Dear Sir or Madam,

Please find enclosed our manuscript “The importance of thinking beyond the water-supply in cholera epidemics: a historical urban case-study” for your consideration as a Research Article.

Cholera is known to be transmitted via multiple pathways, including long-cycle (environmentally mediated waterborne) transmission and short-cycle (foodborne and household) transmission. While well-developed water and sanitations systems could interrupt both pathways, such large-scale improvements are unlikely in the near future for many locales. More immediate and feasible interventions (e.g. reactive vaccination campaigns, water chlorination) may be more effective against one type of transmission than the other. Therefore, there is a growing interest in understanding the relative contributions of each transmission pathway.

Unfortunately disentangling these pathways remains problematic and requires highly detailed data that is rarely collected in outbreak settings. We address this difficulty by fitting mathematical transmission models to epidemiological data from a cholera epidemic in 19th century Copenhagen - a fully susceptible population in a pre-sanitation setting. Coupled with detailed municipal hydrological data, we are able to compare models that include various assumptions about the long- and short-cycle transmission pathways. We find considerable heterogeneity in transmission, and that transmission between neighborhoods did not correlate with water connections, suggesting long-cycle transmission was not the primary driver of this epidemic.

We believe this manuscript justifies publication in PLoS Neglected Tropical Diseases because it:

1. Utilizes unique high-resolution epidemiological and hydrological data to allow a rigorous comparison of transmission models with different pathways.
2. Demonstrates the importance of short-cycle cholera transmission, rather than long-cycle transmission, in propagating a large urban epidemic.
3. Provides a proxy for understanding cholera epidemics in contemporary immunologically naive populations in resource-poor environments.

We hope these findings will encourage public health officials to think beyond water-supply interventions when considering cholera control measures.

Thank you for your consideration

Sincerely,

Matthew Phelps, on behalf of the authors