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Useful discordance: economic justification for whole-genome sequencing of resistant bacteria in institutional outbreak management

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Background: Meticillin-resistant *Staphylococcus aureus* (MRSA) is an important cause of nosocomial infections contributing to significant patient morbidity and mortality. Conventional reference laboratory typing methods for MRSA can lack discrimination when compared with newer techniques such as whole-genome sequencing (WGS). Inconclusive or falsely indicative results can impede effective infection prevention and control. WGS offers the promise of differentiation down to a single nucleotide difference, allowing for accurate mapping of transmission events. The technique can also provide important information pertaining to antimicrobial susceptibility, virulence and identification of high risk clones. However, routine utilisation of WGS is limited by affordability and availability. We describe the investigation and management of a cluster of the USA300 clone of community acquired-MRSA by WGS.

Material/methods: Over a period of 11 days, Panton-Valentine Leukocidin-MRSA colonisation was identified in seven babies across two neonatal units (NNUs) within different hospitals in neighbouring districts. Phenotypic susceptibility patterns and conventional typing data (*spa* and PFGE) indicated that the MRSA recovered from both NNUs were indistinguishable and belonged to a lineage seen

relatively rarely in England (USA300 clone), thus prompting a cross-site outbreak investigation. When no link was identified, WGS was employed.

Results: Phylogenetic analyses clearly indicated two different strains were involved and, despite chronological association, there was no cross-site spread. An evaluation of the absolute costs associated with the investigation and management of presumed cross-site spread was undertaken. In addition to the routine involvement of infection prevention and control, microbiology, NNU and maternity personnel; the presumed cross-site nature of the outbreak necessitated the further participation of reference laboratory scientists, Occupational health and Public health teams. Additional processes undertaken included: parent interviews, equipment screening, environmental screening, site visits, hand hygiene audits, healthcare worker (HCW) training and screening. Four HCWs were potential common links between the two units. All four HCWs were temporarily excluded from clinical duties pending screening results. Total staffing costs attributed to unnecessary processes that resulted from the management of the presumed cross-site outbreak totaled in excess of £16,000. This consisted of expenditure in temporary staffing, and 'opportunity cost' in staff time. Further absolute costs include additional cleaning, carrier eradication and screening expenses. Non-quantifiable costs include reputational damage, emotional costs to parents and HCWs involved.

Conclusions: There has been much work demonstrating the use of WGS for epidemiological mapping during suspected outbreaks. Here we demonstrate its utility in discriminating between cases initially thought to be linked. While the value of routine WGS is debatable, we have highlighted a specific situation where a discordant result provides a strong economic justification for its utilisation. Timely employment of WGS can be justified in presumed outbreak scenarios where discordant results could mitigate resources being unnecessarily spent on non-routine infection prevention and control measures.