



GLOBAL TASK FORCE ON  
**CHOLERA CONTROL**

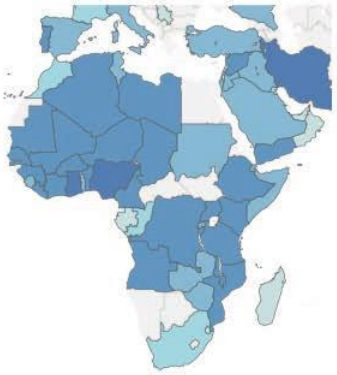
GENOMIC HISTORY OF THE SEVENTH PANDEMIC OF  
CHOLERA

IN AFRICA AND IMPLICATIONS ON CONTROL MEASURES

Marie-Laure Quilici

# CHOLERA IN AFRICA – 7TH PANDEMIC

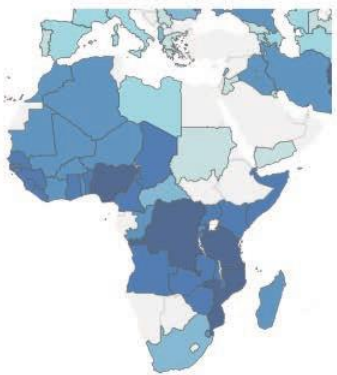
1970-1979



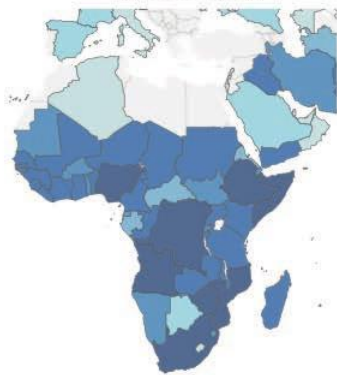
1980-1989



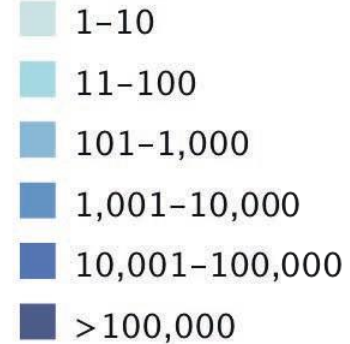
1990-1999



2000-2014

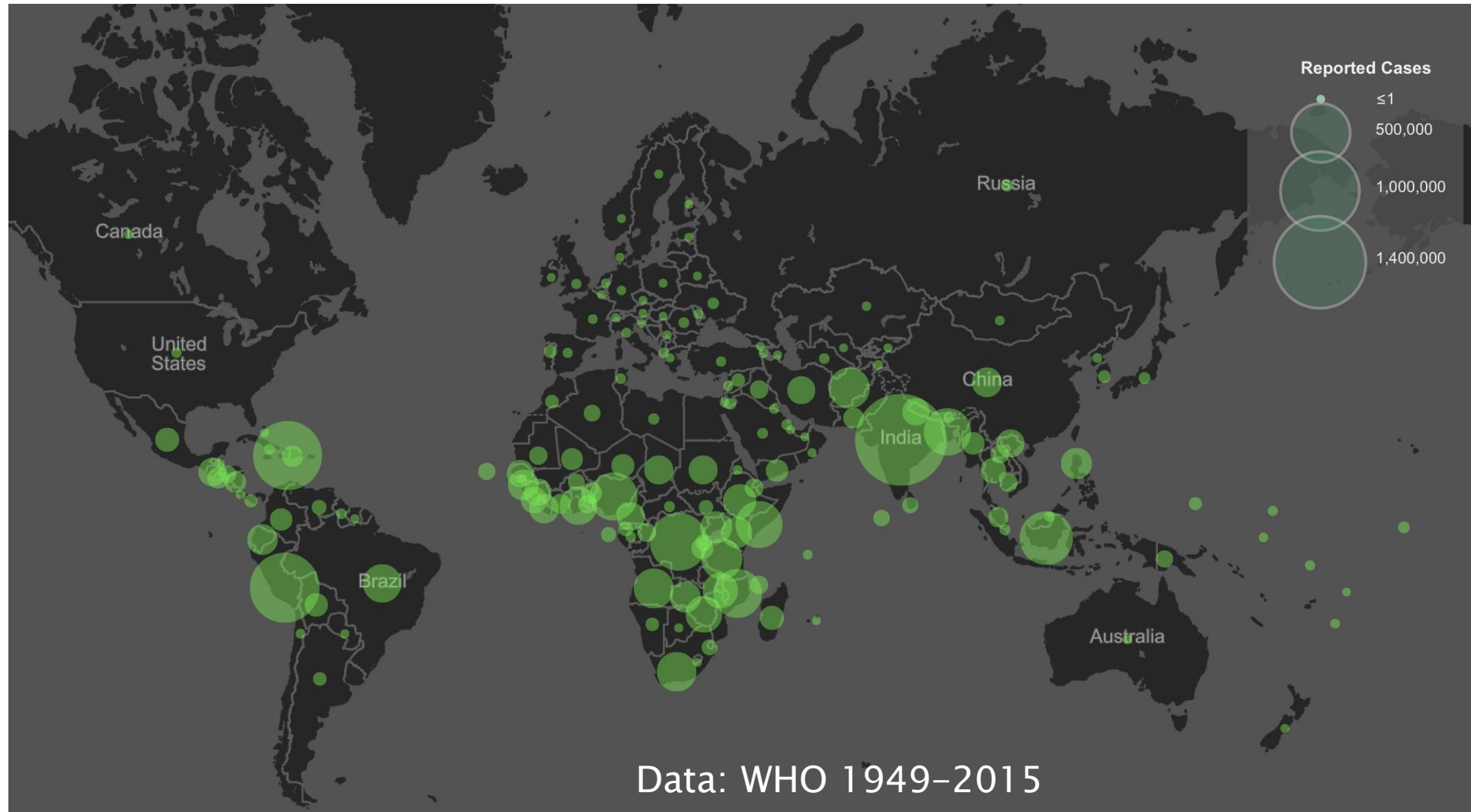


WHO reported cases



**Africa is the continent reporting most of the cholera cases and deaths since the beginning of the seventh pandemic in 1970 (except 1991-1991, Latin America, and 2010-2011, Haiti)**

# How are these related?





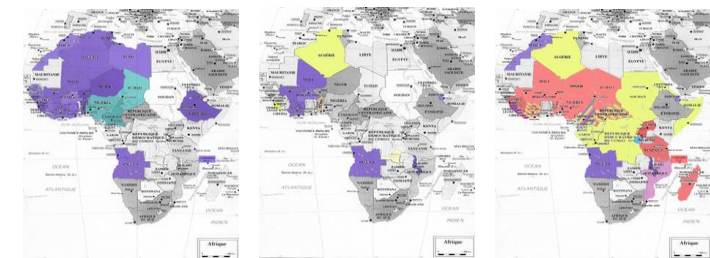
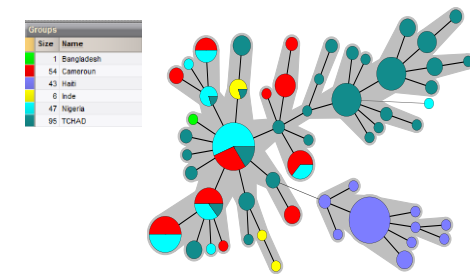
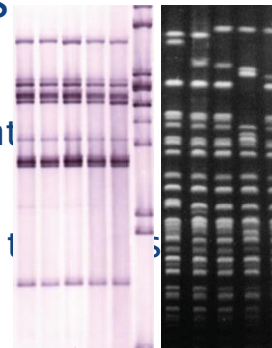
# COMPREHENSIVE CHOLERA PREVENTION AND CONTROL

Include rapid confirmation and the understanding of the dynamics of the epidemics

- Visualization of worldwide circulation and evolution of strains
- Identification of the source of infections
- Dynamics of transmission: origin and expansion mapping, geographical spread of strains in a given country or between countries
- Monitoring of the geographic expansion of strains during and between outbreaks
- Establishing a relationship between the current and previous outbreaks

# EFFECTIVE SURVEILLANCE AND LABORATORY ANALYSIS

- Early detection, rapid diagnosis of suspected cases
- Strain tracking
  - Detection of evolution of strains and emergence of new variants
  - Monitoring of antibiotic resistance
  - Molecular epidemiology and understanding of the dynamics of transmission
    - Serogrouping (O antigens, O1, O139)
    - Biotyping (Classical, El Tor)
    - O1 serotyping (Inaba, Ogawa, Hikojima)
    - Phage typing
    - Multilocus Enzyme Electrophoresis
    - Ribotyping
    - Pulse-field gel electrophoresis
    - Multiple loci VNTR analysis (MLVA)
    - Sequencing of virulence genes
      - *ctxB*, *tcpA*,



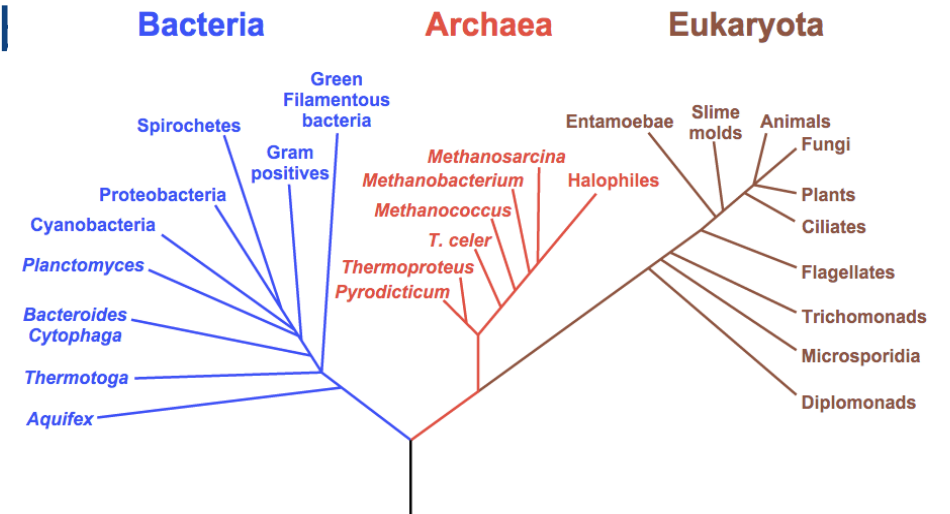
1970-1975    1976-1990    1991-2000

- Evidence of variations between strains and circulation of different strains simultaneously
- No history of the evolutionary relationships between strains

# PHYLOGENY

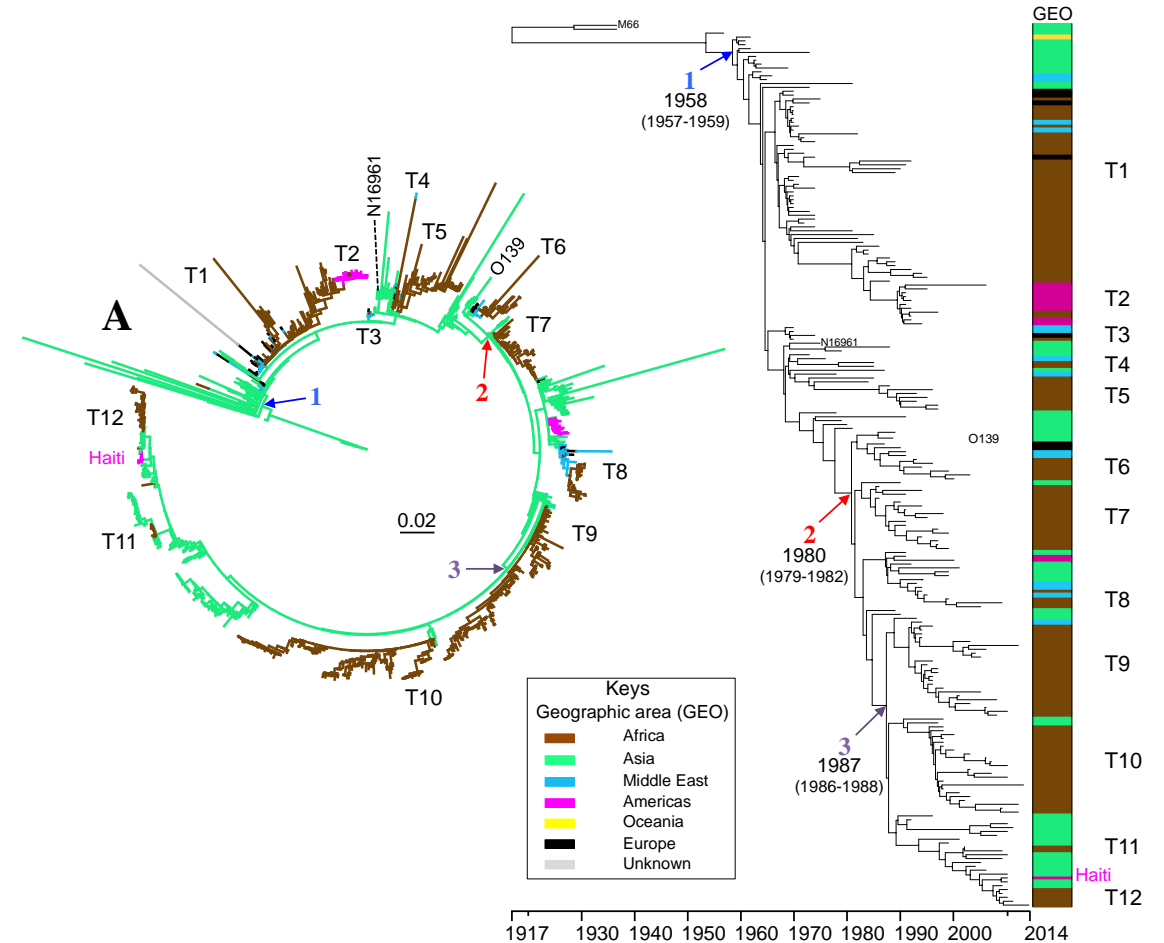
- We have used phylogeny to unify all typing approaches used previously to track and understand cholera (Ribotyping, MLEE, PFGE, MLVA, CTX-typing etc.)
- A phylogenetic tree based on whole genome single-nucleotide variation profile was built, showing the inferred evolutionary relationships among 7<sup>th</sup> pandemic strains
- WGS provides the highest resolution possible

**Phylogenetic Tree of Life**



# SPATIO TEMPORAL ANALYSIS BASED ON BACTERIAL GENOME SEQUENCING

- Collection of historical and contemporary isolates from Africa 1970–2014 (1070 genomes, 655 samples from 45 countries across Africa since 1970)
- Selected to represent the widest possible temporal and geographic distribution of cases reported to the World Health Organization



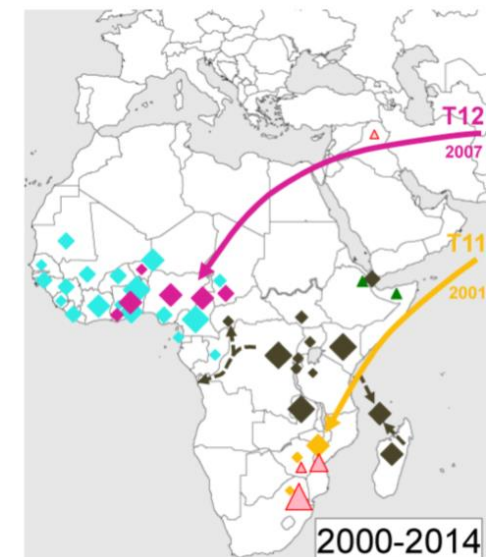
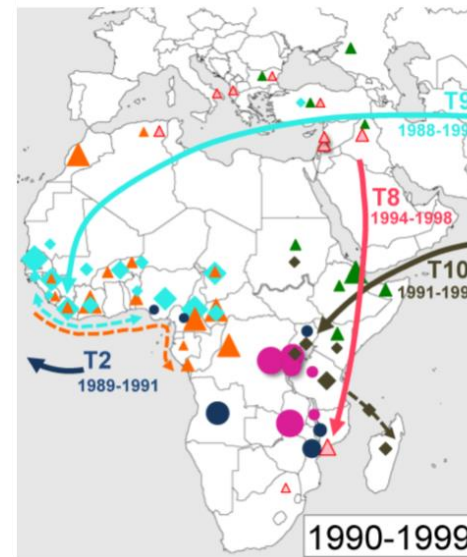
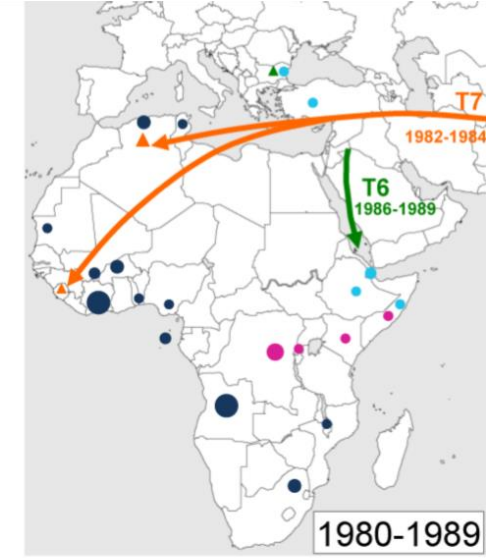
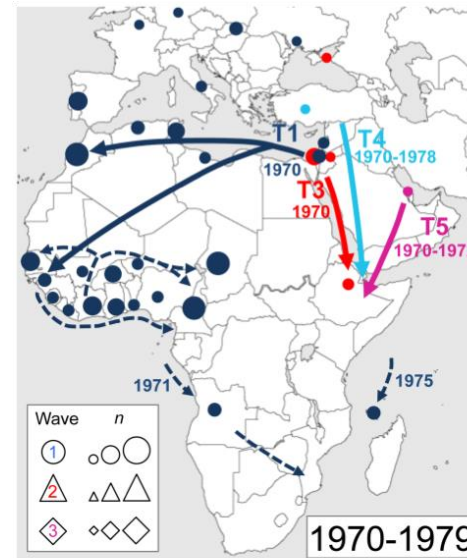
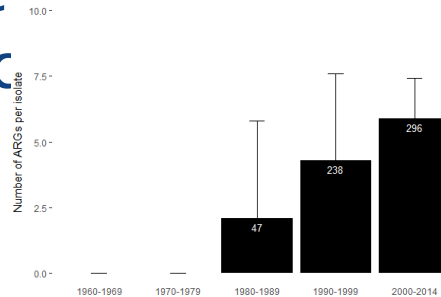
Phylogeny of seventh pandemic *V. cholerae* El Tor isolate

# UNDERSTANDING THE INTRODUCTION AND PROPAGATION ROUTES OF CHOLERA IN AFRICA

A minimum of 11 repeated introductions into West and East/Southern Africa.

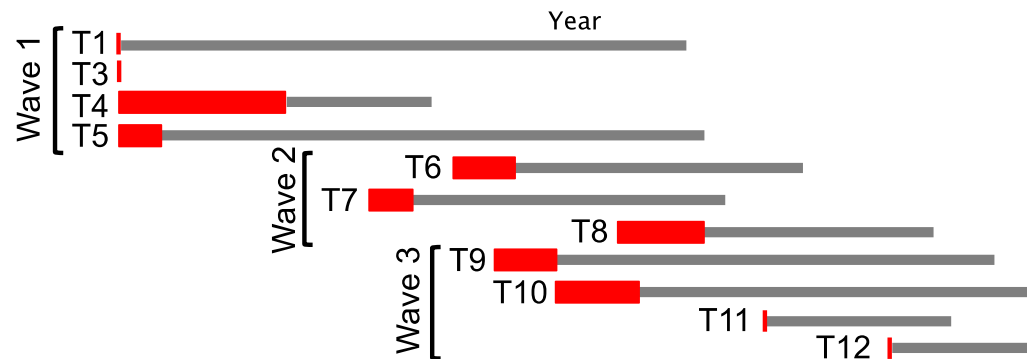
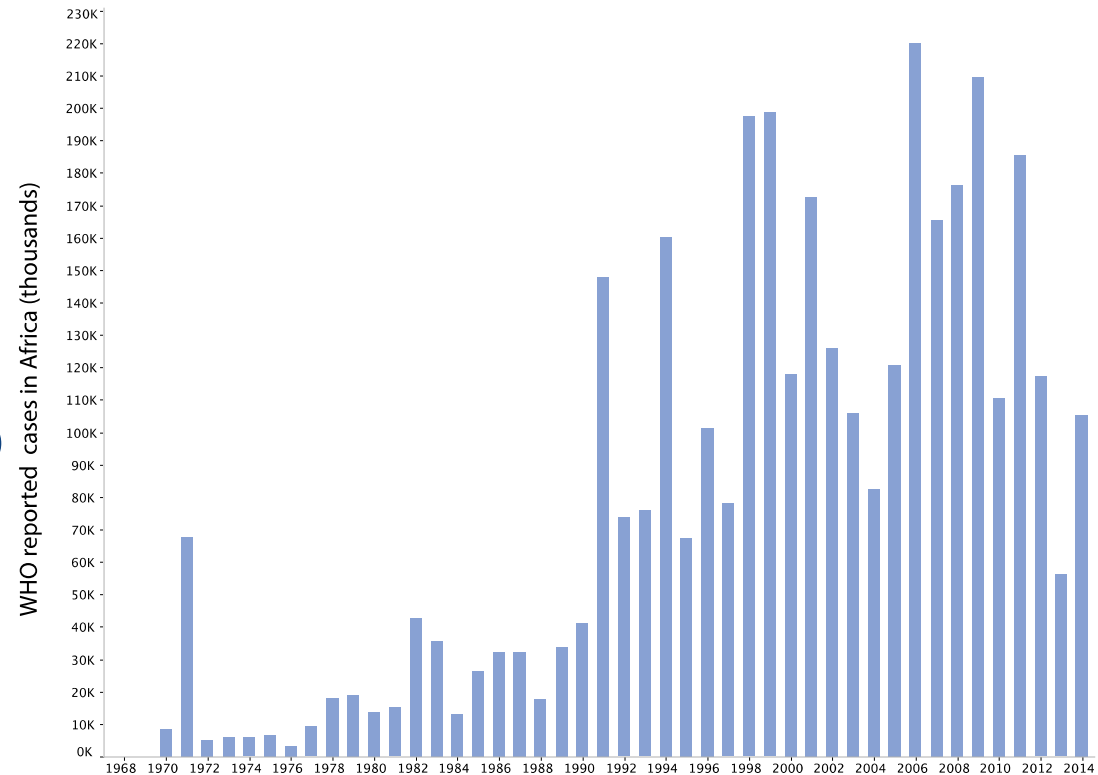
Recurrent patterns of transmission for cholera epidemics : predictable patterns of spread

Increased and imported resistance to antibiotic





- Dates of the various introductions and duration of each lineage
- Strains disappear after variable periods of persistence (up to 28 years)
- These introductions in different regions of Africa correlate with variations and increase in WHO cholera reported cases.



# MAIN FINDINGS

- The seventh pandemic originated from a single ancestral clone
- Cholera in Africa is associated with the recurrent introduction of new strains that had evolved in Asia.
- Aquatic environmental reservoirs are not the primary source of epidemic cholera in Africa
- Human-related factors play a much more important role in cholera dynamics in Africa than climatic and environmental factors

# OUTSTANDING ISSUES

- What are the mechanisms driving cholera introductions into Africa,
- Which factors contribute to outbreak amplification, persistence, and resolution,
- Where are the strains between two epidemics,
- How to explain the limited spatiotemporal spread of strains,
- What are the factors that determine the persistence and then the disappearance of the lineages? What are the respective roles of host and strains?

# WHAT IS THE WAY FORWARD

Strengthening of integrated early warning surveillance systems to limit human-to-human transmission

- Evidence based, integrated approach to Cholera control:
  - Longitudinal and real-time genomic and epidemiological surveillance.
  - Use new approaches to validate interventions.
- Use genomic data to inform current and future control efforts.
  - Develop sentinel sites based on patterns of spread and transmission routes, not necessarily high incidence.
  - Enhance the surveillance in cholera hotspots and in areas where introductions are predictable.
  - Improve outbreak prevention and response through enhance cross-border regional surveillance
- Understanding why new strains evolve and spread across the world from Asia where *V. cholerae* established in the environment.