	505 (38.3)	83 (47.2)	<.001
Endotracheal tube	458 (11.6)	165 (12.5)	34 (19.3)	<.01
Chest tube	69 (1.7)	21 (1.6)	1 (0.6)	.61[b]
PEG tube	299 (7.6)	177 (13.4)	42 (23.9)	<.001
Indwelling urinary catheter	1,044 (26.4)	528 (40.1)	91 (51.7)	<.001
Suprapubic catheter	33 (0.8)	4 (0.3)	2 (1.1)	.08[b]
Colostomy	44 (1.1)	24 (1.8)	5 (2.8)	.03[b]
Tracheostomy	212 (5.4)	85 (6.5)	14 (8.0)	.14
Any percutaneous device[c]	1,979 (50.0)	890 (67.6)	141 (80.1)	<.001
Peripheral line	3,078 (77.7)	1,125 (85.4)	170 (96.6)	<.001
Details of current admission				
Length of stay, median d (IQR)	15 (7-61)	26 (11-73)	22 (12-42.5)	<.001[a]
Length of stay >14 d	1,982 (50.0)	905 (68.7)	121 (68.8)	<.001

(*Continued*)

https://doi.org/10.1017/ice.2022.57 Published online by Cambridge University Press

Table 1. (*Continued*)

Characteristics	Non-colonized (n = 3,962)	Singly-colonized (n = 1,318)	Co-colonized (n = 176)	*P* Value
Admitting healthcare facility				
ACH	2,328 (58.8)	596 (45.2)	120 (68.2)	<.001
ITCF	744 (18.8)	458 (34.8)	53 (30.1)	
LTCF	890 (22.4)	890 (22.4)	3 (1.7)	
No. of beds per room				
1	369 (9.3)	80 (6.1)	24 (13.6)	<.001
2–4	320 (8.1)	73 (5.5)	6 (3.4)	
5–8	2,441 (61.6)	842 (63.9)	114 (64.8)	
>8	832 (21.0)	323 (24.5)	32 (18.2)	
Details of prior admission				
Prior ICU admission	121 (3.1)	20 (1.5)	5 (2.8)	<.01[b]
Prior admission				
None	1,968 (49.7)	374 (28.4)	35 (19.9)	<.001[b]
ACH	1,930 (48.7)	908 (68.9)	135 (76.7)	
ILTCF	64 (1.6)	36 (2.7)	6 (3.4)	
Prior known carriage of antimicrobial-resistant organism				
MRSA	435 (11.0)	446 (33.8)	121 (68.8)	<.001
VRE	55 (1.4)	71 (5.4)	19 (10.8)	<.001[b]
CRE	24 (0.6)	16 (1.2)	7 (4.0)	<.001[b]
Any of the above	482 (12.2)	493 (37.4)	129 (73.3)	<.001
Prior antibiotic use				
Aminoglycosides	840 (21.2)	381 (28.9)	70 (39.8)	<.001
Carbapenems	400 (10.1)	233 (17.7)	65 (36.9)	<.001
Cephalosporins	968 (24.4)	448 (34.0)	86 (48.9)	<.001
Fluoroquinolones	722 (18.2)	400 (30.4)	82 (46.6)	<.001
Penicillin	2,366 (59.7)	978 (74.2)	154 (87.5)	<.001
Vancomycin	810 (20.4)	476 (36.1)	110 (62.5)	<.001
Prior days of antibiotic therapy[d]				<.001
0	1,069 (27.0)	178 (13.5)	2 (1.1)	
1–3	299 (7.5)	50 (3.8)	7 (4.0)	
4–7	557 (14.1)	137 (10.4)	8 (4.5)	
>7	2,015 (50.9)	938 (71.2)	158 (89.8)	
Unknown	22 (0.5)	15 (1.1)	1 (0.6)	
Other risk factors				
Prior emergency surgery	817 (20.6)	338 (25.6)	70 (39.8)	<.001
Surgical care in the prior 90 d	1,352 (34.1)	481 (36.5)	94 (53.4)	<.001
Presence of open wounds	631 (15.9)	407 (30.9)	89 (50.6)	<.001

Note. Values are expressed in no. (%) unless indicated otherwise. MDRO, multidrug-resistant organism; IQR, interquartile range; ACH, acute-care hospital; ILTCF; intermediate or long-term care facility; MRSA, methicillin-resistant *Staphylococcus aureus*; VRE, vancomycin-resistant enterococci; CRE, carbapenemase-producing Enterobacterales; CCI, Charlson comorbidity index; HIV, human immunodeficiency virus; PICC, peripherally inserted central catheter; PEG, percutaneous endoscopic gastrostomy.
[a]Kruskal-Wallis test.
[b]Fisher exact test.
[c]Any percutaneous devices included procedures such as tracheostomy or colostomy, or insertion of any of the following: arterial line, dialysis line, peripherally inserted central catheter, endotracheal tube, chest tube, PEG tube or suprapubic catheter in the preceding 12 months.
[d]Prior days of antibiotic therapy included aminoglycosides, carbapenems, cephalosporins, fluoroquinolones, penicillin, and vancomycin in the preceding 12 months.

https://doi.org/10.1017/ice.2022.57 Published online by Cambridge University Press

Table 2. Multivariable Multinomial Logistic Regression Analysis of Risk Factors for Singly-colonized or Co-colonized Patients With Either MRSA, VRE or CPE[a]

	Singly-colonized				Co-colonized			
	Model 1 (crude)	Model 2 (full)	Model 3 (stepwise)	Model 4 (stepwise, final)	Model 1 (crude)	Model 2 (full)	Model 3 (stepwise)	Model 4 (stepwise, final)
Variables	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age >65 y	1.18 (1.03–1.35)	1.14 (0.98–1.33)	1.16 (1.00–1.35)	1.16 (1.00–1.35)	1.41 (1.00–1.98)	1.36 (0.93–1.99)	1.34 (0.92–1.95)	1.34 (0.92–1.96)
Sex, male	1.48 (1.30–1.68)	1.39 (1.21–1.59)	1.39 (1.21–1.59)	1.41 (1.22–1.62)	2.31 (1.66–3.21)	1.92 (1.34–2.75)	1.92 (1.34–2.74)	1.96 (1.37–2.80)
Year screened								
2014	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
2015	1.09 (0.94–1.27)	1.09 (0.92–1.29)	1.09 (0.92–1.29)	1.10 (0.93–1.30)	1.37 (0.95–1.97)	1.53 (1.03–2.27)	1.53 (1.03–2.27)	1.54 (1.04–2.29)
2016	0.90 (0.77–1.05)	0.84 (0.71–1.00)	0.84 (0.71–1.00)	0.84 (0.71–1.00)	0.81 (0.55–1.21)	0.77 (0.50–1.19)	0.77 (0.50–1.18)	0.77 (0.50–1.18)
CCI >5	1.28 (1.10–1.48)	1.05 (0.88–1.24)	. . .	. . .	1.86 (1.34–2.59)	0.88 (0.60–1.28)	. . .	. . .
Prior use of any percutaneous devices	2.09 (1.83–2.38)	1.44 (1.23–1.67)	1.42 (1.22–1.66)	1.42 (1.22–1.65)	4.04 (2.77–5.88)	1.49 (0.98–2.28)	1.47 (0.97–2.24)	1.44 (0.95–2.19)
Peripheral line	1.67 (1.41–1.98)	0.99 (0.78–1.25)	. . .	. . .	8.14 (3.59–18.43)	0.77 (0.30–1.93)	. . .	. . .
Currently admitted healthcare facility								
ACH	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
ITCF	2.40 (2.08–2.79)	2.21 (1.80–2.71)	2.32 (1.94–2.77)	2.28 (1.91–2.73)	1.38 (0.99–1.93)	1.51 (0.96–2.35)	1.69 (1.14–2.52)	1.61 (1.08–2.40)
LTCF	1.16 (0.98–1.37)	0.91 (0.71–1.17)	0.96 (0.77–1.20)	0.94 (0.75–1.18)	0.07 (0.02–0.21)	0.06 (0.02–0.20)	0.06 (0.02–0.21)	0.06 (0.02–0.20)
No. of beds per room								
1	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
2–4	1.05 (0.74–1.49)	1.14 (0.77–1.68)	1.19 (0.81–1.74)	1.18 (0.81–1.73)	0.29 (0.12–0.71)	0.44 (0.17–1.15)	0.46 (0.18–1.20)	0.45 (0.17–1.17)
5–8	1.59 (1.23–2.05)	1.61 (1.19–2.19)	1.76 (1.32–2.33)	1.73 (1.30–2.29)	0.72 (0.46–1.13)	1.25 (0.72–2.18)	1.35 (0.80–2.26)	1.30 (0.78–2.17)
>8	1.79 (1.36–2.35)	1.55 (1.10–2.18)	1.69 (1.22–2.34)	1.67 (1.21–2.31)	0.59 (0.34–1.02)	1.62 (0.82–3.20)	1.76 (0.92–3.36)	1.71 (0.90–3.25)
Prior ICU admission	0.49 (0.30–0.79)	0.73 (0.41–1.27)	. . .	. . .	0.93 (0.37–2.30)	0.64 (0.22–1.88)	. . .	. . .
Prior admission								
None	Reference	Reference	. . .	. . .	Reference	Reference	. . .	. . .
ACH	2.48 (2.16–2.84)	1.11 (0.93–1.33)			3.93 (2.70–5.73)	1.15 (0.72–1.82)		
ILTCF	2.96 (1.94–4.52)	1.28 (0.80–2.05)			5.27 (2.14–12.98)	1.72 (0.60–4.90)		
Prior days of antibiotic therapy								
0	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
1–3 d	1.00 (0.72–1.41)	1.18 (0.81–1.70)	1.14 (0.80–1.65)	1.17 (0.81–1.68)	12.51 (2.59–60.55)	10.23 (2.03–51.61)	9.96 (2.00–49.58)	10.39 (2.08–51.96)
4–7 d	1.48 (1.16–1.89)	1.52 (1.16–1.99)	1.52 (1.17–1.99)	1.53 (1.17–1.99)	7.68 (1.62–36.27)	5.18 (1.06–25.45)	4.93 (1.02–23.90)	4.89 (1.01–23.68)
>7 d	2.80 (2.34–3.34)	1.82 (1.48–2.25)	1.85 (1.51–2.26)	1.82 (1.49–2.23)	41.91 (10.37–169.38)	12.63 (2.98–53.64)	12.45 (2.99–51.87)	11.72 (2.81–48.85)
Unknown	4.10 (2.08–8.04)	1.92 (0.93–3.97)	1.94 (0.94–4.00)	1.93 (0.93–3.99)	24.30 (2.12–277.99)	6.55 (0.52–83.08)	6.53 (0.53–81.06)	6.33 (0.51–78.43)
Prior emergency surgery	1.33 (1.15–1.54)	1.11 (0.91–1.34)	1.04 (0.88–1.23)	1.05 (0.88–1.24)	2.54 (1.86–3.47)	1.33 (0.90–1.98)	1.40 (0.98–1.98)	1.41 (0.99–2.01)
Surgical care in the past 90 d	1.11 (0.97–1.26)	0.88 (0.74–1.05)	. . .	. . .	2.21 (1.63–3.00)	1.19 (0.81–1.75)	. . .	. . .
Presence of open wounds	2.36 (2.04–2.73)	1.48 (1.26–1.74)	1.51 (1.28–1.77)	1.48 (1.26–1.75)	5.40 (3.97–7.34)	2.41 (1.71–3.40)	2.40 (1.71–3.38)	2.34 (1.66–3.29)
Prior MRSA/VRE/CRE carriage	4.31 (3.73–5.00)	3.43 (2.90–4.05)	3.57 (3.04–4.20)	. . .	19.82 (14.00–28.04)	11.37 (7.74–16.69)	11.63 (8.02–16.87)	. . .
Current admission LOS >14 d	2.19 (1.92–2.50)	1.92 (1.62–2.27)	1.89 (1.60–2.23)	. . .	2.20 (1.59–3.04)	2.58 (1.77–3.76)	2.57 (1.77–3.71)	. . .
Prior MRSA/VRE/CRE carriage and LOS of current admission								
Prior carriage – & LOS ≤14 d	. . .	. . .	. . .	Reference	. . .	. . .	. . .	Reference
Prior carriage – & LOS >14 d				2.22 (1.83–2.70)				6.59 (2.87–15.10)
Prior carriage + & LOS ≤14 d				5.04 (3.91–6.49)				31.90 (14.01–72.64)
Prior carriage + & LOS >14 d				6.32 (4.98–8.02)				50.07 (22.26–112.60)

Note. MRSA, methicillin-resistant *Staphylococcus aureus*; VRE, vancomycin-resistant enterococci; CRE, carbapenemase-producing Enterobacterales; ACH, acute-care hospital; CCI, Charlson comorbidity index; CI, confidence interval; ICU, intensive care unit; ILTCF, intermediate- and long-term care facility; LOS, length of stay; OR, odds ratio.

[a]With non-colonized as the reference category.

Table 3. Stratified Multivariable Multinomial Logistic Regression Analysis of Risk Factors for Singly-colonized or Co-colonized Patients With Either MRSA, VRE or CPE[a] for Patients Admitted to the ACH or ILTCFs

	ACH		ILTCFs	
	Singly-colonized	Co-colonized	Singly-colonized	Co-colonized
Variables	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age >65 y	1.31 (1.04–1.64)	1.38 (0.86–2.21)	1.11 (0.91–1.36)	1.70 (0.89–3.25)
Sex, male	1.08 (0.88–1.33)	1.71 (1.10–2.68)	1.80 (1.48–2.18)	2.26 (1.23–4.15)
Year screened				
2014	Reference	Reference	Reference	Reference
2015	0.84 (0.66–1.06)	1.22 (0.76–1.96)	1.54 (1.21–1.95)	3.31 (1.44–7.59)
2016	0.64 (0.50–0.82)	0.52 (0.31–0.89)	1.16 (0.91–1.47)	2.03 (0.87–4.78)
Prior use of any percutaneous devices	1.49 (1.18–1.88)	1.30 (0.74–2.27)	1.31 (1.07–1.60)	1.26 (0.67–2.40)
No. of beds per room				
1	Reference	Reference	Reference	Reference
2–4	1.34 (0.86–2.07)	0.52 (0.18–1.50)	0.77 (0.26–2.24)	0.12 (0.01–1.46)
5–8	1.79 (1.31–2.43)	1.67 (0.95–2.95)	1.27 (0.48–3.36)	0.28 (0.06–1.23)
>8	2.20 (1.38–3.49)	2.35 (1.02–5.44)	0.92 (0.35–2.43)	0.20 (0.04–0.91)
Prior days of antibiotic therapy				
0	Reference	Reference	Reference	Reference
1–3 d	1.62 (0.81–1.70)	13.64 (1.52–122.09)	1.10 (0.65–1.89)	5.22 (0.31–86.89)
4–7 d	1.95 (1.24–3.06)	2.41 (0.25–22.80)	1.52 (1.05–2.18)	12.70 (1.38–116.58)
>7 d	2.15 (1.44–3.22)	6.48 (0.85–49.26)	1.80 (1.42–2.29)	19.75 (2.64–147.65)
Unknown	. . .	. . .	2.10 (1.02–4.32)	12.62 (0.72–220.47)
Prior emergency surgical care	1.06 (0.85–1.33)	1.67 (1.08–2.60)	1.40 (1.09–1.80)	1.77 (0.95–3.32)
Presence of open wounds	1.30 (1.03–1.65)	2.50 (1.62–3.85)	1.64 (1.30–2.06)	2.19 (1.21–3.98)
Prior MRSA/VRE/CRE carriage and LOS of current admission				
Prior carriage – & LOS ≤14 d	Reference	Reference	Reference	Reference
Prior carriage – & LOS >14 d	2.10 (1.60–2.75)	18.77 (4.20–83.86)	1.28 (0.95–1.73)	0.86 (0.31–2.35)
Prior carriage + & LOS ≤14 d	5.70 (4.27–7.61)	99.22 (23.09–426.36)	3.29 (1.79–6.03)	9.80 (2.89–33.24)
Prior carriage + & LOS >14 days	9.10 (6.58–12.60)	233.34 (53.96–1009.13)	2.53 (1.75–3.66)	3.18 (1.11–9.12)

Note. ACH, acute-care hospital; CI, confidence interval; ILTCFs, intermediate- and long-term care facilities; LOS, length of stay; OR, odds ratio.
[a]With non-colonized as the reference category.

Open wounds and prior use of antibiotics were independent risk factors for single and co-colonization in both the ACH and the ILTCFs, consistent with other studies.[20,22–24] Both acute and chronic wounds, as previously studied, have the propensity to develop biofilms that are communities of microorganisms attached to a surface,[29] and are often associated with increased risk of bacterial growth and infection.[30] Inappropriate antibiotic uses are well-recognized drivers for the emergence of MDROs. Wang et al[31] reported that antibiotics not only elevated the risk of primary MDRO colonization but also increased the likelihood of colonization and infection by other MDROs among LTCFs residents. This report is reflected in our finding that the effect sizes of antibiotic use on co-colonization were significantly higher in ILTCFs patients, posing a concern to infection prevention and control practitioners because of the frequent transfers between ILTCFs and ACH in an interconnected healthcare network. Therefore, good comprehensive antibiotic stewardship programs that enforce the judicious antibiotic use are urgently required in both ACH and ILTCFs.

The prior use of any percutaneous device was a significant predictor of single colonization but was not significantly associated with co-colonization, in both the ACH and ILTCF patients in our study. In contrast, device use was a significant determinant of co-colonization in previous studies conducted in different healthcare settings.[19,22,32,33] Although the reason remains unclear, variation in anatomic sites of sampling across the studies may explain the difference. We further noted that the odds ratio for percutaneous device was attenuated when antibiotics was added to the model in our multivariable analysis of co-colonization. This finding indicates that antibiotic was a stronger predictor, which in turn supported the aforementioned observation of association between a history of antibiotic consumption and co-colonization.

In this study, emergency surgery was a risk factor in the ILTCFs and the ACH for single- and co-colonization, respectively. Surgery has previously been identified as a predictor of MRSA infection,[34,35] and it may represent a breakdown of the host defense mechanism, surgical technique, or postoperative care, and it may mandate more contact-intensive care, which creates the

https://doi.org/10.1017/ice.2022.57 Published online by Cambridge University Press

opportunity for new bacterial acquisition. A higher number of beds per room was associated with single colonization in ACH patients but not in ILTCF residents, which corroborates the findings from earlier studies on VRE and MRSA colonization.[5,36] This association could be the result of different care models between the ACH and ILTCFs in which the residents are encouraged to ambulate and share common facilities such as the rehabilitation gymnasium.

The greater risk of MDRO colonization among LTCF residents and those who had a history of MDRO carriage has been consistently demonstrated,[4,5,7,22] but we revealed, in addition, the synergistic effects of longer LOS and prior MDRO carriage, especially on MDRO co-colonization in the ACH setting. This finding suggests that ACH is a reservoir of multiple MDROs and that targeted MDRO screening and pre-emptive precautionary measures for at-risk patients may reduce co-colonization.

Our study has several strengths. First, including the participants from different healthcare settings allowed us to concurrently assess the prevalence and compare the epidemiology of co-colonization among short- and long-stay populations in an ACH and ILTCFs, respectively, thus ensuring the generalizability of findings. Second, a large sample of patients and an 87% participation rate reduced the risk of selection bias, if any. Third, collection of stool specimen for those who refused rectal swabs minimized the underestimation of VRE and CPE colonization. Fourth, research assistants were trained to standardize data and specimen collection methods, and the identification of bacterial isolates further was confirmed by matrix-assisted laser desorption ionization-time of flight (MALDI-TOF) mass spectrometry, reducing potential measurement errors and outcome misclassifications. Finally, we demonstrated the joint effects of LOS and a history of MDRO carriage on co-colonization, especially among ACH patients. This finding gives new insights into developing infection prevention and control strategies for the at-risk population to reduce MDRO co-colonization and prevent healthcare-associated infections.

This study has several limitations. Clinical data collection was performed retrospectively through reviewing EMR or medical case notes, which might have resulted in missing data if no documentation was made. However, any exposure misclassification was likely nondifferential, moving the observed effects toward the null. Also, the epidemiology of triple-colonized patients could not be elaborated due to their very small number (n = 4). Finally, because different anatomic sites were screened for the different MDROs in accordance with the most commonly colonized sites based on local epidemiology, we could not determine the anatomic site–level prevalence of co-colonization, as revealed by a study in which the incidence of MRSA/VRE concurrent co-colonization was highest in hands,[22] thus warranting further studies.

In summary, we identified common and differential risk factors associated with MDRO co-colonization between an ACH and its affiliated ILTCFs. Although emergency surgery increased the odds of co-colonization in an ACH, a longer duration of antibiotic therapy was a strong risk factor in ILTCF patients. Open wounds, a prior MDRO carriage, and LOS >14 days were risk factors common to all facilities. Infection prevention and control strategies, including pre-emptive contact precautions and active screening of at-risk populations specific to the healthcare setting, could be instituted.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/ice.2022.57

Acknowledgments. We thank all patients who participated in this study and the staff who facilitated the study.

Financial support. This study was funded by the Ministry of Health's Communicable Diseases Public Health (research grant no. CDPHRG/0008/2014). The funders had no role in study design, data collection and interpretation, or the decision to submit the work for publication.

Conflicts of interest. All authors report no conflicts of interest relevant to this article.

References

1. Cohen ML. Changing patterns of infectious disease. *Nature* 2000;406:762–767.
2. Eliopoulos GM, Cosgrove SE, Carmeli Y. The impact of antimicrobial resistance on health and economic outcomes. *Clin Infect Dis* 2003;36:1433–1437.
3. Friedman ND, Temkin E, Carmeli Y. The negative impact of antibiotic resistance. *Clin Microbiol Infect* 2016;22:416–422.
4. Chow A, Htun HL, Hon P-Y, *et al.* Comparative epidemiology and factors associated with major healthcare-associated methicillin-resistant *Staphylococcus aureus* clones among interconnected acute-, intermediate- and long-term healthcare facilities in Singapore. *Clin Microbiol Infect* 2021;27:785.e789–785.e716.
5. Tan D, Htun HL, Koh J, *et al.* Comparative epidemiology of vancomycin-resistant enterococci colonization in an acute-care hospital and its affiliated intermediate- and long-term care facilities in Singapore. *Antimicrob Agents Chemother* 2018;62:e01507–e01518.
6. Koh TH, Hsu LY, Chiu LL, Lin RV. Emergence of epidemic clones of vancomycin-resistant *Enterococcus faecium* in Singapore. *J Hosp Infect* 2006;63:234–236.
7. Aung AH, Kanagasabai K, Koh J, *et al.* Epidemiology and transmission of carbapenemase-producing Enterobacteriaceae in a healthcare network of an acute-care hospital and its affiliated intermediate- and long-term care facilities in Singapore. *Antimicrob Agents Chemother* 2021;65:e0258420.
8. Boswihi SS, Udo EE. Methicillin-resistant *Staphylococcus aureus*: An update on the epidemiology, treatment options, and infection control. *Curr Med Res Pract* 2018;8:18–24.
9. Elstrøm P, Astrup E, Hegstad K, Samuelsen Ø, Enger H, Kacelnik O. The fight to keep resistance at bay, epidemiology of carbapenemase producing organisms (CPOs), vancomycin-resistant enterococci (VRE) and methicillin-resistant *Staphylococcus aureus* (MRSA) in Norway, 2006–2017. *PloS One* 2019;14:e0211741.
10. Liu C, Chambers HF. *Staphylococcus aureus* with heterogeneous resistance to vancomycin: epidemiology, clinical significance, and critical assessment of diagnostic methods. *Antimicrob Agent Chemother* 2003;47:3040–3045.
11. Sng L-H, Koh TH, Wang GCY, Hsu L-Y, Kapi M, Hiramatsu K. Heterogeneous vancomycin-resistant *Staphylococcus aureus* (hetero-VISA) in Singapore. *Int J Antimicrob Agents* 2005;25:177–179.
12. Hiramatsu K, Hanaki H, Ino T, Yabuta K, Oguri T, Tenover FC. Methicillin-resistant *Staphylococcus aureus* clinical strain with reduced vancomycin susceptibility. *J Antimicrob Chemother* 1997;40:135–136.
13. Howden BP, Johnson PDR, Ward PB, Stinear TP, Davies JK. Isolates with low-level vancomycin resistance associated with persistent methicillin-resistant *Staphylococcus aureus* bacteremia. *Antimicrob Agents Chemother* 2006;50:3039–3047.
14. Weinstein RA, Fridkin SK. Vancomycin-intermediate and -resistant *Staphylococcus aureus*: what the infectious disease specialist needs to know. *Clin Infect Dis* 2001;32:108–115.
15. Noble WC, Virani Z, Cree RG. Co-transfer of vancomycin and other resistance genes from *Enterococcus faecalis* NCTC 12201 to *Staphylococcus aureus*. *FEMS Microbiol Lett* 1992;72:195–198.
16. Htun HL, Hon PY, Holden MTG, Ang B, Chow A. Chlorhexidine and octenidine use, carriage of *qac* genes, and reduced antiseptic susceptibility in methicillin-resistant *Staphylococcus aureus* isolates from a healthcare network. *Clin Microbiol Infect* 2019;25:1154.e1151–1154.e1157.

17. Hidron AI, Kourbatova EV, Halvosa JS, *et al.* Risk factors for colonization with methicillin-resistant *Staphylococcus aureus* (MRSA) in patients admitted to an urban hospital: emergence of community-associated MRSA nasal carriage. *Clin Infect Dis* 2005;41:159–166.
18. Young BE, Lye DC, Krishnan P, Chan SP, Leo YS. A prospective observational study of the prevalence and risk factors for colonization by antibiotic resistant bacteria in patients at admission to hospital in Singapore. *BMC Infect Dis* 2014;14:298.
19. Hayakawa K, Marchaim D, Bathina P, *et al.* Independent risk factors for the co-colonization of vancomycin-resistant *Enterococcus faecalis* and methicillin-resistant *Staphylococcus aureus* in the region most endemic for vancomycin-resistant *Staphylococcus aureus* isolation. *Eur J Clin Microbiol Infect Dis* 2013;32:815–820.
20. Reyes K, Malik R, Moore C, *et al.* Evaluation of risk factors for coinfection or cocolonization with vancomycin-resistant *Enterococcus* and methicillin-resistant *Staphylococcus aureus*. *J Clin Microbiol* 2010;48:628–630.
21. Warren DK, Nitin A, Hill C, Fraser VJ, Kollef MH. Occurrence of cocolonization or coinfection with vancomycin-resistant enterococci and methicillin-resistant *Staphylococcus aureus* in a medical intensive care unit. *Infect Control Hosp Epidemiol* 2015;25:99–104.
22. Heinze K, Kabeto M, Martin ET, Cassone M, Hicks L, Mody L. Predictors of methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci cocolonization among nursing facility patients. *Am J Infect Control* 2019;47:415–420.
23. Flannery EL, Wang L, Zöllner S, Foxman B, Mobley HLT, Mody L. Wounds, functional disability, and indwelling devices are associated with cocolonization by methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci in southeast Michigan. *Clin Infect Dis* 2011;53:1215–1222.
24. Furuno J, Perencevich E, Johnson J, *et al.* Methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci cocolonization. *Emerg Infect Dis J* 2005;11:1539.
25. McKinley L, Becerra B, Moriarty H, *et al.* Vancomycin-resistant *Enterococcus* cocolonization rates with methicillin-resistant *Staphylococcus aureus* and *Clostridium difficile* in critically ill veterans. *Am J Infect Control* 2016;44:1047–1049.
26. Rabinowitz RP, Kufera JA, Makley MJ. A hidden reservoir of methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus* in patients newly admitted to an acute rehabilitation hospital. *PM R* 2012; 4:18–22.
27. Meyer E, Ziegler R, Mattner F, Schwab F, Gastmeier P, Martin M. Increase of patients cocolonized or coinfected with methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus faecium* or extended-spectrum β-lactamase–producing Enterobacteriaceae. *Infection* 2011;39:501–506.
28. Wang Y, Oppong TB, Liang X, Duan G, Yang H. Methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci cocolonization in patients: a meta-analysis. *Am J Infect Control* 2020;48:925–932.
29. Flemming H-C, Wingender J. The biofilm matrix. *Nat Revs Microbiol* 2010;8:623–633.
30. Percival SL. Importance of biofilm formation in surgical infection. *Br J Surg* 2017;104:e85–e94.
31. Wang J, Foxman B, Mody L, Snitkin ES. Network of microbial and antibiotic interactions drive colonization and infection with multidrug-resistant organisms. *Proc Nat Acad Sci* 2017;114:10467–10472.
32. Sigurdardottir B, Berg JV, Hu J, *et al.* Descriptive epidemiology and case–control study of patients colonized with vancomycin-resistant *Enterococcus* and methicillin-resistant *Staphylococcus aureus*. *Infect Control Hosp Epidemiol* 2016;27:913–919.
33. Yoon YK, Lee MJ, Ju Y, *et al.* Determining the clinical significance of co-colonization of vancomycin-resistant enterococci and methicillin-resistant *Staphylococcus aureus* in the intestinal tracts of patients in intensive care units: a case-control study. *Ann Clin Microbiol Antimicrob* 2019;18:28.
34. Graffunder EM, Venezia RA. Risk factors associated with nosocomial methicillin-resistant *Staphylococcus aureus* (MRSA) infection including previous use of antimicrobials. *J Antimicrob Chemother* 2002;49:999–1005.
35. Callejo-Torre F, Eiros Bouza JM, Olaechea Astigarraga P, *et al.* Risk factors for methicillin-resistant *Staphylococcus aureus* colonisation or infection in intensive care units and their reliability for predicting MRSA on ICU admission. *Infezioni medicina* 2016;24:201–209.
36. Kibbler CC, Quick A, O'Neill AM. The effect of increased bed numbers on MRSA transmission in acute medical wards. *J Hosp Infect* 1998;39:213–219.

https://doi.org/10.1017/ice.2022.57 Published online by Cambridge University Press