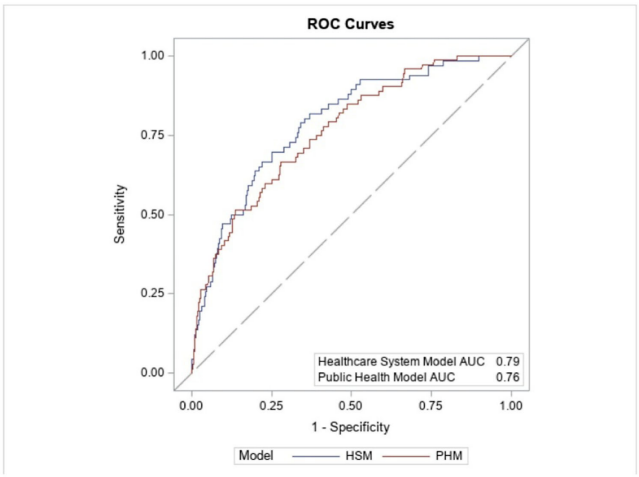

Figure 3: Receiver operating curves for the Public Health Model (shown in red) and the Healthcare System Model (shown in blue)

system model" added 4 additional variables (admission to the ICU in the prior 365 days, malignancy diagnosis, Elixhauser score and inpatient antibiotic days of therapy in the prior 365 days) to the public health model. We used billing codes to determine Elixhauser score, malignancy status, and recent infection diagnoses. We compared model performance using the area under the receiver operating curve (AUC). **Results:** We identified 105 cases and 441,460 controls (Table 1). CRE was most frequently identified in urine cultures (46%). All 4 variables included in the public health model and the 4 additional variables in the healthcare system model were all significantly associated with being a case in unadjusted analyses (Table 1). The AUC for the public health model was 0.76, and the AUC for the healthcare system model was 0.79 (Table 2; Fig. 1). In both models, a prior admission with an infection diagnosis was the most significant risk factor. **Conclusions:** A modified CRE prediction model developed using public health data and focused on prior healthcare exposures performed reasonably well when applied to a different academic healthcare system. The addition of variables accessible in large healthcare networks did not meaningfully improve model discrimination.

Disclosures: None

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Presentation Type:
Poster Presentation - Poster Presentation
Subject Category: Molecular Epidemiology

Surveillance of healthcare-onset clinical cultures using whole-genome sequencing reveals hidden nosocomial transmission

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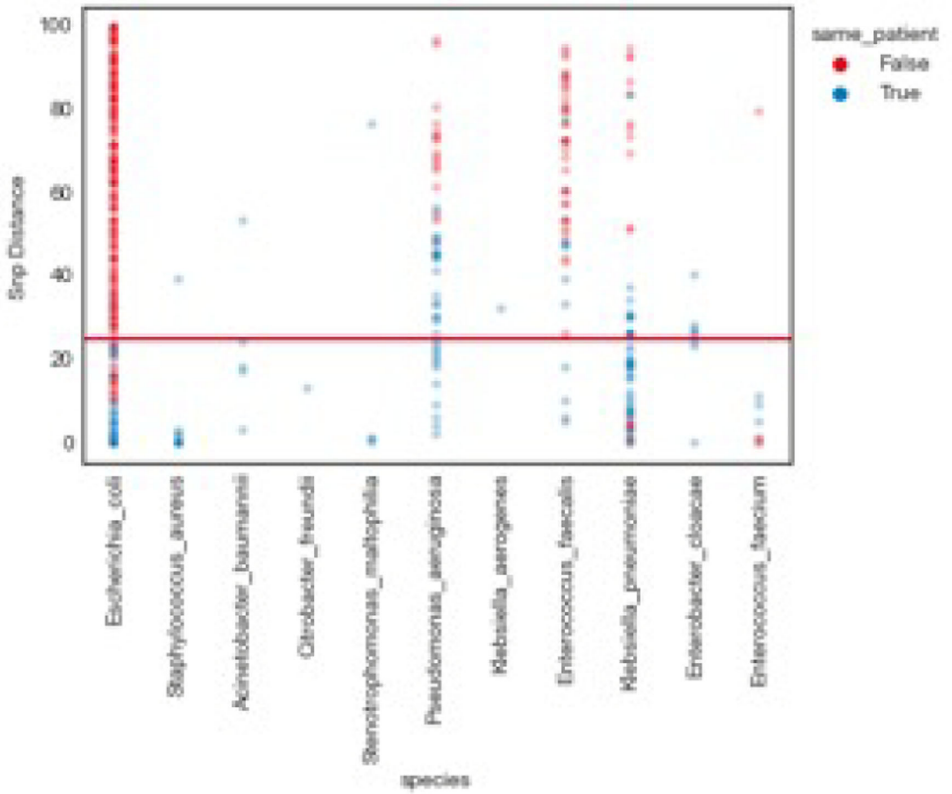
Background: Traditional hospital outbreak-detection methods are typically limited to select multidrug-resistant pathogens in a single unit, which can miss transmission of many medically important healthcare-transmissible pathogens. Whole-genome sequencing (WGS) enables comprehensive genomic resolution for accurate identification of clonal transmission. Previously, lack of scalability limited the use of WGS for hospital surveillance. **Methods:** We conducted prospective surveillance of select bacteria from all inpatient clinical cultures plus all bacteria from clinical cultures from ICUs and oncology units at the University of California Irvine (UCI) Clinical Microbiology Laboratory from September 2021 to February 2022. Due to pandemic stressors, this pilot test was a prelude to a real-time demonstration project. Its goal was to demonstrate the efficiency and scalability of the WGS platform when receiving samples monthly and analyzing results quarterly without the intent for real-time response. Bacterial isolates slated for discard were collected weekly and sent monthly to Day Zero Diagnostics for sequencing. In total, 1,036 samples from 926 patients were analyzed for genomic relatedness, a



scalable and automated analysis pipeline already in use for rapid (days) characterization of genomic-relatedness in small and large sets of isolates. Mapping and SNP calling was performed against high-quality, best-match reference genomes. Sets of samples with pairwise distance of 2 persons with genomically related isolates and were denoted as "clusters." Separately, we also investigated within-patient diversity by quantifying the genomic relatedness of isolates collected from individual patients. **Results:** Isolates represented 28 distinct species. We identified 10 *Escherichia coli* clusters (range, 2–4 patients; median, 2 patients), 2 *Klebsiella pneumoniae* clusters (range, 2–4 patients), and 1 *Enterococcus faecium* cluster (3 patients). All but 1 involved genomically matched isolates from multiple hospital locations. There were 4 *Escherichia coli* ST131 clusters spanning 4 months, including 1 with 4 patients across 3 different hospital locations. At a species level, there were distinct differences between the observed SNP distances between samples isolated from the same versus different patients (Fig. 1). All identified clusters had not been flagged by routine outbreak detection methods used by the UCI infection prevention program. **Conclusions:** Comprehensive WGS-based surveillance of hospital clinical isolates identified multiple potential transmission events between patients not in the same unit at the time cultures were taken. Combining WGS detection and real-time epidemiologic investigation may identify new avenues of transmission risk and could provide early warnings of clonal transmission to prevent larger outbreaks. High-volume surveillance of hospital isolates can also provide species- and context-specific clonality.

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Disclosures: None

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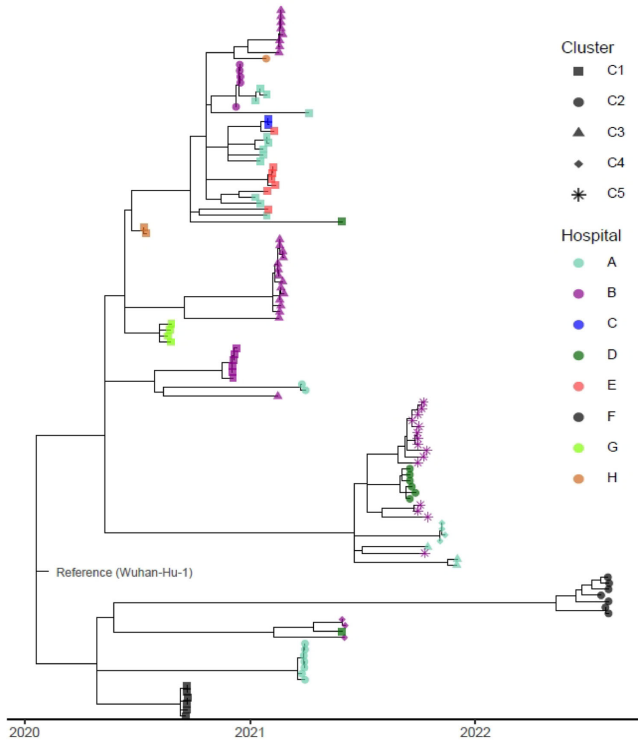

Presentation Type:
Poster Presentation - Poster Presentation

Subject Category: Molecular Epidemiology

Whole-genome sequencing cluster analysis reveals complex healthcare-associated COVID-19 dynamics

Theodore Rader; Graham Snyder; Lee Harrison; Vatsala Rangachar Srinivasa; Marissa Griffith; Lora Pless and Ashley Chung

Background: Identifying and interrupting transmission of severe acute respiratory syndrome coronavirus 2 and resulting disease (COVID-19) in acute-care settings can be challenging due to incubation period, asymptomatic infection, and prevalent community disease. To elucidate routes of infection and interrupt COVID-19 outbreaks with uncertain epidemiological chains of transmission, UPMC utilized reactive whole-genome sequencing (WGS) of viral specimens. **Methods:** UPMC infection prevention teams identified healthcare-associated COVID-19 clusters with uncertain transmission pathways among patients and/or healthcare personnel (HCP) in acute-care hospitals. Nasopharyngeal samples preserved in viral transport media were obtained for genetic analyses. Nucleic acids were extracted and WGS libraries were prepared by targeted enrichment or multiplex PCR methodologies. Resulting sequencing reads were aligned to the Wuhan-1 reference genome, followed by identification of single-nucleotide polymorphisms (SNPs) among the genomes and construction of a phylogenetic tree. Specimens were considered genetically similar if there were ≤2 SNP differences between viral genomes within a cluster. **Results:** Between May 2020 until August 2022, infection prevention teams requested WGS for 17 healthcare-associated clusters of COVID-19 involving 182 individuals across 8 UPMC facilities (median outbreak size, 9 individuals; range, 2–26). Of the 182 individuals, 36 lacked clinical specimens and 30 did not pass WGS quality-control criteria of ≥95% of the reference genome with a minimum of 10× coverage. Of the 116 sequenced genomes, 94 (81%) had virus genetically similar to ≥1 other specimen, including 87 (83.6%) of 104 patient viruses and 7 (58.3%) of 12 HCP viruses, comprising 22 clusters (Fig. 1). The remaining 22 (20.6%) specimens were genetically unrelated. In total, 16 (94.1%) of the 17 epidemiologically identified clusters had 2 or more individuals with a genetically similar virus. Also, 7 (41.1%) of these clusters had genetically similar viral genomes for every individual within each cluster. Also, 9 (52.9%) clusters contained both genetically related and unrelated specimens: 5 of these had more complex genomic profiles (including 4 clusters containing 2 distinct subclusters of ≥2 genetically related viruses) and 1 cluster contained 3 subclusters of ≥2 genetically related viruses. In the outbreak with 3 clusters, 3 SNPs separated specimens from 2 temporally proximal clusters, suggesting possible propagation between clusters (cluster B-3 in Fig. 1). **Conclusions:** WGS can complement traditional epidemiological investigations of healthcare-associated COVID-19 outbreaks, revealing complex transmission dynamics. Future investigations will characterize the impact of WGS on determining specific transmission pathways in acute-care facilities.

Disclosures: None

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Subject Category: MRSA/VRE

Factors associated with SARS-CoV-2 and community-onset invasive *Staphylococcus aureus* coinfection, 2020

Kelly Jackson; Sydney Resler; Joelle Nadle; Susan Petit; Susan Ray; Lee Harrison; Ruth Lynfield; Kathryn Como-Sabetti; Carmen Bernu;

Figure 1. Timing from first SARS-CoV-2 positive test collection to initial invasive *Staphylococcus aureus* specimen collection, community-onset coinfection cases, 11 US counties, March 1–December 31, 2020.