Enhanced Cholera Genomic Surveillance in Africa

Pathogen Genomics in Health Emergencies: Spotlight Cholera

Gerald Mboowa

Broad Institute of MIT and Harvard, MA, USA

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AfricaCDC Centres for Disease Control and Prevention

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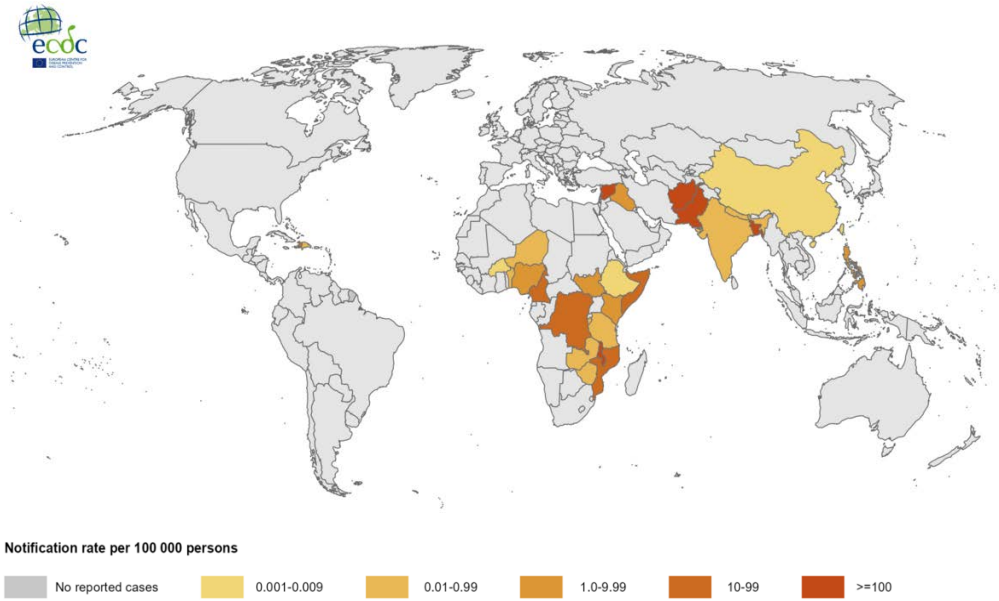
Cholera – Global context

Geographical distribution of cholera cases reported worldwide from 2022 to 2023



Note: Data refer to cases reported in the last 12 months. Administrative boundaries: © Eurographics
The boundaries and names shown on this map do not imply official endorsement or acceptance by the European Union. ECDC. Map produced on 17 January 2023

https://www.ecdc.europa.eu/en/all-topics-z/cholera/surveillance-and-disease-data/cholera-monthly

Recent cholera outbreaks;

- Multiple outbreaks, involving **endemic & non-endemic countries**

- **Higher Case Fatality Rate (CFR)** than in previous years

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Africa

Regional concerns as Zambia's cholera death toll hits 700

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What's fuelling the deadly cholera outbreak in Southern Africa?

Unchecked border movement and poor sewage systems have a new partner in inflicting misery: climate change

A worker carries a bucketful of disinfectant at a cholera treatment centre, in Lusaka, Zambia, Friday, January 12, 2024 [AP Photo]

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Emerging threats Cross-posts Cholera Pandemic preparedness

Scientists urge close monitoring of cholera variants

New cholera variants capable of causing large outbreaks could emerge. Constant monitoring is the only way to prevent possible pandemics. World has seen seven pandemics of the infectious disease.

21 July 2022 · 3 min read by SciDev.Net

Cholera outbreak news in Africa

What Genomics Can Offer in Responding to Cholera Outbreaks: Regional Perspectives

Genomics for outbreak surveillance

- In outbreaks recurrent, genomic surveillance offers:
    - Identification of *V. cholerae*
    - Understanding regional variations in antimicrobial resistance (AMR) patterns
    - Linking cross-border outbreaks to specific sources

Transmission pathways

- *Urban vs. Rural contexts*:
    - Urban areas with high population density, may present unique genomic signatures
    - In rural areas, environmental reservoirs play a significant role, & genomics pinpoints sources
- *Global trade & Migration:* Regional genomic data provides insights into how global trade & human migration influence cholera's spread, informing policy for ports, borders, & migration hubs

Antimicrobial resistance

- Genomics reveal region-specific AMR profiles to adjust treatment guidelines dynamically.
    - Elsewhere, resistance to tetracycline & trimethoprim-sulfamethoxazole has been reported
    - Multidrug-resistant strains may emerge in African settings

Informing vaccination strategies

- Genomics informs vaccine development & deployment by identifying dominant circulating strains in specific regions. For example:
    - Genomic data can highlight antigenic variations that might compromise vaccine efficacy
    - Guides decisions on oral cholera vaccine campaigns in endemic or outbreak settings

Regional genomic capacity & challenges

- Regions like Africa face challenges in genomic capacity, including limited infrastructure & trained personnel.
    - Strengthening capacity through partnerships & training programs is crucial.
- Developed regions or international collaborations can provide technical expertise, funding & infrastructure to enhance regional genomic capabilities

Policy & cross-border collaboration

- Genomics enhances regional & international policy development, fostering data-sharing agreements for real-time outbreak monitoring
- Cross-border genomic collaborations, such as those spearheaded by Africa CDC or WHO-AFRO, ensure coordinated responses in outbreak-prone regions

Establishing capacity for cholera genomic surveillance in Africa

- Affected countries, including **Zambia, Malawi, & Mozambique**, have been severely affected by cholera outbreaks, highlighting the need for improved cholera surveillance & control.

- Explore cholera genomic **diversity, identify lineages & AMR, understand cross-border transmission's** role in outbreaks & assess how genomic data informs surveillance & control strategies.

- CholGen is **tackling critical questions on cholera spread in Africa** through a collaborative, multi-country genomic analysis.

CholGen – Consortium

Africa CDC working with countries & international collaborators established the Cholera Genomic Surveillance Consortium in Africa (**CholGen**)

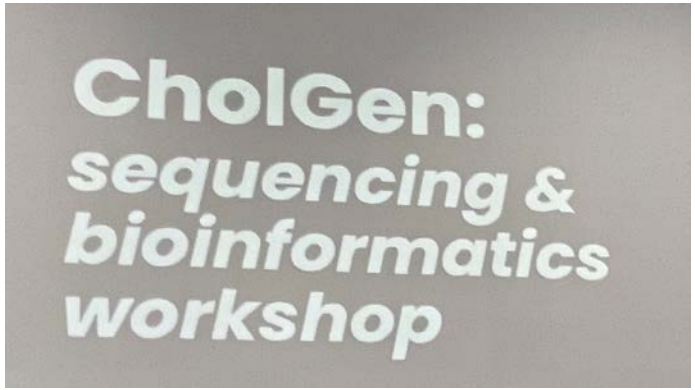
Leveraged local sequencing capacity, built during COVID-19, to generate *V. cholerae* genomes from isolates collected over 5 yrs

CholGen: Uganda, Mozambique, DRC, Nigeria, Cameroon, Malawi & Zambia

CholGen objectives

- Build capacity for bacterial pathogen genomic surveillance & bioinformatics in Africa (Cholera & *K. pneumoniae*)
- Determine the origin/reservoirs, genomic diversity & transmission patterns of *V. cholerae* in Africa (within countries & across borders)

Training – in collaboration with INRB & JHU – Cholera sequencing



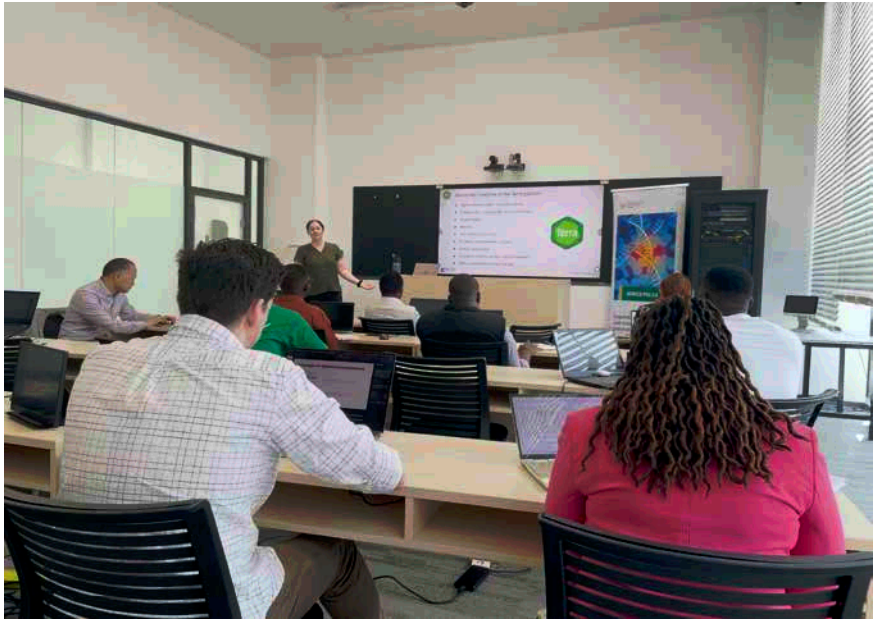
Cholera bioinformatics analysis – CholGen

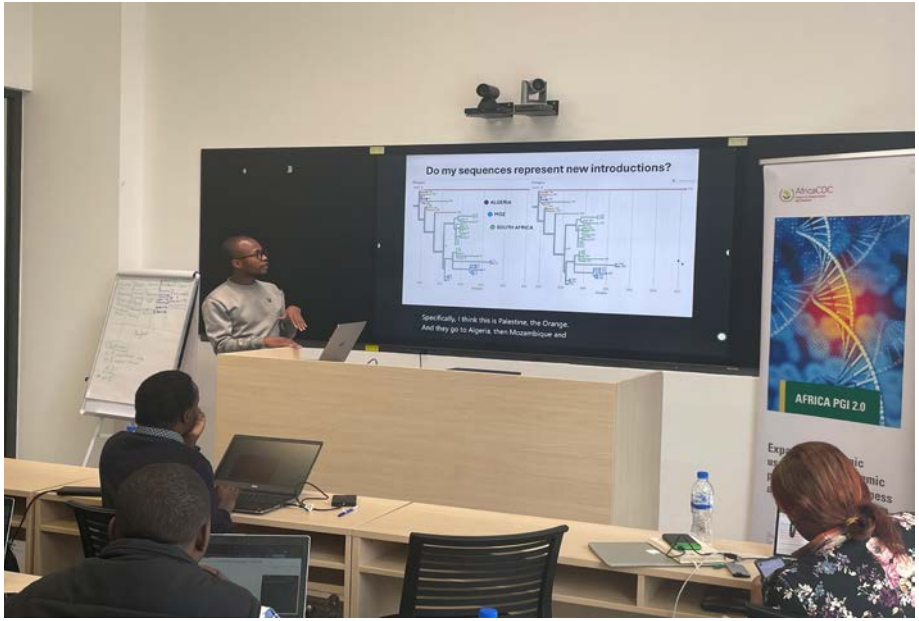
CholGen – Bioinformatics training at Institut National de Recherche Biomédicale (INRB), Sept 18-29, 2023.

Our primary challenge was the absence of a unified bioinformatics data platform for collaboration

Terra: Enabling Public Health Pathogen Genomics in Africa

Cholera bioinformatics training using Terra at Africa CDC Headquarters





Terra Supporting Public Health Pathogen Genomics in the Cloud

Terra: Enabling Public Health Pathogen Genomics in Africa

Cholera bioinformatics analyses

Genomic Sequence Analysis
- ❑ Assembly of raw sequence data from *V. cholerae* isolates
- ❑ Assessment of sequencing quality using tools like FastQC

Pathogen Detection & Typing
- ❑ Identifying the presence of *V. cholerae* in clinical samples
- ❑ Differentiate pathogenic (e.g., O1 & O139) & non-pathogenic serogroups
- ❑ Toxin & virulence genes detection (e.g., *ctxA* & *ctxB* or *tcpA*)

Variant Calling & Annotation
- ❑ Identify single nucleotide polymorphisms (SNPs) & indels
- ❑ Functional annotation of genomes to identify genes & regulatory elements

Phylogenetic Analysis
- ❑ Construct phylogenetic trees to trace evolutionary relationships among cholera strains
- ❑ Temporal & geographic mapping of strains to study outbreaks
- ❑ Core-genome or pan-genome alignment for comparative studies

Antimicrobial Resistance (AMR) Profiling
- ❑ Detection of AMR genes using databases like AMRFinderPlus
- ❑ Prediction of resistance phenotypes based on genomic data

Transmission & Epidemiological Analysis
- ❑ Integration of genomic & epidemiological data to reconstruct transmission dynamics
- ❑ Spatiotemporal modeling to track cholera outbreaks

Plasmid & Mobile Element Analysis
- ❑ Characterize plasmids & other mobile genetic elements carrying virulence or resistance genes

Comparative Genomics
- ❑ Compare genomes of different *V. cholerae* strains to study genetic diversity
- ❑ Identify strain-specific genomic regions

Data Visualization & Reporting
- ❑ Create clear, interpretable visualizations of genomic data (e.g., phylogenetic trees, AMR heatmaps)
- ❑ Generate outbreak reports integrating genomic & epidemiological findings

Reference

***https://www.medrxiv.org/content/10.1101/2024.11.15.24317392v1**

Terra **https://terra.bio/**

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Leveraging Genomics for Enhanced Public Health Decision-Making in Cholera Control Across Africa

Empowering countries with the tools & knowledge to use genomics to make informed decisions that strengthen cholera surveillance & control

What have we accomplished with CholGen in Africa?

Enhanced local expertise in pathogen genomic data analysis.

- ✓ We successfully built capacity for genomic surveillance & bioinformatics, empowering scientists across Africa to conduct & interpret pathogen genomic data independently.

Improved understanding of how cholera spreads within & across country borders.

- ✓ Mapping the genomic diversity & transmission patterns of *V. cholerae* provided valuable insights into the sources & spread of cholera within & across borders.

Strengthened public health response, data sharing & collaboration.

- ✓ With comprehensive genomic data, health agencies are better positioned to respond proactively to outbreaks & implement effective surveillance strategies.

Acknowledgment

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Thank you!