





# The Role of Healthcare Worker-Mediated Contact Networks in the Transmission of Vancomycin-Resistant *Enterococci*

Eili Y. Klein, <sup>1,2,©</sup> Katie K. Tseng, <sup>2</sup> Jeremiah Hinson, <sup>1</sup> Katherine E. Goodman, <sup>1,3</sup> Aria Smith, <sup>1</sup> Matt Toerper, <sup>1</sup> Joe Amoah, <sup>1</sup> Pranita D. Tamma, <sup>1</sup> Scott R. Levin, <sup>1</sup> and Aaron M. Milstone <sup>1</sup>; for the CDC Prevention Epicenters Program and the CDC MInD-Healthcare Program

<sup>1</sup>The Johns Hopkins School of Medicine, Baltimore, Maryland, USA, <sup>2</sup>Center for Disease Dynamics, Economics & Policy, Washington, District of Columbia, USA, <sup>3</sup>University of Maryland School of Medicine, Baltimore, Maryland, USA

**Background.** User- and time-stamped data from hospital electronic health records (EHRs) present opportunities to evaluate how healthcare worker (HCW)-mediated contact networks impact transmission of multidrug-resistant pathogens, such as vancomycin-resistant enterococci (VRE).

Methods. This is a retrospective analysis of incident acquisitions of VRE between July 1, 2016 and June 30, 2018. Clinical and demographic patient data were extracted from the hospital EHR system, including all recorded HCW contacts with patients. Contacts by an HCW with 2 different patients within 1 hour was considered a "connection". Incident VRE acquisition was determined by positive clinical or surveillance cultures collected ≥72 hours after a negative surveillance culture.

**Results.** There were 2952 hospitalizations by 2364 patients who had ≥2 VRE surveillance swabs, 112 (4.7%) patients of which had incident nosocomial acquisitions. Patients had a median of 24 (interquartile range [IQR], 18–33) recorded HCW contacts per day, 9 (IQR, 5–16) of which, or approximately 40%, were connections that occurred <1 hour after another patient contact. Patients that acquired VRE had a higher average number of daily connections to VRE-positive patients (3.1 [standard deviation {SD}, 2.4] versus 2.0 [SD, 2.1]). Controlling for other risk factors, connection to a VRE-positive patient was associated with increased odds of acquiring VRE (odds ratio, 1.64; 95% confidence interval, 1.39–1.92).

*Conclusions.* We demonstrated that EHR data can be used to quantify the impact of HCW-mediated patient connections on transmission of VRE in the hospital. Defining incident acquisition risk of multidrug-resistant organisms through HCWs connections from EHR data in real-time may aid implementation and evaluation of interventions to contain their spread.

**Keywords.** antibiotic resistance; electronic health records; hospital-acquired infections; nosocomial; pathogen surveillance.

Hospital-acquired infections (HAIs) pose a threat to patient safety and are a significant burden to the healthcare system. Approximately 3.5% to 12% of hospitalized patients acquire at least 1 HAI during their stay [1], which can result in prolonged hospital stays and increased rates of mortality. In the United States, HAIs are estimated to burden the healthcare system and patients with an extra 28–45 billion dollars annually [2]. Rising rates of antimicrobial resistance increase the risk of infection, especially in vulnerable patients.

Pathogens can spread in the hospital environment through direct contact between patients, through environmental

Received 26 January 2020; editorial decision 4 February 2020; accepted 13 February 2020. Correspondence: Eili Y. Klein, PhD, Johns Hopkins School of Medicine, 5801 Smith Ave, Davis Suite 3220, Baltimore, MD 21209 (eklein@jhu.edu).

# Open Forum Infectious Diseases®

© The Author(s) 2020. Published by Oxford University Press on behalf of Infectious Diseases Society of America. This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs licence (http://creativecommons.org/licenses/by-nc-nd/4.0/), which permits non-commercial reproduction and distribution of the work, in any medium, provided the original work is not altered or transformed in any way, and that the work is properly cited. For commercial re-use, please contact journals.permissions@oup.com DOI: 10.1093/ofid/ofaa056

sources, or through contact with healthcare workers (HCWs) [3–6]. Because HCWs frequently care for more than 1 patient at a time and have high contact rates with patients, they are considered an important vector for transmission [1]. Transmission between patients is facilitated when HCWs become transiently colonized through contact with colonized or infected patients or contaminated environmental surfaces [7, 8]. However, despite their importance, gaps persist in our understanding of the magnitude of the effect of HCW-mediated contamination events on transmission of pathogenic organisms [9].

Assessing how frequently HCWs connect patients and the resulting impact on pathogen transmission can be challenging in the hospital setting, because surveys, interviews, or direct observations are time- and resource-consuming as well as error-prone. Electronic health records (EHRs) provide readily available data, are updated in real-time, and can be analyzed at both the hospital and unit levels [10] as well as across multicentered institutions [11, 12]. Studies that have used EHR data to study the role of HCWs in organism transmission have demonstrated the utility of EHR data to serve as proxies for HCW movement and behavior, identified patterns in contact

between HCWs, and reinforced the epidemiological relevance of HCW social networks [10–13]. However, although studies have used EHR data to investigate how HCWs connect patients, few have attempted to quantifiably measure the impact of differential HCW-mediated patient connectedness rates on the spread of endemic pathogens in the hospital. Our objective was to examine the magnitude of the role of HCW-mediated contact networks on the spread of vancomycin-resistant *Enterococci* (VRE) within the hospital.

#### **METHODS**

# **Study Setting and Population**

We performed a retrospective analysis of all patients with routine VRE surveillance cultures taken upon admission to 1 of 7 Johns Hopkins Hospital (JHH) units from July 1, 2016 to June 30, 2018. Six of the units were intensive care units (ICUs)— Surgical Critical Care, Medical Critical Care, Neurosurgical Critical Care, Surgical Cardiothoracic Critical Care, Medical Cardiac Critical Care, Surgical Critical Care—and the seventh was the Solid Organ Transplant Specialty Care Area. Although the latter unit is not considered an ICU, it provides ICU-level care and, along with the other units, is part of a longstanding VRE surveillance program that collects patient perirectal samples using Eswabs (COPAN Diagnostics, Murrieta, CA) at admission to the unit and weekly thereafter. All 7 units have private patient rooms and use contact precautions (gown and gloves) for patients identified with multidrug-resistant organisms such as VRE, methicillin-resistant Staphylococcus aureus (MRSA), and carbapenem-resistant organisms. For all patients with ≥1 surveillance swab, we extracted information on their entire hospitalization, including any additional surveillance swab and antibiotic susceptibility results. Patients were defined as having prevalent VRE if their first surveillance swab after hospital admission was positive or they had a positive surveillance swab or clinical culture in the prior year. Incident acquisitions were defined as patients not VREprevalent on admission who had a positive surveillance swab or clinical culture ≥72 hours after their initial negative surveillance swab. Once a patient tested positive, they were considered positive for the duration of their visit regardless of additional test results. Patients with visits across multiple years could newly acquire VRE if their last positive test was more than 365 days prior and they were negative upon initial screen. This study was approved by the Johns Hopkins University School of Medicine Institutional Review Board, with a waiver of informed consent.

# **Clinical Data Collection**

Patient encounter data (past and current) were retrospectively collected using bulk extraction methods from JHH's EHR system. Electronic health record data were available for inpatient and outpatient encounters for all 5 Johns Hopkins

Health System hospitals across Maryland and the District of Columbia to obtain relevant preadmission data. Extracted patient-level data included prior hospitalizations, pre-existing medical conditions, medical diagnoses, procedures, surgeries, vascular lines, surgical drains, mechanical ventilation devices, laboratory results, demographic information, and medication administration.

# **Healthcare Worker-Mediated Contact Data**

Time-stamped HCW interactions with patients were extracted from the JHH EHR system. Interactions were identified by entry of any medication administration, laboratory specimen collection, or flowsheet information by an HCW. Although medication administrations and laboratory specimen collections are generally recorded by the administering HCW and are therefore a fairly accurate means of identifying HCW-patient interactions, flowsheet items are more complex and include several events that are autopopulated. Data captured from flowsheet notations were adjudicated by a physician (J.H.) as to their likelihood of representing direct patient contact, and flowsheet events judged to be automated events (ie, not representative of a patient-HCW interaction) were filtered out. Because a single HCW could administer multiple medications, or collect multiple specimens, or evaluate several different vital signs all within a short period of time, we combined all events that had separate line items in the EHR from a single HCW that occurred within 10 minutes of each other and counted them as a single contact by that HCW with that patient.

Connections between patients were defined as contacts with 2 different patients by the same HCW within 60 minutes. Connections were directed, meaning that a HCW contacting patient A and then patient B within 60 minutes would be counted as a connection for patient B but not patient A. Multiple prior contacts were considered a single connection (ie, if a HCW had more than 1 contact with patient A, even after combining events that occurred within 10 minutes of each other, in the hour preceding contact with patient B, this was counted as a single connection). Healthcare workers were grouped into 5 roles: nurses, technicians, practitioners (ie, physicians, physician assistants, nurse practitioners), therapists, and other. Events recorded in the EHR without attribution to a unique HCW were assumed to be automated reports and were excluded (eg, vital signs autopopulated by monitoring devices). Sensitivity analyses were conducted to evaluate the timing of connections. We calculated connections when the contact occurred in the prior 12 hours, consistent with the typical length of a nurse's shift to capture most connections during a shift, as well as a shorter time window of 30 minutes. In addition, results were analyzed excluding repeat visits to remove any potential confounding effect of prior prevalence or acquisition.

## Statistical Analysis

Descriptive statistics for patient variables were calculated using mean (standard deviation [SD]), median (interquartile range [IQR]), or frequency count (percentage), as appropriate. The number of connections to patients considered VRE positive (ie, VRE prevalent at admission or the time postincident VRE acquisition) was calculated on a daily basis. Multivariable logistic regression was used to calculate the odds of acquiring VRE to assess the association between HCW-mediated connections and VRE acquisition. A priori covariates included in the regression model, based on prior studies of VRE risk factors [14, 15], included the Elixhauser comorbidity score [16], days of dialysis, days with a rectal tube, days with a gastrointestinal tube, days on mechanical ventilation, number of days in an ICU, whether the patient had been in a skilled nursing facility or long-term care facility in the last 180 days, whether contact precautions were ordered, antibiotic use (both overall and by class), and demographic variables including age, gender, and race. Nonnormally distributed variables, including connections and contacts, were log-transformed and standard errors were clustered by patient. Because the number of HCW contacts was correlated with patient length of stay (LOS), Cox regression with time-varying covariates was used to calculate hazard ratios for risk of VRE acquisition adjusting for a similar set of covariates. The proportionality assumption was assessed by building time-dependent covariates into the model. Cox and logistic regression analysis were conducted in Stata (Stata Statistical Software, release 14; StataCorp, College Station, TX).

# **RESULTS**

Over the course of the study period, 9131 patients had 11243 hospital admissions in which they were admitted to at least 1 of the 7 hospital units and had at least 1 VRE surveillance swab obtained. The average patient age was 57, 47% were female, 45% were non-white, and 8% died (Supplementary Table 1). Overall, the average LOS was 12 days (standard deviation [SD], 17), during which the median and average number of HCW contacts per patient per day was 24 (IQR, 18-33) and 26.3 (SD, 12.1), respectively. Nurses had the highest median and average daily contact rates with patients at 17 (IQR, 12-24) and 18.8 (SD, 9.7), followed by technicians (average 3.2 [SD, 2.8], median 3 [IQR, 1-5]) and therapists (average 2.0 [SD, 2.9], median 1 [IQR, 0-3]) (Figure 1). Approximately 40% of all HCW contacts were within 1 hour of a contact with another patient, resulting in a median of 9 (IQR, 5-16) and average of 11.2 (SD, 8.3) connections per day, with nurses the most common connector, followed by technicians and then therapists (Figure 1).

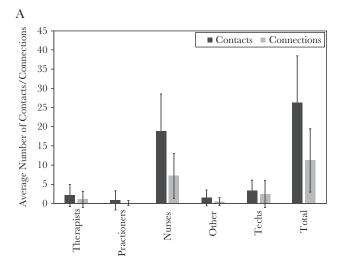
A total of 455 patients were VRE prevalent at 977 admissions (ie, had a positive swab within 2 days of admission or had a positive swab or infection within the past year). These patients were included in calculations of connections to VRE patients, but not in the analysis to assess the factors associated with incident

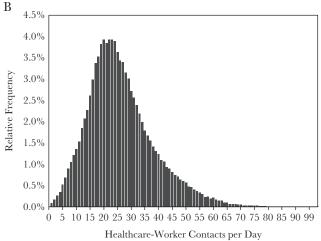
colonization. An additional 7314 admissions by 6312 patients only had a single negative VRE surveillance swab or were hospitalized for less than 72 hours and thus were excluded from the statistical analysis because it was not possible to determine whether patients in this subpopulation acquired VRE or remained uncolonized or infected. The final cohort included 2364 patients accounting for 2952 hospital admissions: 112 (4.7%) of these patients across 165 hospitalizations (5.6%) had an incident VRE acquisition.

Population demographics and contacts with HCWs for the incident and nonincident VRE groups were similar, although the population that acquired VRE had higher proton pump inhibitor (PPI) and antibiotic use rates both in the hospital and in the prior 365 days, longer lengths of stay, more contacts with VRE-prevalent patients both in total and per day (average 3.1 [SD, 2.3] compared with 2.0 [SD, 2.2]), and were more likely to have an isolation order requiring contact precautions (Table 1). The median and mean length of time to acquisition was 11 (IQR, 7–21) and 20.0 (95% confidence interval [CI], 15.1–24.9) days.

Multivariable logistic regression found that a 1% increase in the number of connections to VRE-prevalent patients was associated with 1.64 (95% CI, 1.39-1.92) higher odds of acquiring VRE (Table 2). The nonlinearity of VRE connectivity [17] implies that a single connection to a VRE-prevalent patient was associated with 1.41 (95% CI, 1.26-1.57) higher odds of VRE acquisition. A greater number of connections increased the odds of acquisition, but each additional connection was marginally less impactful; with 5 connections the odds increased to 2.42 (95% CI, 1.82-3.23), and with 10 connections the odds increased to 3.26 (95% CI, 2.22-4.80) (Figure 2). Antibiotic and PPI use in the prior 365 days were also significantly associated with VRE acquisition (Table 2). Of the different antibiotic classes, only macrolides were significantly associated with VRE acquisition (Supplementary Table 2). Although the number of HCW contacts was significantly associated with VRE acquisition, the number of HCW contacts was highly collinear with LOS (although number of connections to VRE-prevalent patients was not strongly correlated), so they could not be assessed independently. However, analysis of the effect of LOS led to qualitatively similar results (Supplementary Table 2). Assessing the impact of the different types of HCWs, we found that only nursing connections were significantly associated with VRE acquisition (Supplementary Table 3). Altering the connection definition to include all connections within 12 hours or shortening the connection time period to 30 minutes resulted in qualitatively similar results (Supplementary Tables 4 and 5). Likewise, only analyzing the first visit from a patient resulted in qualitatively similar results (Supplementary Table 6). Including connections to noncolonized patients had no qualitative impact on the results (Supplementary Table 7).

Cox regression analysis with time-varying covariates indicated that for each additional connection with a VRE patient





**Figure 1.** Healthcare worker (HCW) daily contacts and connections to other patients. The average number of daily contacts and connections to other patients by HCW type. Connections are defined as contacts by an HCW with 2 patients within 1 hour (A). The error bars show the standard deviation of daily contacts or connections as the distribution per patient per day is quite variable and right skewed (B).

per day, the probability of colonization or infection increased by 12% (95% CI, 9–15). Antibiotic and PPI use within the hospital were associated with VRE acquisition, as was dialysis. Similar to the results of the logistic regression, alternative definitions for timing related to defining connections, or limiting the patient visits had no qualitative impact on the results (Supplementary Tables 4–6). Including connections to noncolonized patients showed a small impact of these connections on the hazard risk of VRE acquisition (Supplementary Table 7).

### **DISCUSSION**

Controlling the spread of multidrug-resistant organisms within the hospital is a multifaceted challenge compounded by the fact that sources and transmission paths of many nosocomial infections remain unknown and unrecognized. Prevention strategies recognize that HCWs likely play an important role in transmission, in part based on theoretical models of transmission through HCW-mediated contact networks. However, although research on how HCWs connect patients exists [10–13], more quantitative studies that assess the magnitude of the impact of HCW-mediated connections on transmission are lacking. In this study, we used prevalent and incident VRE colonization and infection, to better understand how HCW network chains drive transmission. Using data collected from the EHRs, we demonstrated that HCW-mediated connections to VRE-prevalent patients were associated with VRE acquisition, and increasing the number of connections further increases the risk of VRE acquisition.

Several studies have shown how HCW movement and connectivity networks may play a role in the transmission of infectious diseases. The majority of these studies have used sensors to track the movement of HCWs and infer how they may impact transmission of disease [18-22]. Although they are of tremendous utility in defining HCW movement, these are relatively expensive and can be difficult to tie directly to patients due to privacy concerns. The EHR, on the other hand, presents opportunities to utilize routinely captured data to assess not only how HCWs move within the hospital, but also which patients they contact and how those patients are connected in a relatively simple and inexpensive manner. For example, Curtis et al used millions of EHR logins to construct HCW movement networks [12]. However, this study only inferred patient contact from use of computers by HCWs near patients and did not examine patient colonization or infection data. Likewise, Cusumano-Towner et al [11] used data derived from EHRs to generate social networks among inpatients based on shared rooms and shared contacts with HCWs, but they did not tie the data directly to transmission of nosocomial infections (ie, MRSA and influenza).

Although EHR data have limitations, because certain activities and contacts are not logged into the system, constructing HCW-mediated contact networks between patients using EHR data provides a scalable surrogate measurement for understanding how patients are connected. Our findings have implications not only for measuring the potential impact of infection control measures, but also for auditing HCW behavior associated with such measures. For instance, the finding that increased connections with VRE-positive patients is associated with VRE acquisition suggests that cohorting of staff may be effective in mitigating the spread of multidrug-resistant organisms, such as VRE. Electronic health record data can be used not only to define groups of patients for cohorting, but also to assess the implementation and effectiveness of cohorting. Data on patient connectedness could also be used for identifying patients at risk of acquisition and targeted for surveillance or as a means of aiding outbreak investigations. For example, one hospital used EHR data to aid in contact tracing for a TB outbreak [13]. In addition, other hospital operations data, such as

Table 1. Patient Demographics

Variable	Incident VRE	Nonincident
Patients	112	2252
Hospitalizations <sup>b</sup>	165	2787
Age, mean (SD)	56.5 (14.1)	56.5 (15.4)
Female	38.8%	44.1%
Race/Ethnicity (self-identified)		
Black, non-Hispanic	43.6%	38.0%
Other	4.2%	12.0%
White, non-Hispanic	52.1%	50.0%
Died	16.4%	12.3%
Length of stay, mean (SD)	39.5 (55.5)	19.7 (21.7)
Elixhauser comorbidity score	1.6 (2.7)	1.3 (2.3)
Long-term care facility (in prior 180 days)	9.1%	3.8%
HCW contacts, daily mean (SD)	26.9 (7.6)	26.4 (8.3)
Connections to other patients, daily mean (SD)	14.2 (5.8)	12.3 (5.4)
Connections to VRE colonized patients, total (SD)	26.6 (38.7)	9.8 (21.4)
Connections to VRE colonized patients, daily mean (SD)	3.1 (2.3)	2.0 (2.2)
Isolation order	51.5%	35.5%
Antibiotics (DDDs) before hospitalization (prior 365 days)	47.6 (104.5)	15.5 (33.1)
Carbapenems	4.9 (16.8)	1.4 (6.9)
Cephalosporins	6.9 (12.6)	3.6 (10.5)
Macrolides	3.6 (11.5)	0.8 (2.9)
Trimethoprim/sulfamethoxazole	0.5 (1.8)	0.1 (0.5)
Vancomycin	4.3 (7.1)	2.1 (5.5)
Antibiotics (DDDs) during hospitalization <sup>c</sup>	30.6 (66.5)	20.5 (40.3)
Carbapenems	3.5 (10.7)	1.8 (8.5)
Cephalosporins	4.6 (7.3)	4.4 (9.9)
Macrolides	3.0 (8.6)	1.0 (4.4)
Trimethoprim	0.4 (1.4)	0.2 (0.8)
Vancomycin	3.1 (5.3)	2.6 (6.1)
Proton pump inhibitors (DDDs) before hospitalization (prior 365 days)	38.3 (57.6)	14.5 (29.0)
Proton pump inhibitors (DDDs) during hospitalization <sup>c</sup>	25.3 (42.8)	19.7 (33.7)

Abbreviations: DDD, defined daily dose; HCW, healthcare worker; SD, standard deviation; VRE, vancomycin-resistant *Enterococcus*.

environmental cleaning or movement of hospital equipment, in which data may be electronically captured but not integrated into the EHR, can be readily incorporated into analyses to assess the impact of other infection control interventions. The utility of defining HCW-mediated contact networks may also benefit problem solving in healthcare optimization including the placement of resources critical for healthcare delivery and the architectural design (or redesign) of hospital units. More important, by using data regularly collected in most EHRs, the

Table 2. Multivariable Regression Results for Predicting Vancomycin-Resistant *Enterococcus* Acquisition

Variable	Logistic	Cox
	Odds Ratio (95% CI)	Hazard Ratio (95% CI)
HCW contacts <sup>a</sup>	1.45 (1.05–2.01)	1.00 (0.98-1.01)
Connections to VRE patients <sup>a</sup>	1.64 (1.39–1.92)	1.12 (1.08–1.15)
Isolation order <sup>b</sup>	1.27 (0.89–1.83)	_
Days with/presence of rectal tube <sup>a</sup>	0.78 (0.62–0.98)	1.16 (0.63–2.13)
Days with/presence of GI tube <sup>a</sup>	0.75 (0.61–0.93)	0.66 (0.33–1.32)
Days with/presence of dialysis <sup>a</sup>	1.11 (0.93–1.31)	1.77 (1.05–3.00)
Days with/presence of mechanical ventilation <sup>a</sup>	0.84 (0.65–1.09)	1.33 (0.74–2.38)
Antibiotics (DDDs) <sup>c</sup>	1.40 (1.20–1.64)	1.14 (1.02–1.27)
Proton pump inhibi- tors (DDDs) <sup>c</sup>	1.17 (1.03–1.34)	1.11 (1.08–1.15)
Long-term care facility in prior 180 days	1.24 (0.63–2.43)	1.37 (0.71–2.64)
Elixhauser comor- bidity score	0.98 (0.91–1.05)	0.99 (0.93–1.07)
Female	0.78 (0.55–1.10)	0.70 (0.49-0.98)
Age, mean (SD)	1.00 (0.99-1.01)	1.00 (0.99-1.01)
Race/Ethnicity Black, non-Hispanic as reference	Reference	Reference
Other	0.26 (0.12-0.61)	0.28 (0.11-0.70)
White, non-Hispanic	0.81 (0.56–1.18)	1.05 (0.73–1.50)
Days/present in ICU <sup>a</sup>	0.83 (0.69-1.00)	1.11 (0.71-1.74)

Abbreviations: CI, confidence interval; DDD, defined daily dose; GI, gastrointestinal; HCW, healthcare worker; ICU, intensive care unit; SD, standard deviation; VRE, vancomycinresistant enterococci.

<sup>a</sup>Indicates that in the Cox model, this is a discrete time-varying variable (eg, whether the patient was in the ICU or received dialysis on a particular day), whereas in the logistic regression, the variable was the sum of days and was logged in the logistic regression.

results are generalizable, and translation of this research to operational infection prevention and control interventions is scalable across institutions.

#### imitations

Although our use of EHR data to construct HCW-mediated patient networks is advantageous for several reasons, EHR data do have important limitations that should be considered when interpreting our results. Most importantly, EHR data does not catalog every HCW-patient interaction, and timestamps associated with those that are captured may not always coincide with the actual time of contact. This is likely of greater concern for certain types of interactions (eg, multiple HCWs coordinating on a single task) and certain classes of HCW (eg, practitioners) who tend to document at a delay. As a result, we likely underestimated the number of HCW interactions overall,

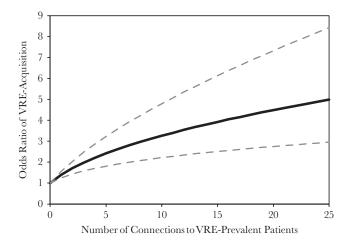
<sup>&</sup>lt;sup>a</sup>Includes patients that had at least 2 negative surveillance swabs for VRE ≥72 hours apart during an encounter.

<sup>&</sup>lt;sup>b</sup>Previously incident patients that had been out of the hospital for more than 1 year were eligible to be included again if their initial swab was negative.

<sup>&</sup>lt;sup>c</sup>For patients that acquired VRE, this is the total up until the acquisition swab and/or culture that tested positive was collected.

<sup>&</sup>lt;sup>b</sup>Variable was not available as time-varying parameter and did not meet proportionality hazard assumption and was thus excluded in the Cox models.

<sup>&</sup>lt;sup>c</sup>In logistic regression, this was the total antibiotic consumed in the prior 365 days before hospitalization, and in the Cox regression, this was the daily intake before incidence.



**Figure 2.** Odds ratio of vancomycin-resistant *Enterococcus* (VRE) acquisition relative to total number of VRE connections. The odds of acquiring VRE for a patient increased with the number of healthcare worker-mediated connections a patient had to VRE-prevalent patients compared with no connections. In other words, a single connection increased the odds most significantly, and although additional connections increased the odds of acquisition further, the marginal impact of each additional contact was less.

and biases in the collected data could impact calculations of patient connectivity, particularly for practitioners. In addition, although we minimized the inclusion of automated data in this study via clinical adjudication, it is important to note that many streams of EHR data (eg, vital signs) are now automated from medical devices and cannot be relied on as a marker of physical human interaction. Nevertheless, connectivity data generated from the EHR provide a surrogate measure of HCW-mediated contacts that is representative of the true underlying connectivity of patients. The other major limitation regards patient colonization status, because VRE surveillance swabs were only collected during the time period patients were hospitalized in the study units. Thus, the measurement of connections with VRE-colonized patients outside these units may underestimate the risk of acquisition because colonization status of many of these connections was unknown. Colonization status was determined by VRE surveillance swabs that are only taken at certain intervals, meaning patients that acquired VRE may have been colonized for several days before being detected. In addition, we assumed that once a patient was identified as colonized or infected with VRE, they remained positive (and thus a potential source) for 365 days regardless of other tests, which may have misclassified some patients relative to actual colonization status. Finally, as with most diagnostic tests, results may sometimes be incorrect, producing both false positives and false negatives, which again may have resulted in some patients being misclassified. However, the impact of misclassified patients is likely low because including connections to nonprevalent VRE patients, which should control for these misclassified patients, did not produce significant qualitative differences. Only in the time-varying covariate Cox regression case is there a suggestion that this may play a minor role in transmission (Supplementary Table 6). Additional research is needed to understand whether improvements in identification of VRE-prevalent patients could alter the capacity to reduce transmission.

## **CONCLUSIONS**

Containing the spread of infectious diseases within the hospital is a multifaceted challenge. Understanding how HCWs connect patients can elucidate how infectious diseases, such as VRE and other multidrug resistant organisms, spread in the hospital. We demonstrated that EHR data can inform how HCWs connect patients to spread VRE. Although EHR data have limitations, they provide a scalable and generalizable data source for understanding how patients are connected and can be used to reduce HAIs.

# **Supplementary Data**

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Supplementary Table 1. Patient Demographics of All Patients With  $\geq \! 1$  Surveillance Swab

Supplementary Table 2. Effect of Length of Stay and Antibiotics, Multivariable Logistic Regression

Supplementary Table 3. Multivariable Regression Results (When 12-Hour Connectivity)

Supplementary Table 4. Multivariable Regression Results (When 12-Hour Connectivity)

Supplementary Table 5. Multivariable Regression Results (When 30-Minute Connectivity)

Supplementary Table 6. Effect of Limiting Data to First Visit

Supplementary Table 7. Multivariable Regression Results Including Connections to Nonprevalent VRE Patients

#### **Acknowledgments**

Financial support. This work was funded by the Centers for Disease Control and Prevention (CDC) Epicenters Program (Grant Number 1U54CK000447) and the CDC MInD-Healthcare Program (Grant Number 1U01CK000536).

**Potential conflicts of interest.** All authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

### References

- World Health Organization. The burden of health care-associated infection worldwide. Available at: http://www.who.int/gpsc/country\_work/burden\_hcai/ en/. Accessed 8 August 2018.
- Stone PW. Economic burden of healthcare-associated infections: an American perspective. Expert Rev Pharmacoecon Outcomes Res 2009; 9:417–22.
- Ulrich N, Vonberg RP, Gastmeier P. Outbreaks caused by vancomycin-resistant *Enterococcus faecium* in hematology and oncology departments: a systematic review. Heliyon 2018; 3:e00473.
- Kaki R, Yu Y, O'Neill C, Lee C, Mertz D; Hamilton Health Sciences Infection Prevention and Control Team. Vancomycin-resistant enterococcus (VRE) transmission and risk factors in contacts of VRE carriers. Infect Control Hosp Epidemiol 2014; 35:876–9.
- Otter JA, Yezli S, Salkeld JAG, French GL. Evidence that contaminated surfaces contribute to the transmission of hospital pathogens and an overview of strategies to address contaminated surfaces in hospital settings. Am J Infect Control 2013: 41:S6–11.
- Srinivasan A, Song X, Ross T, Merz W, Brower R, Perl TM. A prospective study to determine whether cover gowns in addition to gloves decrease nosocomial

- transmission of vancomycin-resistant enterococci in an intensive care unit. Infect Control Hosp Epidemiol **2002**; 23:424–8.
- Duckro AN. Transfer of vancomycin-resistant enterococci via health care worker hands. Arch Intern Med 2005; 165:302.
- Hayden MK, Blom DW, Lyle EA, Moore CG, Weinstein RA. Risk of hand or glove contamination after contact with patients colonized with vancomycin-resistant enterococcus or the colonized patients' environment. Infect Control Hosp Epidemiol 2008; 29:149–54.
- Barnes S, Golden B, Wasil E. Exploring the effects of network structure and healthcare worker behavior on the transmission of hospital-acquired infections. IIE Trans Healthc Syst Eng 2012; 2:259–73.
- Geva A, Wright SB, Baldini LM, et al. Spread of methicillin-resistant Staphylococcus aureus in a large tertiary NICU: network analysis. Pediatrics 2011; 128:e1173–80.
- Cusumano-Towner M, Li DY, Tuo S, et al. A social network of hospital acquired infection built from electronic medical record data. J Am Med Inform Assoc 2013; 20:427–34.
- 12. Curtis DE, Hlady CS, Kanade G, et al. Healthcare worker contact networks and the prevention of hospital-acquired infections. PLoS One 2013; 8:e79906.
- Usiak SC, Romero FA, Schwegman P, et al. Utilization of electronic health record events to conduct a tuberculosis contact investigation in a high-risk oncology unit. Infect Control Hosp Epidemiol 2017; 38:1235–9.
- Karki S, Houston L, Land G, et al. Prevalence and risk factors for VRE colonisation in a tertiary hospital in Melbourne, Australia: a cross sectional study. Antimicrob Resist Infect Control 2012; 1:31.

- Chanderraj R, Millar JA, Patel TS, et al. Vancomycin-resistant enterococcus acquisition in a tertiary care hospital: testing the roles of antibiotic use, proton pump inhibitor use, and colonization pressure. Open Forum Infect Dis 2019; 6:ofz139.
- 16. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. Med Care 1998; 36:8–27.
- Elswick RK Jr, Schwartz PF, Welsh JA. Interpretation of the odds ratio from logistic regression after a transformation of the covariate vector. Stat Med 1997; 16:1695–703.
- Isella L, Romano M, Barrat A, et al. Close encounters in a pediatric ward: measuring face-to-face proximity and mixing patterns with wearable sensors. PLoS One 2011; 6:e17144.
- Polgreen PM, Hlady CS, Severson MA, Segre AM, Herman T. Method for automated monitoring of hand hygiene adherence without radio-frequency identification. Infect Control Hosp Epidemiol 2010; 31:1294–7.
- Vanhems P, Barrat A, Cattuto C, et al. Estimating potential infection transmission routes in hospital wards using wearable proximity sensors. PLoS One 2013; 8:e73970
- Voirin N, Payet C, Barrat A, et al. Combining high-resolution contact data with virological data to investigate influenza transmission in a tertiary care hospital. Infect Control Hosp Epidemiol 2015; 36:254–60.
- Hornbeck T, Naylor D, Segre AM, et al. Using sensor networks to study the effect of peripatetic healthcare workers on the spread of hospital-associated infections. J Infect Dis 2012: 206:1549–57.