

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

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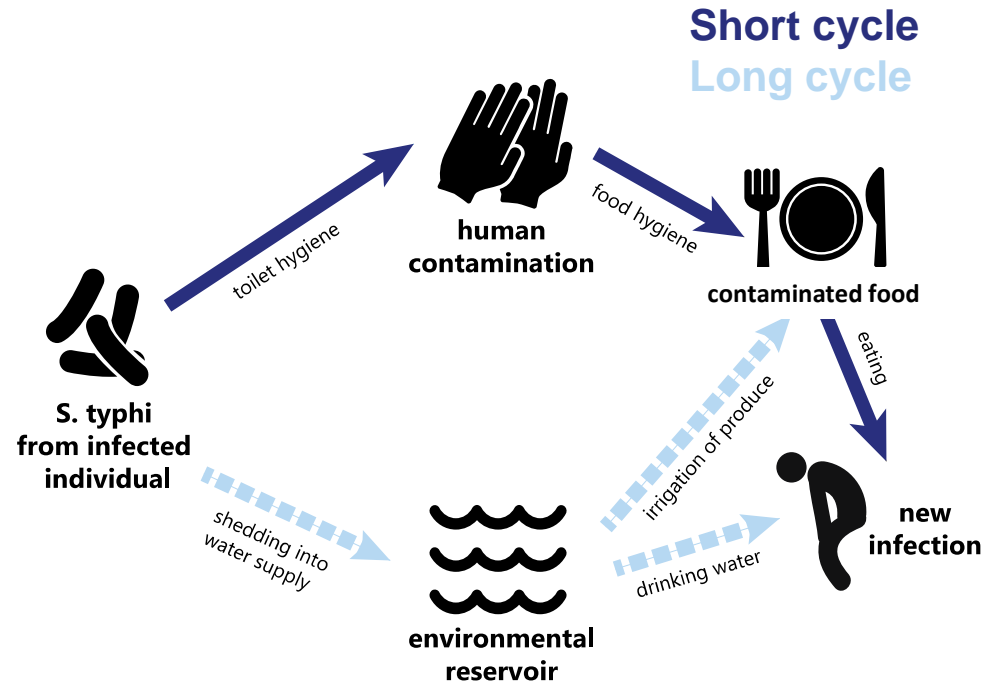
11th International Conference on Typhoid and Other Invasive Salmonellosis

Transmission of S. Typhi

“Short-cycle” and “long-cycle”

Unknown in most locations

Understanding transmission pathways: targeted interventions, vaccine impact estimates



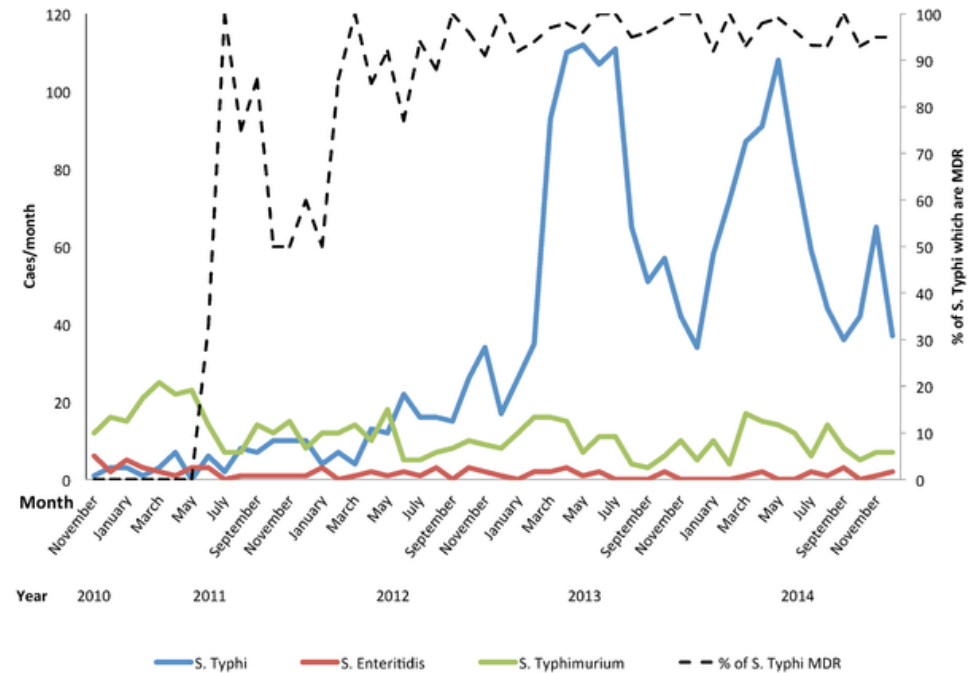
Blantyre context

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

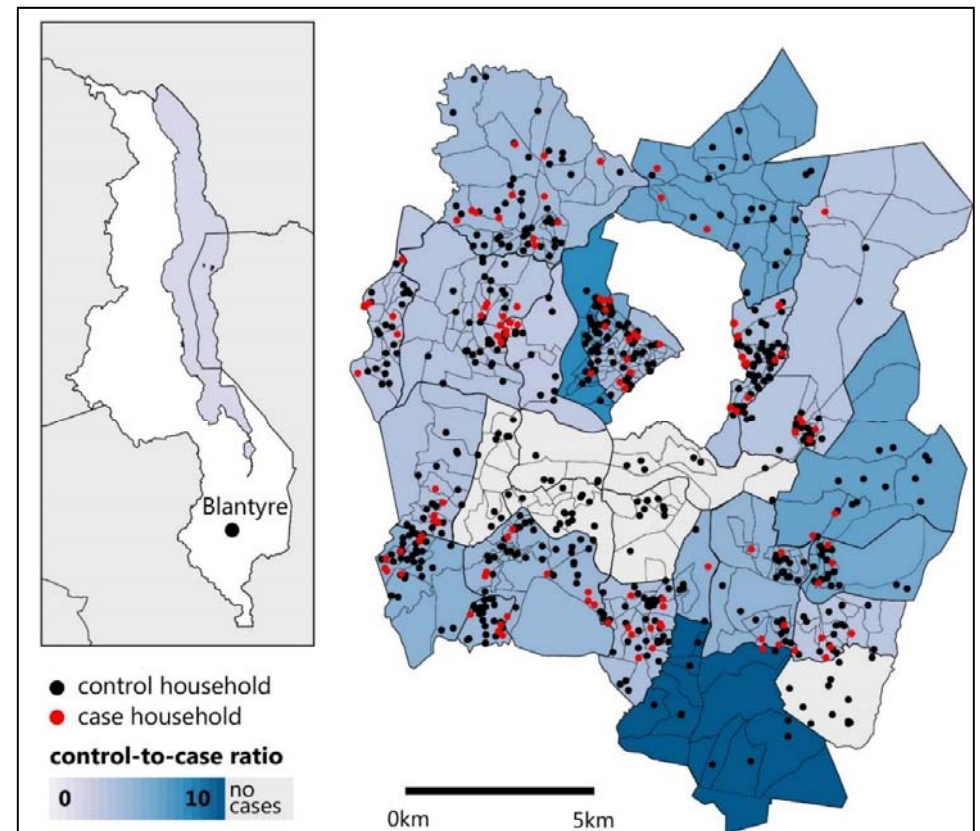
Data collection by Fran Olgemoeller et al.

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%)



Cohort study

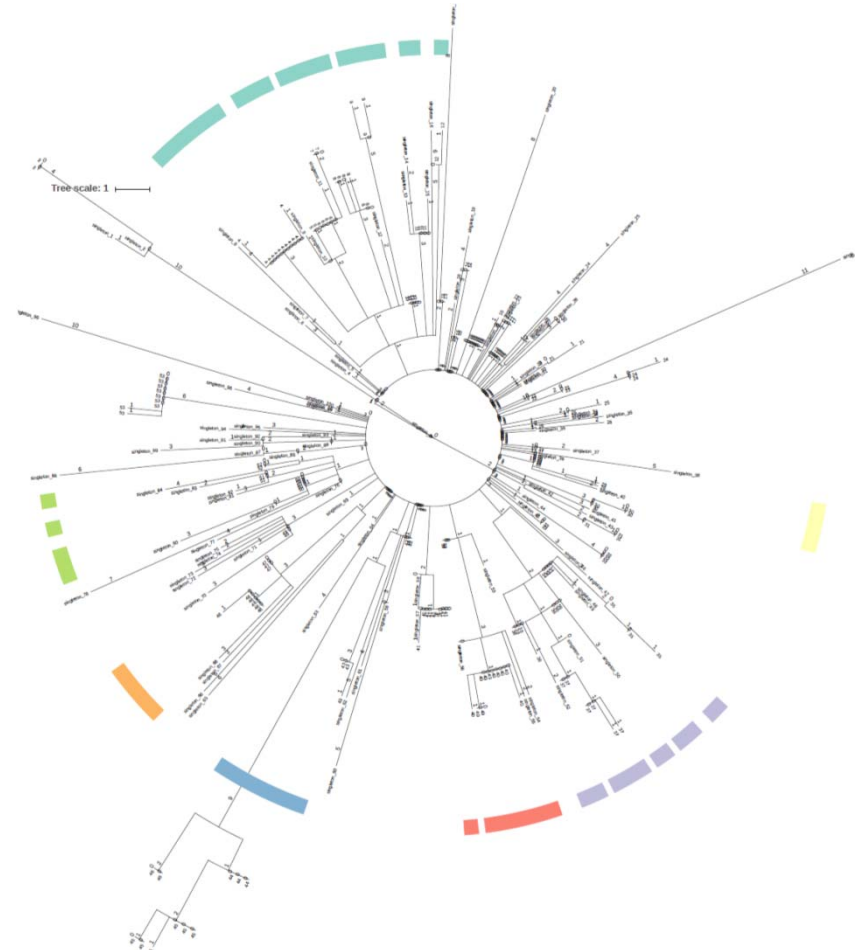
Data collection by Fran Olgemoeller et al.

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



Tree generated by Alex Wailan, Sanger

Predicting genetic relatedness

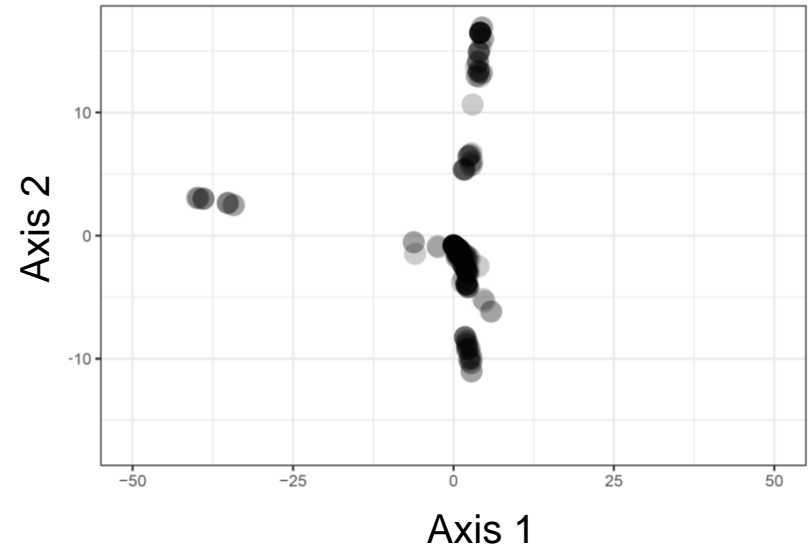
Preliminary analysis: SNP distance and physical distance are significantly correlated

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

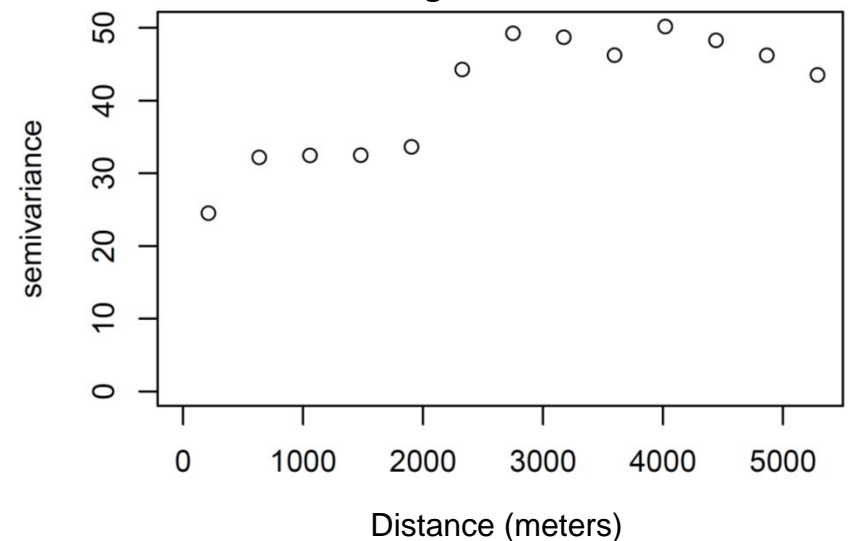
Evidence of spatial correlation up to 2500 meters

What possible transmission mechanisms operate on this scale?

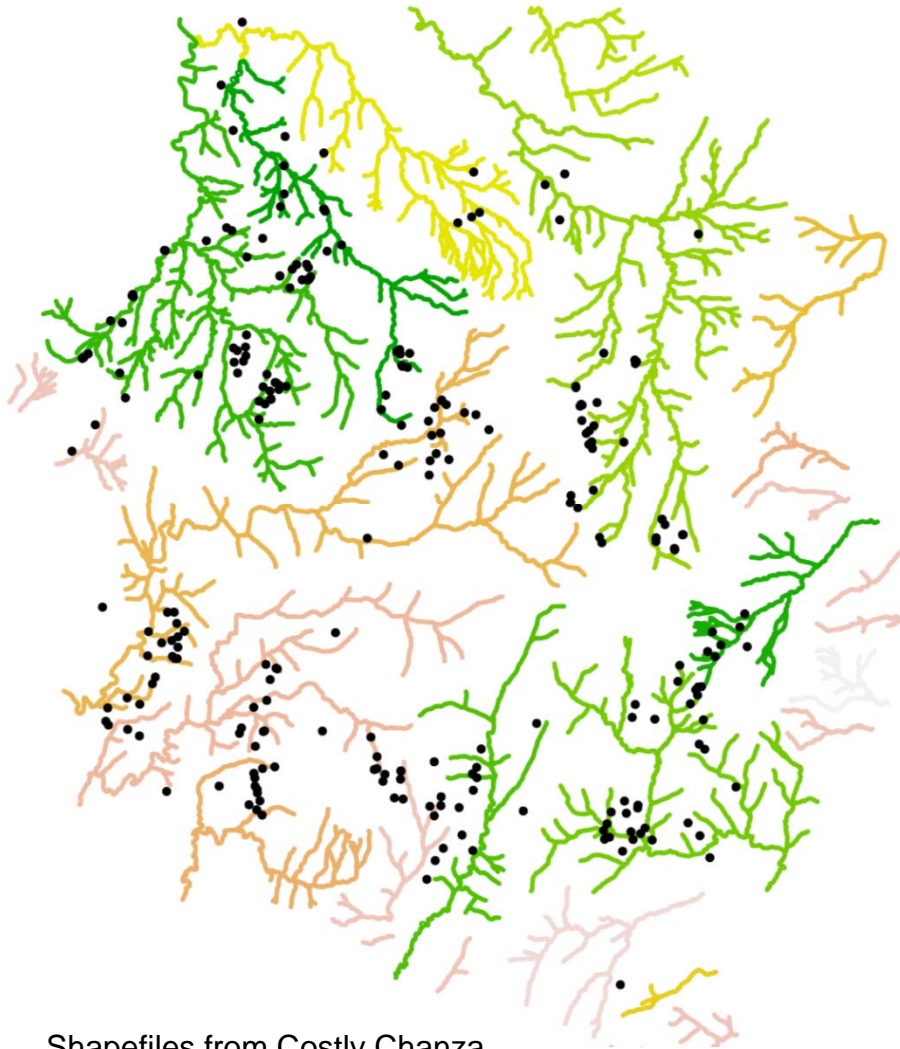
Multidimensional scaling



Variogram of Axis 2



Exploring possible predictors



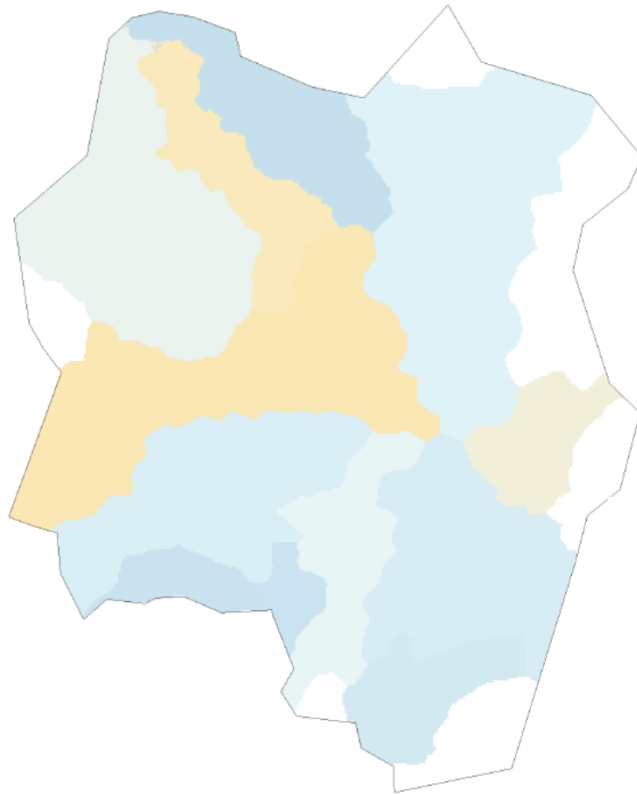
Shapefiles from Costly Chanza

Hypothesis driven by case-control results

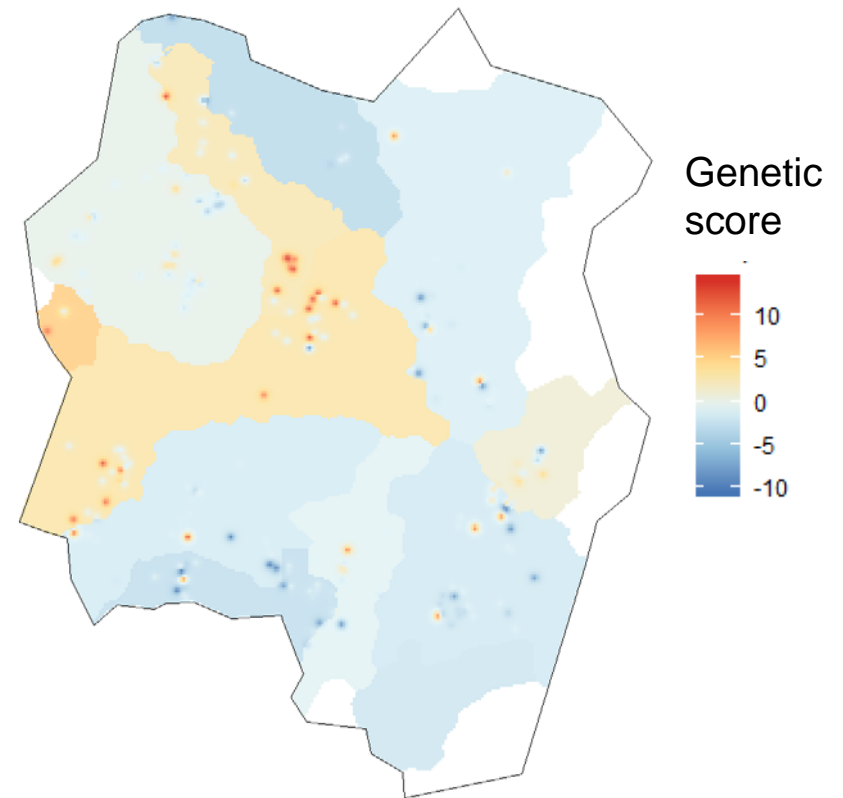
Explore ability of river networks across city to predict genetic relatedness

Findings: Nearest river is a significant predictor of genetic score across the city

Contribution of river catchment



Total prediction

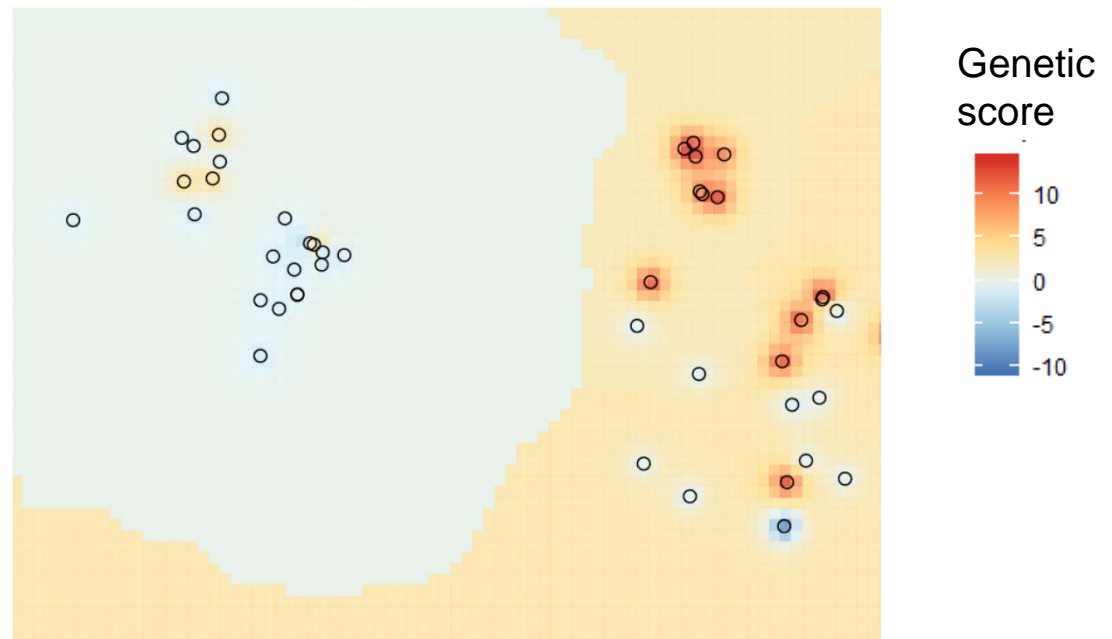
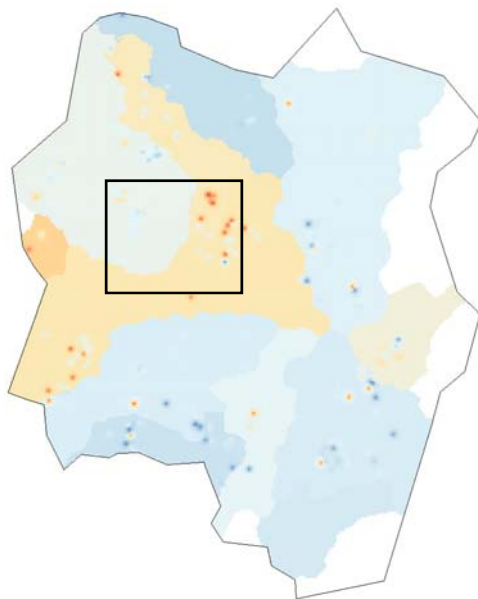


Interpreting model results

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!