WGS for infection prevention and control in Africa

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In *The Lancet Microbe*, Uduak Okomo and colleagues[1] present a study on the nosocomial transmission of multiresistant strains of *Klebsiella* spp and *Burkholderia cepacia* in a neonatal hospital ward in The Gambia. Prompted by the microbiological detection of 94 bacteraemia episodes (49 due to *B cepacia* and 45 due to extended spectrum β-lactamase [ESBL]-producing *K pneumoniae*) with a high associated mortality over a 10-month period in 2016, the authors started an outbreak investigation and used whole-genome sequencing (WGS) to elucidate strain relatedness and to source the origin of the outbreaks. Okomo and colleagues found that extrinsic contamination during handling of previously sterile intravenous fluids was the most likely source of the outbreaks. Additionally, they found that *B cepacia* had been present on the ward for several years, suggesting that many previous infections might have gone undiagnosed and unnoticed. The researchers detected that the *Klebsiella* outbreak was actually caused by two distinct strains (*Klebsiella pneumoniae* [ST39] and *Klebsiella quasipneumoniae* subsp *similipneumoniae* [ST1535]), which had been introduced more recently on the ward than *B cepacia*. Okomo and colleagues concluded that poor hand hygiene and inaccuracies during sterile procedures might have given rise to the high number of severe infections due to these bacteria. These causes of infection are likely to apply to many health-care settings in low-income and middle-income countries, and more clinical research on the application of WGS for infection prevention and control is urgently warranted.

Although WGS is now frequently being used in high-income settings for infection control measures, its application in resource-constrained tropical areas has mainly been restricted to research settings—eg, to assess the dissemination of certain microorganisms in different environments.[2] The newly published study is among the first ones to apply WGS as a tool for outbreak investigation in clinical practice in Africa. Okomo and colleagues' finding that the *B cepacia* outbreak strain had been present on the ward for several years underscores the need for quality-controlled, timely, and reliable microbiological diagnostics in low-income settings.[3] Indeed, previous calls for prioritisation of laboratory testing facilities in Africa[4] should be complemented by the introduction of modern molecular methods such as WGS, which allow for the investigation of strain characteristics and relatedness.

Because of technical difficulties in obtaining qualitatively adequate blood cultures—particularly on a neonatal ward—such as a high risk of contamination with skin flora during the sampling procedure and a reduced test sensitivity attributable to the small amount of blood volume that can be obtained from newborn children, the true rate of bloodstream infections might have been higher than reported by Okomo and colleagues. With regard to the microbiological culture techniques used, there is a possibility that some *B cepacia* infections might have been missed; this pathogen grows slowly on most agar media and might require more time than the reported incubation period of 48 h to become visible and be accurately identified.[5]

B cepacia is a non-fermentative Gram-negative bacterium that typically gives rise to severe pulmonary infections in individuals with cystic fibrosis. However, outbreaks due to extrinsic contamination (eg, incorrect handling[6]) or intrinsic contamination (eg, during the manufacturing process of disinfectants[7]) have been frequently reported. The bacterium is usually resistant to a wide panel of antibiotics, and the mortality associated with *B cepacia* is thus high, particularly in resource-constrained settings. Okomo and colleagues found the *B cepacia* isolates in their study to be susceptible to all tested antibiotics, but reported a mortality of 50% for the 36 patients with *B cepacia* bacteraemia for whom outcome data were available, suggesting discordance between in-vitro susceptibility and in-vivo response to antimicrobial treatment.

Klebsiella spp belong to the Gram-negative Enterobacterales and rank high among the clinically relevant bacteria with multidrug resistance. Strains producing ESBLs and, even more worrisome, carbapenemases such as *Klebsiella pneumoniae* carbapenemase (KPC), New Delhi metallo-β-lactamase (NDM), and OXA-48 commonly cause outbreaks in health-care settings, and are increasingly being detected in sub-Saharan Africa.[8] A 2019 WGS-based study[9] from Nigeria showed that 24·6% of all ESBL-producing isolates obtained from clinical infections also carried carbapenemase-encoding genes, which considerably limited the remaining antibiotic treatment options.

Although the two outbreak *Klebsiella* strains in the investigation by Okomo and colleagues remained sensitive to carbapenems, they produced ESBLs and showed additional resistance to fluoroquinolones and aminoglycosides. Unfortunately, outcome data were only available for nine out of 45 patients, with five recorded deaths.

While the study from The Gambia highlights the paramount importance of applied WGS to identify and control such outbreak scenarios, the actual WGS work was done in the UK. In the future, efforts should be made to implement WGS facilities in selected centres across sub-Saharan Africa to ensure the availability of regional diagnostic centres of excellence that are readily available to assist in independent, clinically relevant outbreak investigations. Although WGS was restricted to a few large research consortia a decade ago, this technique has now been democratised[10] and can easily be used by individual research groups, but high associated costs are still of concern. It is also important to note that the successful implementation of a WGS pipeline requires not only the technical availability of a suitable sequencer, but also sufficient data management and bioinformatics resources for efficient genome assembly and annotation.

In conclusion, the study by Okomo and colleagues underscores that WGS-based investigations are clinically useful tools to monitor, source, control, and prevent outbreaks caused by widespread multidrug-resistant bacteria in Africa. Hence, strategies to foster the availability of WGS in low-income countries should be encouraged.

I declare no competing interests.

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