

Cholera disease burden and circulation of *V. cholerae* strains in Africa

A body of work based on collaborations between Institut Pasteur, Johns Hopkins University, World Health Organization and several other institutions with Médecins Sans Frontières and Epicentre^{1,2}

BACKGROUND

- Cholera remains a persistent health problem in sub-Saharan Africa and worldwide.
- The seventh cholera pandemic has heavily affected Africa, with no knowledge about the origin and continental spread of the disease until recently.
- We are also lacking a good understanding of the areas that suffer a larger disease burden, since these places should be prioritized to make progress towards cholera control.
- Cholera can be controlled through appropriate water and sanitation, or by oral cholera vaccination, which provides transient (~3 years) protection.

OBJECTIVES

- The results presented here aim to gain a better understanding of the circulation of *V. cholerae* strains in Africa, to map cholera burden in sub-Saharan Africa and to assess how geographical targeting could lead to more efficient interventions.

METHODS

MAPPING THE BURDEN OF CHOLERA IN SUB-SAHARAN AFRICA

Data sources

– We combined information on cholera incidence in sub-Saharan Africa (excluding Djibouti and Eritrea) from 2010 to 2016 from datasets from WHO, Médecins Sans Frontières, ProMED, ReliefWeb, Ministries of Health, and from the scientific literature.

Data analysis

- We divided the study region into 20 km × 20 km grid cells and modelled annual cholera incidence in each grid cell assuming a Poisson process adjusted for covariates and spatially correlated random effects.
- We combined these findings with data on population distribution to estimate the number of people living in areas of high cholera incidence (>1 case per 1000 people per year).
- We further estimated the reduction in cholera incidence that could be achieved by targeting cholera prevention and control interventions at areas of high cholera incidence.

GENOMIC ANALYSIS OF THE SEVENTH CHOLERA PANDEMIC OF IN AFRICA

- We used genomic data from 1070 *Vibrio cholerae* O1, including 651 isolates collected in 45 of 54 African countries between 1966 and 2014.
- We used two approaches to obtain a robust phylogenetic framework for the inference of propagation routes:
 - Maximum likelihood phylogenetic analysis was performed on the 1,070 genomes with 9,300 single-nucleotide variants (SNVs), evenly distributed over the genome.
 - A Bayesian phylogenetic approach to provide divergence times for a spatially and temporally representative subset of 228 isolates.

RESULTS

MAPPING THE BURDEN OF CHOLERA IN SUB-SAHARAN AFRICA

- We included 279 datasets covering 2283 locations in our analyses, in sub-Saharan Africa (excluding Djibouti and Eritrea).
- A mean of 141 918 cholera cases (95% credible interval [CrI] 141 538-146 505) were reported per year.
- 4.0% (95% CrI 1.7-16.8) of districts, home to 87.2 million people (95% CrI 60.3 million to 118.9 million), have high cholera incidence.
- By focusing on the highest incidence districts first, effective targeted interventions could eliminate 50% of the region's cholera by covering 35.3 million people (95% CrI 26.3 million to 62.0 million), which is less than 4% of the total population.

References

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2. Weill FX, Domman, Njamkepo E, Tarr C, Raugier J, Fawal N, Keddy KH, Salje H, Moore S, Mukhopadhyay AK, Bercion R, Luquero FJ, Ngandjio A, Dosso M, Monakhova E, Garin B, Bouchier C, Pazzani C, Mutreja A, Grunow R, Sidikou F, Bonte L, Breurec S, Damian M, Njanpop-Lafourcade BM, Sapriel G, Page AL, Hamze M, Henkens M, Chowdhury G, Mengel M, Koeck JL, Fournier JM, Dougan G, Grimont PAD, Parkhill J, Holt KE, Piarroux R, Ramamurthy T, Quilici ML, Thomson NR. Genomic history of the seventh pandemic of cholera in Africa. *Science*. 2017 Nov 10;358(6364):785-789.

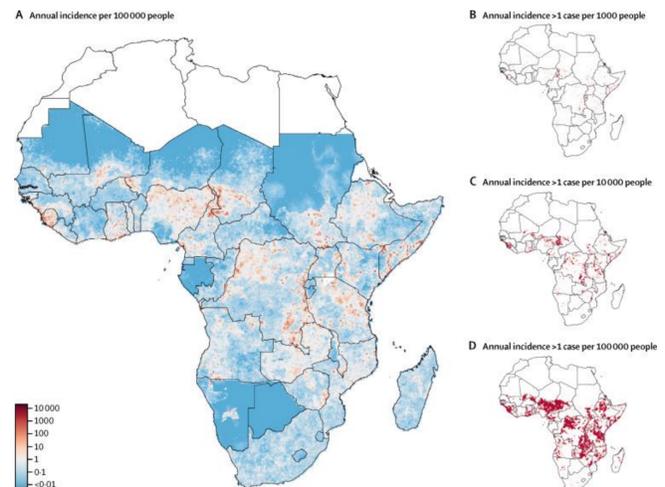


Figure 1. (A) Mean annual cholera incidence per 100 000 people in sub-Saharan Africa between 2010 and 2016, and (B) locations with mean annual incidence of more than one per 1000 people, (C) more than one per 10 000 people, or (D) more than one per 100 000 people.

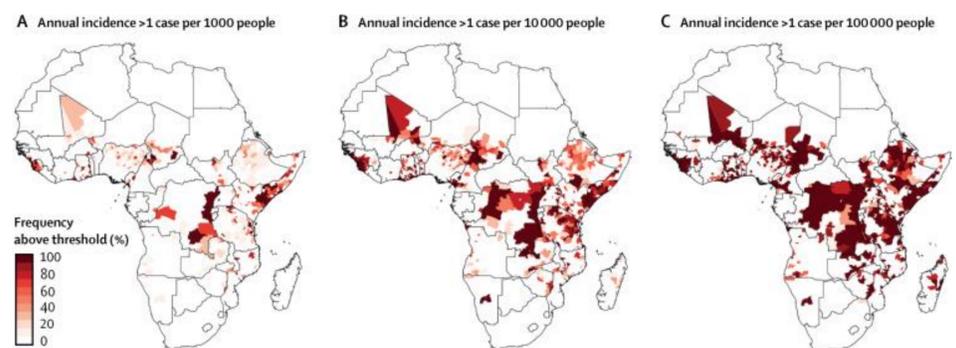


Figure 2. Districts with mean annual cholera incidence above certain thresholds. Shading indicates statistical robustness of classification as a 'hotspot,' with darker shading representing more statistical support

GENOMIC ANALYSIS

- The past epidemics in Africa were attributable to a single expanded lineage.
- Sub-lineages were introduced at least 11 times since 1970, into two main regions, West Africa and East/Southern Africa, causing epidemics for periods of up to 28 years, and then disappeared.
- The last five introductions into Africa, all from Asia, involved multidrug-resistant sublineages that replaced antibiotic-susceptible sublineages after 2000.
- Recurrent circulation patterns were identified (Fig 4).

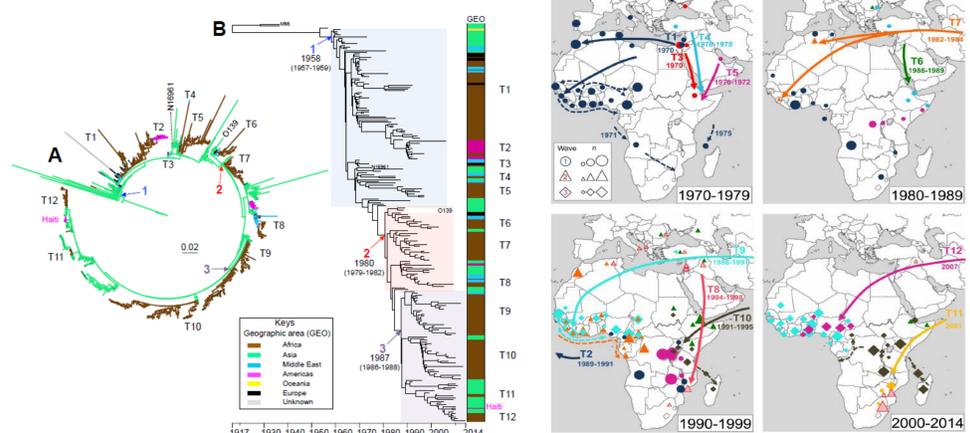


Figure 3. Phylogeny of seventh pandemic *V. cholerae* El Tor isolates. (A) Maximum likelihood phylogeny of the 1,070 genomes studied. (B) Maximum clade credibility tree produced with BEAST for a subset of 228 representative isolates

Figure 4. Inferred propagation routes of seventh pandemic *V. cholerae* O1 El Tor populations to, from and within Africa. The 11 introduction events within Africa and 1 from Africa are indicated by the letter T.

CONCLUSION

- This phylogenetic framework describes the periodicity of lineage introduction and the stable routes of cholera spread, which should inform the rational design of control measures for cholera in Africa.
- Although cholera occurs throughout sub-Saharan Africa, its highest incidence is concentrated in a small proportion of the continent. Prioritizing high-risk areas could substantially increase the efficiency of cholera control programs.