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2476. Universal detection of healthcare-related bacterial transmissions using *de novo* assembly with short-read whole genome sequencing

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Background. Whole genome sequencing (WGS) is the gold standard for molecular evidence of pathogen transmission. To date, most WGS investigations within healthcare settings have used low cost short-read technologies (e.g., Illumina), aligning reads to a high quality reference genome. However, this relies on either public repositories having closely-related high quality references, which is not guaranteed for arbitrary clinical isolates, or additional long-read sequencing. *De novo* assembly avoids reliance on references, but the utility of fragmented assemblies of short reads is not well-established in hospital outbreak investigations.

Methods. 24 clusters of clinical isolates were identified by automated and routine methods at 17 U.S. hospitals and underwent paired-end WGS on Illumina platforms, followed by two parallel analyses. For a reference-free analysis, *de novo* assembly was performed with Shovill, assemblies were clustered with Mash, core-genome alignments were created with Harvest, and finally single nucleotide polymorphism (SNP) distances were visualized using the PathoSPOT phylogenomics toolkit to highlight likely transmission events. For a reference-guided analysis, references were selected for each isolate using StrainGST, and SNPs called by read alignment were used to define phylogenomic distances. Finally, conclusions from both analyses were compared.

Results. 92 bacterial isolates underwent WGS, of which 86 (93%) completed *de novo* assembly and passed quality control, comprising 10 isolates of *Acinetobacter baumanii*, 4 of *Klebsiella oxytoca*, 46 of *Klebsiella pneumoniae*, and 26 of *Staphylococcus aureus*. Reference-free analysis with PathoSPOT identified close relatedness consistent with transmission in 13 of 24 clusters (54%), while the reference-

guided analysis identified the same in 12 clusters (50%). Overall, 21 clusters (88%) showed concordance between reference-free and reference-guided methods. Cohen's kappa indicated substantial agreement (0.75; 95% CI, 0.49–1.0).

Conclusion. *De novo* assembly of short reads is tenable for WGS investigation of hospital outbreaks, elides the need for reference genomes or long-read sequencing, and compares favorably with SNP calling via read alignment for detecting likely healthcare-related transmissions.

Disclosures. **Laura E. McLean, M.Ed.**, HCA Healthcare: Stocks/Bonds **Susan S. Huang, MD MPH**, Medline Industries, Inc: Conducted studies whereby participating nursing homes and hospital patients received cleaning & antiseptic products| Xttrium Laboratories: Conducted studies where participating nursing homes and hospital patients received antiseptic products **Yonatan H. Grad, MD, PhD**, Day Zero Diagnostics: Board Member|GSK: Advisor/Consultant