Identification of transmission pathways for Vancomycin-resistant enterococcus in a hospital group from network theory

Michael Dahlweid, MD¹, Stefan Zahnd, PhD¹, Matthias Kaempf¹, Chris Debatin¹, Jonas Marschall, MD²

¹ Insel Data Science Center, Bern University Hospital, Bern, Switzerland
² Department of Infectious Diseases, Bern University Hospital, Bern, Switzerland

Abstract
To identify transmission vectors and characterize risk factors for Vancomycin-resistant enterococcus (VRE) acquisition, a computational network model to determine the “betweenness centrality” as a proxy for VRE dissemination has been developed, and network analysis was added to the arsenal of traditional infection control tools. This network model allowed the identification of risk factors for interpersonal transmission of VRE, and the applicability of data-based infection control has been tested. The model can be assumed to work with other hospital-acquired infections as well, for which further studies are being conducted.

Introduction
Vancomycin-resistant enterococci (VRE) are multi-drug-resistant micro-organisms that cause nosocomial infections and spread through healthcare workers or the environment¹. VRE infections are the fourth leading cause of mortality from antibiotic-resistant pathogens in the United States and in 2013, the CDC categorized vancomycin-resistant Enterococcus as a “serious threat”, suggesting the need for increased monitoring and prevention activities². Understanding VRE epidemiology, transmission in health care settings, and risk factors for colonization and infections are keys to prevention³.

In 2018, a previously locally unknown sub-type of VRE (sequence type 796) caused a nosocomial outbreak in our hospital group. Our intention was to control the nosocomial infection as quickly as possible after its introduction, given the challenges associated with VRE endemicity⁴. Thus, we aimed to go beyond traditional hospital epidemiology methodologies⁵, and established an interaction graph system based on electronic patient data to identify VRE infection hot spots and dissemination vectors. Our goals were to characterize risk factors for VRE acquisition, elicit potential hot spots of transmission, and delineate an optimized approach to tracing contacts.

Methodology
To examine the underlying variables contributing to the VRE dissemination, we developed a network model in which patients, medical devices, employees, and rooms constitute the nodes. The edges of the network represent the patient-room, patient-device, patient-employee, employee-device, employee-room, and device-room interactions. Note that there is no patient-patient interaction since the patients are never in direct contact with each other.

The data for the model were obtained from different electronic information systems during the outbreak period (1/2018-9/2018). Data sources include Electronic Medical Records, the Patient and Staff Scheduling System, the Rostering System, the Electronic Patient Administration System, and the Laboratory Information System (LIS). The LIS provided the screening results thus the annotation of each patient to be VRE-positive was assumed. Data from all other systems represents the patient pathway through the hospital(s) during the treatment process and is used to define the network to identify the transmission for Vancomycin-resistant enterococcus. Patients who tested VRE-positive during this period were compared to controls, defined as having had 0-3 negative screenings.

The following three methods were applied:
1. Risk factors for VRE colonization were determined by fitting uni- and multivariate logistic regression models
2. Hotspots: Transmission pathways and hot spots were identified by analyzing the relative importance of nodes in our network model. The metric consists of calculating the ratio of infected edges to all edges for all nodes where infected edges are characterized by the nodes being in direct connection with at least a VRE-positive patient node.
3. Network Modelling: We sought to understand whether cases with characteristics and connections similar to VRE patients were missed during contact tracing using betweenness centrality metrics. According to Borgatti⁶, betweenness centrality is the correct metric to identify nodes in a network that are critical in terms of occurrence in shortest pathways across the whole network thus this is the preferred metric for infection transmission scenarios.
Results

Table 1. Size of the data set (network)

<table>
<thead>
<tr>
<th>#</th>
<th>Node</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
<td>53667</td>
<td></td>
</tr>
<tr>
<td>Device</td>
<td>440</td>
<td></td>
</tr>
<tr>
<td>Employee</td>
<td>2054</td>
<td></td>
</tr>
<tr>
<td>Room</td>
<td>1689</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>#</th>
<th>Edge</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient-Room</td>
<td>554548</td>
<td></td>
</tr>
<tr>
<td>Patient-Device</td>
<td>139826</td>
<td></td>
</tr>
<tr>
<td>Patient-Employee</td>
<td>274813</td>
<td></td>
</tr>
<tr>
<td>Employee-Device</td>
<td>157477</td>
<td></td>
</tr>
<tr>
<td>Employee-Room</td>
<td>376943</td>
<td></td>
</tr>
<tr>
<td>Device-Room</td>
<td>262340</td>
<td></td>
</tr>
</tbody>
</table>

Results of logistic regression:

Independent predictors of VRE colonization were ICU admission (OR 4.9, with 95% confidence interval [3.7, 6.5], p < 0.001), number of records in the database (as a proxy for severity-of-illness, OR 1.1 [1.1, 1.1], p < 0.001), length of hospital stay (log(10) OR 2.7 [2.0, 3.5], p < 0.001), age (OR 1.3 per 10 years [1.2, 1.4], p < 0.001), weeks of antibiotic administration (OR 1.2 [1.1, 1.3], p < 0.001), along with marginally significant effects for both gender (male, OR 1.4 [1.1, 1.9], p = 0.02) and number of employee contacts (OR 1.1 [1.0, 1.2], p = 0.04).

We compared 340 VRE patients to 53,667 controls. (Table 1) By using complex network analysis, we were able to establish three main pathways by which the 340 VRE cases are connected: healthcare personnel, medical devices, and patient rooms. This multi-dimensional network extends beyond our current contact tracing strategy, which captures inpatients based on geographical proximity. We calculated the ratio of infected edges to all edges identified hotspot i.e. individual rooms, devices and employees allowing to intensify and targeted room cleaning, to review device disinfection protocols, and to test employees for carriage.

<table>
<thead>
<tr>
<th>Node ID</th>
<th>Node Type</th>
<th>Betweenness Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>EKG Service</td>
<td>Room</td>
<td>9.50</td>
</tr>
<tr>
<td>Examination Room</td>
<td>Room</td>
<td>8.00</td>
</tr>
<tr>
<td>142152</td>
<td>Device</td>
<td>6.92</td>
</tr>
<tr>
<td>Operating room X</td>
<td>Room</td>
<td>3.53</td>
</tr>
<tr>
<td>BL04</td>
<td>Room</td>
<td>2.30</td>
</tr>
<tr>
<td>D 123</td>
<td>Room</td>
<td>2.23</td>
</tr>
<tr>
<td>A</td>
<td>Employee</td>
<td>2.08</td>
</tr>
<tr>
<td>Operating room Y</td>
<td>Room</td>
<td>2.05</td>
</tr>
<tr>
<td>B</td>
<td>Employee</td>
<td>1.97</td>
</tr>
<tr>
<td>GASTRO</td>
<td>Room</td>
<td>1.97</td>
</tr>
<tr>
<td>ZAS-01</td>
<td>Room</td>
<td>1.74</td>
</tr>
</tbody>
</table>

Table 2. Results of Network Modeling

Clear ranked list allows a deep dive to define actionable interventions on the individual nodes

Conclusion

By utilizing a computational model to determine the “betweenness centrality” as a proxy for VRE dissemination within our hospital network and to identify high-risk patients as potential screening targets, we could show its usefulness to help hygiene stewardship during a VRE outbreak. Three main risk factors for being a VRE carrier (ICU admission, length of hospital stay, and antibiotic exposure) and three important links between VRE cases (healthcare personnel, medical devices, and patient rooms) have been identified. The model is being introduced as a standard tool for hospital epidemiology at our hospital group, and further evaluation is being performed to validate its utility and robustness.

Outlook

Beside further optimization of the transmission vector and hot spot analysis, we plan to develop a machine learning approach in order to predict (and thus reduce) infection risk on individual patient level. Data scarcity might be a serious caveat to successfully apply supervised learning, therefore generative adversarial networks (GANs) and/or Monte Carlo simulation will be tested. In addition, the model can be assumed to work with other hospital-acquired infections as well, for which further studies are being conducted.

References


(7) Hossmann T1, Atkinson A, Herbel S, Salazar-Vizcaya L, Dahlweid M, Marschall J. Data science for outbreak investigation: Identifying risk factors, tracing contacts and eliciting transmission pathways in a vancomycin-resistant enterococci (VRE) outbreak. ESCMID. 2019