**Cholera – Johns Hopkins Bloomberg School of Public Health**

This phenomenological, spatial model assumes that the mean annual incidence rate of suspected cholera in a given location represents a baseline cholera risk, and that cholera incidence may be projected by considering direct and indirect vaccine effects and waning effectiveness over time, population size changes and spatial turnover, and secular trends in country-level cholera incidence rates. The model is based a previously published cholera vaccine impact model [1].

For the 35 modeled countries in sub-Saharan Africa, the baseline spatial cholera risk was the estimated mean annual suspected cholera incidence rate from 2010-2016 downscaled from the 20 km by 20 km to 5 km by 5 km grid cell scale [2]. Baseline spatial cholera risk for Bangladesh was derived from unpublished estimates of the mean annual clinical cholera incidence rate in 5 km by 5 km grid cells across Bangladesh from 2014-2018 using a Bayesian hierarchical model similar to that in [2]. Acute watery diarrhea (AWD) cases were acquired from the Directorate General Health Services (DGHS) of Bangladesh from participating public and private hospitals in all 64 districts, and culture-confirmed *V. cholerae* surveillance data were obtained from systematic sampling of AWD patients at 22 sentinel hospital sites that represent an enteric disease surveillance system. We applied the national mean annual incidence rate in Bangladesh to 5 km by 5 km grid cells in India in a population-weighted manner. For the 10 remaining modeled countries, annual country-level reports of cholera to WHO [8] were used to estimate mean annual cholera incidence rates, and the rate was assumed to apply homogeneously to all 5 km by 5 km cells in the country.

Vaccine doses were administered to second-level administrative units (i.e., districts) with the greatest cholera-affected population sizes. Affected population size was defined as the product of the proportion of the country population living in the district, as calculated from 2020 WorldPop population estimates and GADM district shapefiles [3,4], and the mean annual incidence rate across all 5 km by 5 km cells in the district. We assumed that vaccination campaign coverage was 80% and that a district could not receive vaccines more than once every three years.

As in [1], indirect vaccine protection was modeled with a logistic function fit to the relative reduction in incidence among unvaccinated individuals and OCV coverage in a 5 km by 5 km grid cell, based on data from vaccine trials in India and Bangladesh [5,6]. Also as in [1], waning vaccine efficacy was obtained by fitting a log-linear decay function to 2-dose vaccine efficacy reported 0 to 5 years after vaccination according to a previously published meta-analysis [7].

Model uncertainty in the 200 stochastic simulations is derived from different posterior draws for baseline cholera risk, and four simulation settings that cross two dimensions – temporal incidence rate trend and stochastic outbreak variability -- with two options each (i.e., 50 simulations per setting).

In one dimension, we consider a constant or modeled temporal incidence rate trend from 2000 to 2100, the VIMC projection period. The constant trend assumes that baseline spatial cholera risk is constant over the 100-year period. The modeled trend fits a log-linear regression model with country-level group effects to all available annual country-level reports of cholera to WHO [8]. The model fit was then used to calculate a multiplier for each projection year relative to the 2014 reference year, and the multiplier was then used to project the country’s baseline spatial cholera risk forwards and backwards from 2014.

The second dimension considered sub-Saharan African countries did or did not have stochastic outbreak variability. Using published data on suspected cholera outbreaks in sub-Saharan Africa from 2010 to 2020 [9], we calculated the annual probability of an outbreak and annualized multipliers for outbreak and non-outbreak attack rates relative to the baseline cholera risk in each second-level administrative unit. For each simulation with outbreak variability, the model performed stochastic draws over a single 10-year period to determine which years a given district had an outbreak. This same 10-year pattern was recycled over the 101-year projection period (e.g., 2000-2009, 2010-2019, etc had the same pattern). Outbreak and non-outbreak multipliers were then multiplied with the baseline spatial cholera risk accordingly. Only 21 African countries had stochastic outbreak variability in our model.

The cholera vaccine impact model is limited in that it does not explicitly model immunity due to natural infection. Additionally, temporal variation in baseline cholera risk is considered only in countries and simulations that include stochastic outbreak variability even though cholera transmission can vary substantially from year to year.

The model package `ocvImpact` and scripts may be be found on Github at <https://github.com/HopkinsIDD/gavi_vimc_cholera.git>.

1. Lee EC, Azman AS, Kaminsky J, Moore SM, McKay HS, Lessler J. The projected impact of geographic targeting of oral cholera vaccination in sub-Saharan Africa: A modeling study. PLoS Med. 2019;16: e1003003.

2. Lessler J, Moore SM, Luquero FJ, McKay HS, Grais R, Henkens M, et al. Mapping the burden of cholera in sub-Saharan Africa and implications for control: an analysis of data across geographical scales. Lancet. 2018;391: 1908–1915.

3. World Health Organization. Annual Cholera Reports. World Epidemiological Record; 2020. Available: https://www.who.int/publications/journals/weekly-epidemiological-record

4. WorldPop. [cited 13 Apr 2021]. Available: https://www.worldpop.org/

5. GADM maps and data. Available: https://gadm.org/

6. Ali M, Emch M, von Seidlein L, Yunus M, Sack DA, Rao M, et al. Herd immunity conferred by killed oral cholera vaccines in Bangladesh: a reanalysis. Lancet. 2005;366: 44–49.

7. Ali M, Sur D, You YA, Kanungo S, Sah B, Manna B, et al. Herd protection by a bivalent killed whole-cell oral cholera vaccine in the slums of Kolkata, India. Clin Infect Dis. 2013;56: 1123–1131.

8. Bi Q, Ferreras E, Pezzoli L, Legros D, Ivers LC, Date K, et al. Protection against cholera from killed whole-cell oral cholera vaccines: a systematic review and meta-analysis. Lancet Infect Dis. 2017;17: 1080–1088.

9. Zheng Q, Luquero FJ, Ciglenecki I, Wamala JF, Abubakar A, Welo P, et al. Cholera outbreaks in sub-Saharan Africa during 2010-2019: A Descriptive Analysis. International Journal of Infectious Diseases. 2022. doi:10.1101/2021.10.25.21265347