

***Salmonella enterica* Serotype Typhi in South Africa: Defining Cases, Clusters and Outbreaks**

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Background: *Salmonella enterica* serotype Typhi (*Salmonella* Typhi) is endemic in South Africa. Incidence rates are ~0.1 per 100,000. Nonetheless, typhoid fever outbreaks are reported, complicated by imported cases from ongoing outbreaks on the country's borders. This study was undertaken to establish whether molecular methods could differentiate between local and imported cases, to support the epidemiological investigation.

Methods: In January 2016, a renewed programme of case follow-up and contact tracing was introduced. Active laboratory-based surveillance complemented these efforts through phenotypic and genotypic analysis (Pulsed-Field Gel Electrophoresis [PFGE] and Multiple-Locus Variable-Number Tandem Repeats Analysis [MLVA] and WGS) of *Salmonella* Typhi isolates from cases and contacts.

Results: By mid-November 2016, 90 typhoid fever cases had been reported in South Africa. Cases appeared predominantly associated with the 2012 Zimbabwean clone. Two typhoid fever clusters were identified in Gauteng and Western Cape (WC) provinces respectively. One Gauteng cluster was related to a domestic worker returning from Zimbabwe, the second to endemic infection: the index case had travelled locally. Both clusters were highly related on PFGE and MLVA. The first WC typhoid fever cluster included both cases and carriers in an extended family. PFGE patterns and MLVA profiles were identical. The second WC cluster showed a different *Salmonella* Typhi PFGE pattern and MLVA profile compared with the first and was considered unrelated. MLVA profiles of these isolates showed single locus variations, but were interpreted as related to one other. One WC cluster and both Gauteng clusters were related to Zimbabwean outbreak cluster. WGS results confirmed these relationships.

Conclusions: MLVA and PFGE could not differentiate between endemic typhoid fever, secondary to the Zimbabwean outbreak, or imported cases. Further WGS analysis is planned to compare these clusters with other *Salmonella* Typhi isolates identified in 2016 and locally acquired versus imported isolates from previous years.