Infection Control & Hospital Epidemiology (2024), **45**, 135–136
doi:10.1017/ice.2023.261

SHEA

Commentary

Whole-genome sequencing surveillance: Growing evidence for a future potential practice standard of infection prevention

Alexander J. Sundermann DrPH, CIC[1] and Waleed Javaid MD[2]

[1]Division of Infectious Diseases, Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania and [2]Division of Infectious Diseases, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York

Whole-genome sequencing (WGS) surveillance, once a technology reserved for research laboratories, is now making significant strides in practical healthcare applications. Its unique capability to identify otherwise undetected outbreaks and trace the transmission of healthcare-associated infections (HAIs) has demonstrated considerable utility. Current literature suggests an increasing number of institutions are employing WGS, albeit primarily in a retrospective manner.[1] If deployed in real time, WGS surveillance holds considerable promise in cost savings and HAI reduction.[2]

In this issue of *Infection Control and Hospital Epidemiology*, Lee et al[3] provide additional evidence of WGS surveillance as a valuable infection prevention tool. In their study, Lee et al analyzed 8 years of real-time WGS surveillance data for carbapenemase-producing Enterobacterales (CPE) at their large hospital in Australia. As screening or clinical CPE isolates were detected, isolates underwent WGS for bacterial or plasmid relatedness, and infection prevention and control (IPC) measures were initiated for suspected transmission. Their data revealed 9 outbreaks ranging from 2 to 16 patients. One notable outbreak described a New Delhi metallo-β-lactamase plasmid outbreak that spanned 250 days across multiple hospital locations with interspecies transmission. Through WGS surveillance, the investigators traced this outbreak back to an outpatient clinic, which they report would have been missed with the use of traditional IPC methods.

An interesting facet of their study involves the description of the use of WGS data to direct IPC measures, particularly the use of environmental cultures, more precisely. The healthcare environment is well known to harbor pathogens implicated in HAI outbreaks.[4] Environmental culturing is currently recommended only when the results can be used to confirm a hypothesis or will lead to an actionable intervention.[5] This is partly because it may be difficult to determine causation from a positive environmental culture given the temporality of the culture (if taken after the outbreak has ended) and difficulty in determining directionality (ie, transmission from the patient to the environment versus environment to patient). Moreover, matching environmental isolates to patient isolates is challenging without using WGS. However, recent studies have shown that WGS surveillance of patient isolates combined with WGS of targeted environmental isolates may yield insights into outbreak dynamics.[6,7] Lee et al provided an outbreak example in which 2 patient isolates, months apart, were genetically linked. Environmental cultures yielded the same genetically linked isolate from the healthcare environment, indicating a persistent environmental source. Here, the use of WGS of patient isolates and environmental isolates allowed the IPC team to identify environmental reservoirs and implement control measures.

Speed is of the essence in outbreak management, and the quick WGS turnaround time in the study by Lee et al was a significant asset, decreasing from a median of 14 days to 9 days over the study period. While isolates are being processed in the genomic bioinformatic pipeline, outbreak transmission may still occur while no interventions are in place. Consideration of this factor is crucial when adopting bacterial versus viral WGS surveillance. Incubation and transmissibility phases of newly acquired viral cases may be shorter than the threshold of a rapid turnaround time in the bioinformatic pipeline (eg, <14 days), such that any interventions made on an outbreak would be past this initial phase and ineffective. However, the timeline of a bacterial outbreak may be protracted, allowing for a more extended time margin in analysis and subsequent intervention before additional spread occurs.

Lee et al state that the most significant hurdle of adoption of WGS surveillance is the interpretation of genomic data. The use of automated bioinformatics analysis pipelines and perhaps the emergence of commercial WGS services may lower this barrier. Nonetheless, healthcare professionals specializing in infection prevention and hospital epidemiology must be trained to interpret WGS data accurately.

As we anticipate the future, one significant barrier to the adoption of WGS surveillance is the lack of financial incentives for healthcare institutions to invest in this technology. The initial capital requirements for an internal WGS surveillance program are not insignificant, encompassing training, infrastructure, and equipment costs. Although some industry companies exist to alleviate this hurdle, there are still associated costs with this approach. Nonetheless, a growing body of literature suggests that the long-term economic benefits and enhanced patient outcomes justify this investment.[2,8] A persistent challenge facing the field of infection prevention is persuading healthcare administrators to allocate resources toward disease prevention rather than treatment modalities. The research by Lee et al offers a case study in overcoming this challenge. They demonstrated to their institutional leadership the utility of WGS surveillance by presenting data on active outbreaks that would likely have remained undetected without this technology. For those in IPC seeking to initiate a WGS program, a similar strategy could be employed: presenting data on

Corresponding author: Alexander J. Sundermann; Email: ALS412@pitt.edu

Cite this article: Sundermann AJ, Javaid W. Whole-genome sequencing surveillance: Growing evidence for a future potential practice standard of infection prevention. *Infect Control Hosp Epidemiol* 2024. 45: 135–136, doi: 10.1017/ice.2023.261

potential, yet undetected, outbreaks that may evade traditional IPC surveillance methodologies could serve as a compelling justification for investment.[9]

Several factors must be considered when adopting WGS surveillance. As WGS surveillance expands, we must consider the equitable use and implementation across healthcare systems. How do we ensure that smaller hospitals or those in less affluent areas have the same access to this potentially lifesaving infection prevention technology? How do we ensure that patient data are appropriately and securely shared from one institution to the next? As WGS databases grow, many institutions may store genomic and epidemiologic data locally. What are the best practices to share these data that optimize the analysis of outbreaks? Additionally, should only clinical isolates be sequenced or those patients with colonization be sequenced as well?

Organizations such as The Council for Outbreak Response: Healthcare-Associated Infections and Antimicrobial-Resistant Pathogens (CORHA) can offer valuable guidance, providing standardized protocols for outbreak response and data sharing. CORHA combines multiple federal agencies and professional societies to create resources for standards in outbreak response. CORHA has begun building their Principles and Practices for Healthcare Outbreak Response, which guides those surveying and responding to outbreaks.[10] These documents provide insight to optimize current practices and reference those institutions wishing to start a surveillance program. The Society of Healthcare Epidemiology of America (SHEA), Association of Professionals in Infection Control (APIC), and other healthcare and hospital-based institutions could provide input on standardizing WGS in line with IPC principles.

Lee et al underscore the urgency for future research to establish a direct connection between real-time WGS surveillance and a measurable decrease in HAIs. Implementing such a study design presents a challenge, particularly when trying to demonstrate the 'what-if' scenario—the counterfactual—of an outbreak that has already been identified and mitigated. One possible approach would be to employ a multicenter case–control design comparing 2 hospitals. However, the inherently sporadic and unpredictable nature of outbreaks complicates the task of selecting a control hospital that closely mirrors the operational intricacies of the test hospital. Given these challenges, relying on robust observational data from WGS surveillance real-time and retrospective studies may be more pragmatic. When combined with financial modeling, these data can be used to build a compelling argument for the routine implementation of WGS surveillance.

In conclusion, as more research, such as the study by Lee et al, contributes to our understanding of the impact of WGS surveillance on HAIs, we must ask ourselves: When will WGS surveillance become the standard in infection prevention and control, given its potential to substantially enhance patient safety?

Acknowledgements.

Financial support. No financial support was provided relevant to this article.

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

References

1. Sundermann AJ, Chen J, Miller JK, *et al.* Whole-genome sequencing surveillance and machine learning for healthcare outbreak detection and investigation: a systematic review and summary. *Antimicrob Steward Healthc Epidemiol* 2022;2:e91.
2. Price V, Ngwira LG, Lewis JM, *et al.* A systematic review of economic evaluations of whole-genome sequencing for the surveillance of bacterial pathogens. *Microb Genom* 2023;9:mgen000947.
3. Lee AS, Dolan L, Jenkins F, Crawford B, van Hal SJ. Active surveillance of carbapenemase-producing Enterobacterales using genomic sequencing for hospital-based infection control interventions. *Infect Control Hosp Epidemiol* 2023. doi: 10.1017/ice.2023.205
4. Suleyman G, Alangaden G, Bardossy AC. The role of environmental contamination in the transmission of nosocomial pathogens and healthcare-associated infections. *Curr Infect Dis Rep* 2018;20:12.
5. Environmental sampling: guidelines for environmental infection control in healthcare facilities. Centers for Disease Control and Prevention website. https://www.cdc.gov/infectioncontrol/guidelines/environmental/background/sampling.html. Published April 9, 2019. Accessed September 18, 2023.
6. Cassone M, Wang J, Lansing BJ, *et al.* Diversity and persistence of MRSA and VRE in skilled nursing facilities: environmental screening, whole-genome sequencing and development of a dispersion index. *J Hosp Infect* 2023;138:8–18.
7. Doughty EL, Liu H, Moran RA, *et al.* Endemicity and diversification of carbapenem-resistant *Acinetobacter baumannii* in an intensive care unit. *Lancet Reg Health West Pac* 2023;37:100780.
8. Fox JM, Saunders NJ, Jerwood SH. Economic and health impact modelling of a whole-genome sequencing-led intervention strategy for bacterial healthcare-associated infections for England and for the USA. *Microb Genom* 2023;9:mgen001087.
9. Sundermann AJ, Chen J, Kumar P, *et al.* Whole-genome sequencing surveillance and machine learning of the electronic health record for enhanced healthcare outbreak detection. *Clin Infect Dis* 2022;75:476–482.
10. CORHA principles and practices for healthcare outbreak response. Council for Outbreak Response: Healthcare-Associated Infections and Antimicrobial-Resistant Pathogens (CORHA) website. https://www.corha.org/resources/corha-principles-and-practices-for-outbreak-response/. Accessed September 18, 2023.

https://doi.org/10.1017/ice.2023.261 Published online by Cambridge University Press