Clinical and genomic data to understand transmission patterns of typhoid fever and inform targeted environmental sampling in Blantyre, Malawi

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March 26, 2019
11th International Conference on Typhoid and Other Invasive Salmonelloses
Transmission of S. Typhi

“Short-cycle” and “long-cycle”
Unknown in most locations
Understanding transmission pathways: targeted interventions, vaccine impact estimates
Blantyre context

Increase in cases starting ~2011, majority MDR

Dominant transmission routes unknown

Cohort study including GPS coordinates of households of typhoid fever cases and whole genome sequences starting in mid-2015

Nested case-control study conducted through MLW to assess risk factors

Feasey et al, 2015
Case-control study
Data collection by Fran Olgemoeller et al.

Nested case control study of children 8 years of age and younger

Exposure related variables spanning water usage, food storage, other risk factors

Largest odds ratio (other than healthcare-seeking): water usage pattern for cooking and cleaning

- Those using river water for cooking and cleaning had highest 4.7 (95% CI 1.7-12.6) odds of being a case
- Spending the day in school or daycare had lower odds (OR 2.6 [CI: 1.3-5.2]) but highest attributable risk (51%)
Aim: to better understand typhoid transmission patterns in Blantyre using spatial and genomic data

Motivation: the more similar isolates are genetically, the closer they are along a transmission network

Clinical isolates from Blantyre, Malawi were whole genome sequenced and geo-located

Seven major clades identified in Blantyre, approximately 50 clonal isolates
Predicting genetic relatedness

Preliminary analysis: SNP distance and physical distance are significantly correlated

Multidimensional scaling to create variables representing position in genetic “space”

Evidence of spatial correlation up to 2500 meters

What possible transmission mechanisms operate on this scale?
Exploring possible predictors

Hypothesis driven by case-control results

Explore ability of river networks across city to predict genetic relatedness

Shapefiles from Costly Chanza
Findings: Nearest river is a significant predictor of genetic score across the city
Interpreting model results

Spatial-genetic model: allows for explained variation (large scale, river catchment) and unexplained (small-geographic scale).

Both components important for explaining genetic relatedness across the city

Small scale correlation up to approximately 200 meters: clustering distances of schools and daycares?
Take-aways for understanding typhoid transmission in Blantyre:

Cooking and cleaning water may be as important (or more important) than drinking water as an exposure route for typhoid fever in some locations.

Pairing spatial and genomic data is useful for investigating spatial scales of transmission in new locations.

River network predicts the large-scale spatial correlation seen in Blantyre, and combined with risk data provides evidence that rivers may be facilitating transmission of typhoid fever.

Smaller scale spatial correlation exists: household units, school/daycare facilities, more work needed to identify these routes.
Targeting environmental sampling for understanding exposure

Look to rivers! Pilot testing to inform larger sampling initiative.

Spatial heterogeneity in incidence: target rivers linked with the most reported cases

Primary questions:
• Upstream/downstream samples to test for potential accumulation or die-off of S. Typhi downstream
• Understand drivers in temporal variation in signal: diurnal or rainfall-based variation in detection? Preliminary analysis shows temporal signal with rain, “flushing” of pit latrines
Thank you!