Combining epidemiologic and genomic data to define epidemiologically relevant units of cholera transmission in Africa

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Background





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Background

Recent phylogenetic analysis found distinct introduction events into Africa







Background



Based on these findings, authors inferred propagation routes of seventh pandemic V. cholerae O1 El Tor in the African continent



Motivation

• Despite recent evidence, much remains unknown about cholera transmission dynamics within Africa.





Motivation

- Despite recent evidence, much remains unknown about cholera transmission dynamics within Africa.
- While there is clear evidence of multiple introductions to the continent that have helped sustain the seventh cholera pandemic in Africa, epidemiologic data suggests that there are also areas that maintain endemic cholera.





Motivation



- Connected areas likely have correlated transmission dynamics. These basic epidemiologic units of transmission may:
 - Propagate outbreaks from intercontinental introductions
 - Maintain endemic circulation that seed outbreaks elsewhere on the continent





Objective

Identify geographically connected areas of cholera transmission in Africa





Data sources

Combine molecular data with epidemiologic and ecologic data of cholera incidence.

- Molecular data:
 - Cholera sequencing data from public repositories
- Epidemiologic data
 - WHO reported cholera case counts by year and country













Zimbabwe						
Zambia –						
Uganda —						
Togo —						
Tanzania –						
Sudan —						
South Sudan -						
South Africa -						
Somalia						
Sierra Leone						
Senegal -						
Rwanda						
Rep. of the Congo						
Nigeria -						
Niger -						
Namibia -						
Mozambique -						
Mauritania –						
Mali —						
Malawi						
Liberia –						
Kenva						
Guinea-Bissau						
Guinea -						
Ghana -						
Gabon -						
Ethiopia						
Eswatini –						
Equatorial Guinea						
DRC -						
Diibouti —						
Cote D'Ivoire						
Chad -						
Central African Republic						
Cameroon						
Burundi						
Burkina Faso –						
Botswana						
Benin -						
Angola						
3	1970	1980	1990	2000	2010	2020
	1310	1300	1990	2000	2010	2020
	Reported 100	1000 5000 10000 25000	50000 75000 100000 Tran	nsmission T1 T3 T4 T5 ent Lineage	T6 T7 T8 T9 T10	T11 T12 T1







Inferring occurrence & prevalence of cholera sub-lineages to define epidemiologically relevant transmission units





Approach

- Model occurrence and prevalence of distinct cholera sub-lineages in countries through time using a Hidden Markov Model.
 - Accounting for historical information of cholera presence
- Targets of inference:
 - strength of connectivity driving transmission between locations
 - underlying occurrence and prevalence of cholera sub-lineages in each country in all years



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Transition Process





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Model Results

Zambia — Uganda —					
Togo —					
Tanzania —					
Sudan					
South Stidan					
Somalia -					
Sierra Leone –					
Senegal					
Observed Rep of the Congo -					
Niger -					
SUD-IINEOGE Namibia –					
Mozambique -					
bresence Mali –					
Malawi –					
Liberia -					
Kenya –					
~Since 2000~ Guinea-Bissau -					
Ghana					
Gabon —					
Ethiopia					
Eswatini –					
Equatorial Guinea					
Djibouti -					
Cote D'Ivoire -					
Chad -					
Central African Republic –					
Burundi -					
Burkina Faso -					
Botswana					
Benin —					
Angola —	2000	2005	2010	2015	
	Reported 100 Cholera Cases	1000 5000 10000 25000	50000 75000 100000 Transm Event I	ission T6 T8 T9 T10 T1 Lineage	1 T12 T13

Model Results



Burundi Burkina Faso Botswana Benin Angola		
Cote Divore Chad Central African Republic Cameroon		
Equatorial Guinea DRC Djibouti		
Ghana Gabon Ethiopia		
Control Contro Control Control Control Control Control Control Control Control Co		
lineage		
inferred sub-		
Observed & Rep. of the Congo Nigeria		
South Africa Somalia Sierra Leone		
logo Tanzania Sudan South Sudan		
Zimbabwe Zambia Uganda		

19



Model Results



0

Inferred

prevalence

~Since 2000~

20







Ongoing Analysis

- Continue to refine and validate our model, incorporating additional elements to capture transmission dynamics and connectivity between locations.
- Simulate transmission between countries based on inferred connectivity from our model.





Limitations

- Ultimately, sequencing remains sparse and cholera cases are often underreported.
 - Areas with extremely sparse data can impact the ability of our model to infer underlying presence of distinct sub-lineages.



Year

• Additional sequencing efforts can help improve our understanding of phylodynamic processes driving cholera transmission in Africa.



Implications & Future Directions

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- Transmission units informing cholera control:
 - Proactive intervention:
 - identify areas where increases in cases ightarrow increase in local cholera risk in connected areas
 - Maximize indirect effects:
 - targeted vaccination and water/sanitation campaigns



• Assess drivers of cholera endemicity to determine the influence of new and re-introductions versus local undetected persistence



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Thank You



