Supporting Information for El Niño Southern Oscillation and Cholera in East Africa

Sean M. Moore¹, Andrew S. Azman¹, Ben F. Zaitchik², Eric D. Mintz³, Joan Bunkard³, Dominique Legros⁴, Alexandra Hill⁴, Heather McKay¹, Francisco J. Luquero^{5,6}, David Olson⁷, Justin Lessler¹

1. SI Materials and Methods

1.1 Cholera data summary

The cholera data used to generate the fine-scale maps of cholera incidence were collated from 360 separate datasets (details and data are available at http://www.iddynamics.jhsph.edu/projects/cholera-dynamics/data). Annual case counts reported to the World Health Organization (WHO) from 2000-2014 were included for each country in sub-Saharan Africa [\(1\).](https://paperpile.com/c/dWuoaQ/ks3xi) We received sub-national reporting data from the Ministries of Health of Benin, Democratic Republic of Congo, Mozambique, and Nigeria and additional sub-national reporting data for several countries were shared by the WHO. Médecins Sans Frontières and Epicentre provided cholera data from outbreaks occurring between 2000 and 2014. Cholera reporting data for South Africa and Madagascar were obtained from publicly available sources [\(2–5\).](https://paperpile.com/c/dWuoaQ/nn3Wd+3CFAJ+9FKqS+Ha45G) Publicly available reporting data were also obtained for refugee camps managed by the UN Refugee Agency (UNCHR; 20 records) and publicly available cholera outbreak reports were obtained from ReliefWeb and ProMED [\(6, 7\).](https://paperpile.com/c/dWuoaQ/HZ04H+US4Fy) Finally, cholera data was also obtained from the primary literature [\(8–14\).](https://paperpile.com/c/dWuoaQ/tOImo+DxDwn+a9Hsb+jtdhV+ReZS3+2pikM+mgtap)

A total of 17,033 annual observations from 3,071 unique locations from 2000-2014 were included in the main analysis. Of these observations, 7,691 were from 2,525 unique locations in non-El Niño years and 9,342 were from 2,616 unique locations in weak-orstronger El Niño years. These 3,071 unique locations include 44 different countries, 327 first-level administrative units, 1948 second-level administrative units, and 752 locations at the third-level administrative unit or lower (Fig. S1). A summary of the cholera data used to model the spatial distribution of cholera incidence is provided by country (Table S1) and year (Table S2). Shapefiles of official administrative boundaries were obtained from the Database of Global Administrative Areas [\(15\)](https://paperpile.com/c/0zmJ5D/7LdLH) for the majority of countries. However, alternative administrative shapefiles were used for Cameroon, Ghana, Kenya, Mauritania, Malawi, Rwanda, Senegal, South Africa, Sudan, Togo, Tanzania, Uganda, and Zimbabwe for at least part of the study period. Alternative shapefiles were used

because they either included new administrative districts not yet included in the GADM shapefiles or older districts no longer in the GADM shapefiles. The boundaries of locations that did not correspond to official administrative units (e.g. a health district, hospital, or village) were either identified using shapefiles (in the case of health districts in Chad and the Democratic Republic of Congo or city communes/neighborhoods in Guinea-Bissau, Ghana, and Mali) or assigned to the highest available official administrative unit containing the location. For example, cases occurring in a village would be assigned to the smallest official administrative unit that the village is located within (typically a 2nd or 3rd level administrative unit such as county or sub-district).

For our regional analyses we divided Africa into six regions (North, southern, East, West, Central, and Madagascar). The first five regions are the main continental divisions used by the United Nations Statistics Division (UNSD) and for each of these we used the UNSD grouping with the exception of Madagascar. Madagascar is grouped with East Africa by UNSD; however, we considered Madagascar separately from continental East Africa because of its physical separation from the rest of the continent. The continental East African countries based on the regional categorization used by UNSD are: Burundi, Djibouti, Eritrea, Ethiopia, Kenya, Malawi, Mozambique, Rwanda, Tanzania, Somalia, Uganda, Zambia and Zimbabwe.

Fig. S1. (A) Map of cholera data sets during El Niño years from 2000-2014 used in this analysis based on spatial resolution. **(B)** Map of cholera data sets during non-El Niño years. Colors represent the lowest administrative level data available for a given area (data from multiple administrative levels).

Table S1. Summary of cholera dataset by country in El Niño and non El Niño years. Locations is unique administrative units and observations is the number of unique administrative unit by year combinations. Cases is number of cases in all units combined, with cases in nested administrative units counted multiple times, leading to over counting of cases in some circumstances. Case numbers presented here are for summary purposes only and are not actual estimates. Max level is smallest administrative unit with an observation.

Table S2. **Summary of cholera dataset by year.** Locations is unique administrative units and cases is number of cases in all units combined, with cases in nested administrative units counted multiple times.

Table S3: Table of cholera cases reported since the start (1-April-2015) of the current El Niño event. Only countries for which we have reported data, including zeros, are included in the table.

Fig. S2. Percentage of population with access to improved drinking water. Data from (16) .

Fig. S3. Percentage of population with access to improved sanitation. Data from [\(16\).](https://paperpile.com/c/0zmJ5D/RkJp3)

1.2 Mapping Implementation

The hierarchical Bayesian spatial model was implemented using Rstan version 2.7 [\(17\)](https://paperpile.com/c/0zmJ5D/lww4r) by running four chains with 2000 iterations each for both El Niño and non-El Niño years. The covariates included as parameters were percent of the population with access to improved drinking water, percent of the population with access to improved sanitation, log population density, distance to the coast, and distance to a large body of water.

In El Niño years there was a negative correlation between incidence and access to improved drinking water (β ₁=-1.09, 95% CI: -1.76 – -0.25; Fig. S4A), but a positive correlation between incidence and access to improved sanitation ($β₂=2.01$, 95% CI: 1.32‒3.00; Fig. S5A). There was also a positive correlation between log population density and cholera incidence ($β₃=0.61$, 95% CI: 0.44–0.70; Fig. S6A). Finally, there was a significant negative correlation between incidence and distance to the coast $(\beta_{4}$ = 0.12, 95% CI: -0.17– -0.09; Fig. S7A) and a non-significant correlation between incidence and the distance to a major body of water (β ₅=-0.02, 95% CI: -0.19–0.11; Fig. S8A). During non-El Niño years there was a negative correlation between incidence and access to improved drinking water ($β_1 = -1.15$; 95% CI: $-1.93 - -0.35$; Fig. S4B), but a positive correlation between incidence and access to improved sanitation ($β₂=1.01$; 95% CI: 0.42–1.66; Fig. S5B). There was also a positive correlation between log population density and cholera incidence ($β₃=0.69$, $95%$ CI: 0.54–0.81; Fig. S6B). Finally, there was a non-significant relationship between incidence and distance to the coast $(\beta_{4}=0.004, 95\% \text{ C}$: -0.05–0.05; Fig. S7B) and a significant correlation between incidence and the distance to a major body of water (β ₅=-1.90, 95% CI: -2.19–-1.59; Fig. S8B). Spatial autocorrelation was very strong during both El Niño (ρ=0.991, 95% CI: 0.982‒0.995) and non-El Niño years (ρ=0.995, 95% CI: 0.993‒0.998).

The relationship between cholera incidence and access to improved drinking water was negative in both El Niño and non-Niño years, suggesting that increasing access to improved water lowers the risk of cholera transmission. The positive relationship between cholera incidence and access to improved sanitation appears paradoxical; however, this relationship is only positive when accounting for the significant relationships between incidence and access to drinking water, population density, and distance to the coast or other major waterbody in the multiple regression. When examined in isolation, there is no significant positive or negative correlation between cholera incidence and access to improved sanitation (Pearson's ρ=0.01 for both El Niño and non-Niño years), as seen in Fig. S5. The significant negative relationship between cholera incidence and distance to a major waterbody during non-El Niño years suggests that major waterbodies are sources of cholera risk. However, they were not a significant source of risk during El Niño years while proximity to the coast was, perhaps because

cholera incidence shifted towards the coast of East Africa and away from large inland waterbodies such as Lake Chad and the Congo River.

Fig. S4. Relationship between mean annual cumulative cholera incidence (per 100,000) and percent of population with access to improved drinking water during **(A)** El Niño and **(B)** non-El Niño years.

Fig. S5. Relationship between mean annual cumulative cholera incidence (per 100,000) and percent of population with access to improved sanitation during **(A)** El Niño and **(B)** non-El Niño years.

Fig. S6. Relationship between mean annual cumulative cholera incidence (per 100,000) and log population density during **(A)** El Niño and **(B)** non-El Niño years.

Fig. S7. Relationship between mean annual cumulative cholera incidence (per 100,000) and distance to the coast during **(A)** El Niño and **(B)** non-El Niño years.

Fig. S8. Relationship between mean annual cumulative cholera incidence (per 100,000) and distance to a major body of water during **(A)** El Niño and **(B)** non-El Niño years.

The mean annual incidence rate during El Niño years was 25.2 per 100,000 (see Fig. S9A for a map of incidence), totaling 215,546 cases (95% CI: 209,770–221,704; see Fig. S9B for a map of cases). The mean annual incidence rate in non-El Niño years was 24.5 per 100,000 (see Fig. S10A for a map of incidence), totaling 209,791 cases (95% CI: 202,087-219,047; see Fig. S10B for a map of cases). Plots of the standard deviation and coefficient of variation (*cv*=σ/μ) of mean annual incidence for all El Niño years and non-El Niño years are presented in Figs. S11-S12. The coefficient of variation is lower in areas with high incidence and high in areas with low population density such as the Sahara and Southern Africa. The geographic distribution of both mean annual cholera incidence and the number of cholera cases varied significantly between El Niño and non-El Niño years (Fig. S13).

To test the sensitivity of our results to single El Niño or La Niña events we re-ran the model while holding out each single pair of years representing either an El Niño event or a non-El Niño event (8 pairs of years; with the exception of the non-El Niño year, 2008, between the 2006-2007 and 2009-2010 El Niño events, where only a single year was withheld from the analysis). The mean annual incidence during El Niño years was sensitive to holding out particular El Niño events in only a few geographic areas, and none of the sensitive areas were within one of the regions where cholera incidence was classified as positively-sensitive to El Niño events (Fig. S14A). Similarly, the mean annual incidence during non-El Niño years was highly sensitive to holding out particular non-El Niño years in only a few scattered geographic areas (Fig. S14B). The overall geographic shift in cholera incidence between El Niño and non-El Niño years does not appear to be overly sensitive to single El Niño events (Fig. S15). However, some areas did see a bigger increase or decrease in incidence during El Niño years when the average from the holdout analysis was compared to the full analysis (Fig. S16). In particular, some areas in the southern Sahara and the Kalahari with very low population densities experienced a larger shift towards cholera in El Niño years in the holdout analysis where non-El Niño years were held out, indicating that cholera incidence during non-El Niño years in these regions is likely driven by a single (small) outbreak, making temporal shifts in incidence sensitive to the years included in the analysis (Fig. S16B).

Table S4. Country-level estimates of annual cases and incidence for El Niño and non El Niño years. Countries are sorted by region and the difference between mean annual cases within region.

Fig. S9. (A) Mean annual incidence per 100,000 and **(B)** annual cases in all El Niño years from 2000-2014.

Fig. S10. (A) Mean annual incidence per 100,000 and **(B)** annual cases in all non-El Niño years from 2000-2014.

Fig. S11. **(A)** Standard deviation and **(B)** coefficient of variation of mean annual incidence in all El Niño years from 2000-2014. Coefficient of variation is $c_v = σ/μ$.

Fig. S12. **(A)** Standard deviation and **(B)** coefficient of variation of mean annual incidence in all non-El Niño years from 2000-2014. Coefficient of variation is $c_v = σ/μ$.

Fig. S13. Difference in **(A)** log of mean annual incidence and **(B)** mean number of cases between El Niño and non-El Niño years.

Fig. S14. (A) Coefficient of variation for mean annual incidence during El Niño years when different El Niño years are held out of analysis. **(B)** Coefficient of variation for mean annual incidence during non-El Niño years when different non-El Niño years are held out of analysis. Areas where mean annual incidence is < 1/1,000,000 were excluded from analysis and are displayed in white. Red and blue outlines are regions

either positively- or negatively-sensitive to El Niño from main analysis included here for comparison to sensitivity analysis.

Fig. S15. (A) Difference in log of mean annual incidence between El Niño and non-El Niño years (same as Fig. S13A). **(B)** Mean difference in log of mean annual incidence between El Niño and non-El Niño years from sensitivity analysis where individual El Niño events were held out. Red and blue outlines are regions either positively- or negatively-sensitive to El Niño from main analysis included here for comparison to sensitivity analysis.

Fig. S16. (A) Comparison of the shift in the log of mean annual incidence between El Niño and non-El Niño years for the full analysis versus the sensitivity analysis when individual El Niño events were held out. **(B)** Comparison of shift in log of mean annual incidence between El Niño and non-El Niño years for full analysis and sensitivity analysis when individual non-El Niño events were held out. Orange regions have a stronger positive change (or a smaller negative change) during El Niño years in the mean result from sensitivity analysis than in the full analysis, purple regions have a stronger negative change (or smaller positive change) in the sensitivity analysis than the full analysis. Red and blue outlines are regions either positively- or negatively-sensitive to El Niño from main analysis included here for comparison to sensitivity analysis.

Fig. S17: Areas with positive (red) and negative (blue) ENSO sensitivities based on classification of smoothed normalized cholera incidence with a kernel smoothing bandwidth of **(A)** 50 km, **(B)** 100 km, **(C)** 150 km, **(D)** 200 km, **(E)** 250 km, or **(F)** 300 km.

2. SI Further Results

2.1 Local Climate Anomalies and El Niño Incidence

In addition to rainfall, we also examined the association between ENSO-related cholera anomalies from 2000-2014 and temperature, soil moisture, evapotranspiration, and NDVI anomalies. Temperature plays an important role in the survival time of *Vibrio cholerae* outside of a human host, so may facilitate or hinder cholera transmission [\(18\).](https://paperpile.com/c/0zmJ5D/DtHei) The soil moisture, evapotranspiration, and NDVI measures provide alternatives to rainfall in approximating the level of either drought stress or the extent of standing surface water and flooding that occurs during El Niño years in comparison to non-El Niño years. Standardized temperature anomalies during El Niño years were small compared to standardized rainfall anomalies (53.3% of rainfall anomalies were larger than the maximum temperature anomaly of 4.2%), and positive anomalies were limited geographically to a few regions including coastal South Africa, southern Mozambique, the Rift Valley, and highlands in Kenya and Ethiopia (Fig. S18). Soil moisture, evapotranspiration, and NDVI anomalies all showed a similar geographic pattern to that of rainfall anomalies, with positive anomalies during El Niño years concentrated in East Africa and negative anomalies concentrated in Southern Africa and the Sahel (Figs. S19-21). However, negative NDVI anomalies in the Sahel were shifted slightly southward and negative evapotranspiration anomalies were shifted northward into North Africa and the Sahara desert. The distribution of NDVI and evapotranspiration anomalies were moderately correlated with rainfall anomalies (Pearson r=0.56 and r=0.46), while soil moisture anomalies were only weakly correlated with the distribution of rainfall anomalies (Pearson r=0.21). Temperature anomalies were not strongly correlated with any of the other climate variables (Pearson r<0.2).

No climate variables were significantly associated with cholera incidence at the riverbasin scale based on a simple linear regression. However, in addition to the significant association between positive cholera anomalies during El Niño years and the lower and upper quartiles of rainfall anomalies presented in the main text, there was also a significant increase in cholera incidence in areas in the lowest quartile of NDVI (relative rate (RR): 2.5; 95% CrI: 1.4—4.5), and in areas in the upper quartile of NDVI (RR: 2.2; 95% CrI: 1.2—3.8), evapotranspiration (RR: 2.1; 95% CrI: 1.1—3.9), and temperature (RR: 2.8; 95% CrI: 1.5—5.2) (Fig. S22).

Fig. S18. Normalized temperature anomalies (percent deviation from long-term mean from 2000-2014) during El Niño years from 2000-2014.

Fig. S19. Normalized percent soil moisture anomalies (percent deviation from long-term mean from 2000-2014) during El Niño years from 2000-2014.

Fig. S20. Normalized evapotranspiration anomalies (percent deviation from long-term mean from 2000-2014) during El Niño years from 2000-2014.

Fig. S21. Normalized NDVI anomalies (percent deviation from long-term mean from 2000-2014) during El Niño years from 2000-2014.

Fig. S22. River-basin level log cholera incidence anomalies during El Niño years as a function of the strength of anomalies of **(A)** rainfall, **(B)** evapotranspiration, **(C)** NDVI, **(D)** soil moisture, and **(E)** temperature. All climate anomalies are grouped into quartiles from strongest negative to strongest positive anomalies. Upper and lower quartiles marked by an asterisk have a significant difference in log cholera incidence than the middle quartiles.

Although the overall relationships between climate anomalies and cholera incidence at the river-basin scale were weak, their strength and direction varied by geographic region. Negative rainfall anomalies were associated with higher cholera incidence in East Africa, Central Africa, North Africa, and West Africa, while positive rainfall anomalies were associated with higher incidence in East and Southern Africa (Fig. 3C main text). Negative evapotranspiration anomalies were associated with a nonsignificant increase in cholera incidence in East, North, southern, and West Africa (Fig. S23), and a significant decrease in incidence in Central Africa (RR: 0.15, 95% CrI: 0.03—0.64; Fig. S23). Positive evapotranspiration anomalies were associated with significantly lower incidence in West Africa (RR: 0.29; 95% CrI: 0.10—0.83), and a significant increase in southern Africa (RR: 6.1; 95% CrI: 1.6—23.2). Negative NDVI anomalies were associated with significantly higher cholera incidence in West Africa (RR: 3.0; 95% CrI: 1.2—7.0), and non-significantly higher incidence in Central Africa (Fig. S24). Positive NDVI anomalies were associated with significantly lower incidence in West Africa (RR: 0.24; 95% CrI: 0.07—0.80). Increased soil moisture levels were associated with a significant decrease in cholera incidence in West Africa (RR: 0.28, 95% CrI: 0.11—0.69; Fig. S25). Temperature anomalies were not associated with statistically significant changes in cholera incidence in any geographical region (Fig. S26).

In addition to varying by geographical region, the association between cholera incidence and rainfall anomalies also varied by the local climatology. Cholera incidence was positively associated with positive rainfall anomalies except for in the wettest regions, which include much of coastal West Africa and the Congo Basin (Fig. S27). Cholera incidence was also higher in normally wetter areas with the largest negative rainfall anomalies (potential drought conditions). This dependency on local climatology may explain why positively-sensitive areas were only associated with increased rainfall anomalies in East Africa, where normal rainfall is mostly low-moderate (Fig. S28).

Fig. S23. River-basin level log cholera incidence anomalies during El Niño years by region versus the strength of evapotranspiration anomalies. All climate anomalies are grouped into quartiles from strongest negative to strongest positive anomalies.

Fig. S24. River-basin level log cholera incidence anomalies during El Niño years by region versus the strength of NDVI. All climate anomalies are grouped into quartiles from strongest negative to strongest positive anomalies.

Fig. S25. River-basin level log cholera incidence anomalies during El Niño years by region versus the strength of soil moisture anomalies. All climate anomalies are grouped into quartiles from strongest negative to strongest positive anomalies.

Fig. S26. River-basin level log cholera incidence anomalies during El Niño years by region versus the strength of temperature anomalies. All climate anomalies are grouped into quartiles from strongest negative to strongest positive anomalies.

Fig. S27. **(A)** Map of annual rainfall quartiles in sub-Saharan Africa. **(B)** Relationship between rainfall and cholera anomalies for different areas classified by annual rainfall (rainfall quartiles). Positive relationships exist for dry to moderately-wet areas (low to mid-high quartiles), while relationship is negative for wettest areas (highest quartile). Cholera incidence also increases with larger negative anomalies in the driest and wettest areas.

Fig. S28. Rainfall anomalies in El-Niño-sensitive and El-Niño-insensitive cholera clusters by geographical region. Positive rainfall anomalies are concentrated in Madagascar and positively-sensitive areas of continental East Africa.

2.2 Sea surface temperatures

The association between cholera incidence during El Niño years and coastal sea surface temperature anomalies (Fig. S29) was examined for grid cells within 200 km of the coastline. For each land grid cell within 200km of the coastline, a corresponding SST value was calculated by averaging the SST anomalies of any ocean grid cell within 400km of the land cell (this buffer was necessary because distances were measured from the center of each grid cell). Coastal SST anomalies are positively correlated with cholera anomalies, but only weakly (Pearson r=0.04). There was little difference between the distribution of cholera anomalies in coastal areas with SST anomalies of greater than ± 0.1℃ compared to areas with SST anomalies <0.1℃(Fig. S30A), but the largest increases in cholera incidence are concentrated in areas with SST anomalies >0.2℃ (Fig. S30B).

Fig. S29. Mean sea surface temperature (SST) anomalies during El Niño years from 2000-2014.

Fig. S30. Cholera anomalies in coastal areas (within 200km of coast) during El Niño years in areas with sea surface temperature (SST) anomalies of **(A)** >0.1℃ below normal, >0.1℃ above normal or ≤0.1℃, and **(B)** >0.2℃ above normal or ≤0.2℃ above normal. There were no SST anomalies of >0.2℃ below normal.

2.3 Sensitivity to the Definition of El Niño Years

In the main text, cholera incidence in all El Niño and non-El Niño years from 2000-2014 was mapped at a 20 x 20 km scale to examine spatially-explicit ENSO-associated variations in cholera incidence. For this main analysis El Niño years were identified using the minimum ONI threshold of 0.5˚C for a weak El Niño event. To determine whether the relationship between ENSO and cholera incidence varied with the strength of the ENSO anomaly we also compared cholera incidence in non-El Niño years to incidence in years with a moderate or stronger El Niño event, thereby excluding weak El Niño events. From 2000-2014 only the 2002-2003 and 2009-2010 El Niño events were of moderate strength and no El Niño events prior to the 2015-2016 event reached the strong or very strong category based on ONI values.

Overall, the mean number of cholera cases (186,204; 95% CI: 162,832-210,956) during moderate El Niño years was lower than the number of cases during non-El Niño years (209,791; 95% CI: 202,087-219,047). This was also lower than the mean number of cases observed during all El Niño years (215,546; 95% CI: 209,770-221,704), indicating that overall cholera incidence is higher during weak El Niño events than during moderately strong El Niño events. The geographic distribution of cholera incidence differed strongly between non-El Niño (Fig. S10) and moderate El Niño years (Figs. S31,32). The largest increases in cholera cases during moderate El Niño years compared to non-El Niño years occurred in Mozambique (11,925 additional cases; 95% CI: 9,677-12,702) and Ethiopia (9,961 additional cases; 95% CI: 9,296-10,428), while the largest decreases occurred in South Africa (25,548; 95% CI: 24,136-26,122) and Sierra Leone (16,209 fewer cases; 95% CI: 15,514-17,174). On a per-capita basis the largest increases occurred in Liberia (206.7 additional cases per 100,000; 95% CI: 203.1-210.8) and Djibouti (116.0 additional cases per 100,000; 95% CI:63.3-167.6), and the largest decreases were in Sierra Leone (280.8 fewer cases per 100,000; 95% CI: 268.8-297.5), Guinea-Bissau (190.0 fewer cases per 100,000; 95% CI: 187.3-192.7), and Swaziland (158.0 fewer cases per 100,000; 95% CI: 95.5-282.7). Regionally, there was an increase of 40,392 cases (95% CI: 30,975-57,520) in continental East Africa, but a decrease of 19,050 (95% CI: 16,098-22,423) cases in West Africa and 29,765 (95% CI: 27,294-32,155) in Southern Africa. The estimated number of cholera cases per country during moderate El Niño years and the difference in cases and incidence compared to non-El Niño years is presented in Table S5.

Table S5. Country-level estimates of annual cases and incidence for moderate El Niño versus all non El Niño years. Countries are sorted by region and the difference between mean annual cases (during all El Niño years versus non El Niño years) within region.

Fig. S31. (A) Mean annual incidence per 100,000 and **(B)** annual cases in moderate El Niño years from 2000-2014.

Fig. S32. Difference in **(A)** log of mean annual incidence and **(B)** mean number of cases between moderate El Niño and non-El Niño years.

The broad-scale geographic distribution of cholera anomalies during moderate El Niño years was similar to their distribution during all El Niño years, with a large increase in East Africa and decreases in West and Southern Africa (Table S6). However, the mean increase of over 9,400 cases seen in Central Africa during El Niño years becomes a decrease of over 11,000 cases during moderate El Niño years, largely because 20,819 fewer cases are expected in Angola during moderate El Niño years compared to all El Niño years. Several other countries experience large differences in cholera incidence during moderate El Niño years compared to all El Niño years, including over 14,000 fewer cases in Ethiopia and 10,900 additional cases in Zimbabwe during moderate El Niño years.

The El-Niño-sensitive clusters during moderate El Niño years were geographically similar to the El-Niño-sensitive clusters during all El Niño years (Fig. S33). The largest positively-sensitive cluster occurs in East Africa from Ethiopia south to Mozambique and the largest negatively-sensitive cluster occurs in Central Africa. There are however several differences between the two analyses; northern Nigeria is mostly neutral or positively-sensitive instead of negatively-sensitive, there is a new positively-sensitive region in southern Africa that was previously neutral or negatively-sensitive, and the far West African coast including Senegal, Gambia, Guinea-Bissau, and Guinea switches from being positively-sensitive to negatively-sensitive. During a year with a moderate El Niño event, cholera incidence within positively-sensitive clusters increased, on average, five-fold from 1.0 per 10,000 to 3.6 per 10,000 (relative rate [RR] 3.4, 95% CI: 2.9-4.1) corresponding to 67,825 excess cases during a typical moderate El Niño year (Fig. S34). In El-Niño-insensitive areas, cholera incidence was slightly lower during El Niño years (2.0 vs. 2.7 per 10,000, RR 0.7, 95% CI 0.6-0.8) and in negatively-sensitive clusters incidence decreased from 3.8 per 10,000 to 0.7 per 10,000 (RR 0.2, 95% CI 0.17-0.22), a reduction of 63,007 cases.

Table S6. Country-level estimates of annual cases and incidence for all El Niño versus moderate-plus El Niño years. Countries are sorted by region and the difference between mean annual cases (during all El Niño years versus non El Niño years) within region.

Fig. S33. Comparison of clusters of positive (red) and negative (blue) ENSO sensitivities during (A) all El Niño years or (B) moderate El Niño years only. Clustering based on classification of smoothed normalized cholera incidence with a kernel smoothing bandwidth of 150 km.

Fig. S34. Mean annual cholera cases per 10,000 during moderate El Niño and non-El Niño years in different El-Niño-sensitive clusters. Boxes represent ±2 SE and whiskers are 95% confidence interval.

As with the analysis of all El Niño years, the positive rainfall anomalies during moderate El Niño years are concentrated in positively-sensitive cholera clusters (Fig. S35A). This association between positive rainfall anomalies and increased cholera incidence only holds in East Africa, while areas of increased cholera incidence in West, Southern, and North Africa experience below average rainfall (Fig. S35B). In addition, in East Africa and Madagascar decreased rainfall is associated with increases in cholera incidence while in Southern and West Africa below average rainfall is associated with decreases in cholera incidence. At the river-basin scale, increases in cholera incidence during moderate El Niño years were associated with positive rainfall anomalies (highest rainfall anomaly quartile) in East and Southern Africa (Fig. S36). In the analysis of all El Niño years only Madagascar had decreased incidence in river basins with increased rainfall, but during moderate El Niño years Madagascar, Central Africa, and West Africa all experienced lower cholera incidence in basins with increased rainfall. North Africa experienced an increase in cholera incidence regardless of the size of rainfall anomaly, while Central Africa and East Africa experienced an increase in cholera incidence in river basins with below average rainfall. The association between positive rainfall anomalies and increased cholera incidence in East and Southern Africa river basins was robust to the use of all El Niño years or moderate El Niño years only, as was the association between negative rainfall anomalies and increased incidence in Central, East, and North Africa. Only the increased incidence in West Africa river basins with negative rainfall anomalies seen during all El Niño years was not observed in moderate El Niño years.

Fig. S36. River-basin level log cholera incidence anomalies during moderate El Niño years by region versus the strength of rainfall anomalies. All climate anomalies are grouped into quartiles from strongest negative to strongest positive anomalies.

Negative evapotranspiration, soil moisture and NDVI anomalies were associated with higher cholera incidence in North and East Africa but significantly lower incidence in Central Africa, while positive evapotranspiration anomalies were associated with higher incidence in East, North, and Southern Africa and lower incidence in Madagascar and West Africa (Figs. S37-39). Positive soil moisture anomalies were only positively associated with higher incidence in East Africa and were negatively associated with cholera incidence in Madagascar (Fig. S38), while positive NDVI anomalies were positively associated with higher incidence in East and North Africa and negative associated with incidence in Central Africa, Madagascar, and West Africa (Fig. S39). Negative temperature anomalies were associated with higher incidence in East and North Africa, and positive temperature anomalies were associated with higher incidence in East, North, and Southern Africa, but associated with lower incidence in Madagascar (Fig. S40).

Central Africa East Africa Madagascar North AfricaSouthern AfricaWest Africa

Fig. S37. River-basin level log cholera incidence anomalies during moderate El Niño years by region versus the strength of evapotranspiration anomalies. All climate anomalies are grouped into quartiles from strongest negative to strongest positive anomalies.

Fig. S38. River-basin level log cholera incidence anomalies during moderate El Niño years by region versus the strength of soil moisture anomalies. All climate anomalies are grouped into quartiles from strongest negative to strongest positive anomalies.

Fig. S39. River-basin level log cholera incidence anomalies during moderate El Niño years by region versus the strength of NDVI anomalies. All climate anomalies are grouped into quartiles from strongest negative to strongest positive anomalies.

Fig. S40. River-basin level log cholera incidence anomalies during moderate El Niño years by region versus the strength of temperature anomalies. All climate anomalies are grouped into quartiles from strongest negative to strongest positive anomalies.

Coastal SST anomalies were positively correlated with cholera incidence in moderate El Niño years (Pearson r=0.10), a small increase in the strength of the correlation compared to all El Niño years (Pearson r=0.04). The largest increases in cholera incidence were concentrated in areas with SST anomalies >0.2℃(Fig. S41).

Fig. S41. Cholera anomalies in coastal areas (within 200km of coast) during moderate El Niño years in areas with sea surface temperature (SST) anomalies of **(A)** >0.1℃ below normal, >0.1℃ above normal or ≤0.1℃, and **(B)** >0.2℃ above normal or ≤0.2℃ above normal. There were no SST anomalies of >0.2℃ below normal.

2.4 Association of country-level cholera anomalies with ENSO strength

We examined the association between ENSO strength and cholera incidence for all of Africa using a longer country-level annually-aggregated dataset [\(19\),](https://paperpile.com/c/0zmJ5D/EdUsw) with a focus on continental East Africa due to the region's large positive El-Niño-sensitive cluster. To determine whether the association between cholera incidence and ENSO strength varied by the effect of ENSO on the local climate, each country in sub-Saharan Africa was grouped by the mean strength of the normalized rainfall anomalies during El Niño events. The country-level rainfall anomaly was calculated as the mean of the normalized rainfall anomaly over all the country's grid cells weighted by population density. Countries were grouped as having either positive or negative rainfall anomalies during El Niño events. In addition, continental East African countries were also analyzed separately by rainfall anomaly with Tanzania, Kenya, Ethiopia, Somalia, Malawi, Rwanda, Eritrea, and Djibouti in the positive rainfall anomaly group and the remaining countries placed in the low rainfall anomaly group.

These annual grouped time series from 1970-2014 were detrended to remove the positive overall trend in cases since the initial spread in the 1970s. The detrended time series were calculated by taking the residuals from a generalized linear regression of annual cases fit by year with a natural cubic spline with four degrees of freedom. Wavelet analyses (using a morlet wavelet) of the annual time series of cholera cases for all of Africa and for East Africa revealed that there were no significant multi-annual cycles prior to 1990, but both time series displayed significant multi-annual cycles for at least part of the post-1990 time period (Figs. S42,43). In addition, there was also a significant coherence between ENSO and cholera cycles in East Africa after 1990, but not before (Fig. S43C). Therefore, we examined the association between ENSO strength (mean of the three highest absolute ONI values per year) and detrended cholera cases for East Africa and all of Africa for both the entire time period from 1970- 2014 and for only the second half of the time period (1992-2014). The association between ENSO strength and cholera was stronger for the period from 1992-2014 than it was for the entire time period, so the more conservative results from the former analysis were presented in the main text.

Fig. S42. (A) Wavelet analysis of monthly ENSO cycle (ONI values) showing a significant multi-annual cycle with a period of 4-6 years during the 1980s and 1990s. **(B)** Wavelet analysis of annual sub-Saharan cholera cases showing significant 2-3 year cycles during early-1990s and late 2000s. **(C)** Wavelet coherence analysis of ENSO and annual cholera cases showing coherence of a 4-5 year cycle in the 1980s.

Fig. S43. (A) Wavelet analysis of monthly ENSO cycle (ONI values) showing a significant multi-annual cycle with a period of 4-6 years during the 1980s and 1990s. **(B)** Wavelet analysis of annual cholera cases in East Africa showing a significant multiannual cycles during the 1990s and 2000s. **(C)** Wavelet coherence analysis of ENSO and annual East Africa cholera cases showing coherence of a 1-2 year cycle and potentially an 8-year cycle in the 2000s.

There was a significant nonlinear association between ENSO strength and cholera cases from 1992-2014 in countries with increased rainfall during El Niño years (r^2 =0.33), but no significant relationship in countries without increased rainfall during El Niño years $(r^2=0.02;$ Fig. S44A). There was also a significant nonlinear (U-shaped) association between ENSO strength and cholera cases from 1992-2014 in East African countries with increased rainfall during El Niño years (r^2 =0.38), but only a weak association between ENSO strength and cholera in East African countries without increased rainfall $(r^2=0.10;$ Fig. S45A). In both East Africa and all of sub-Saharan Africa the association between ENSO strength and cholera is nonlinear, with higher cholera incidence during years with strong negative or positive ENSO events. The association between ENSO strength and cholera in rainfall-positive countries of East Africa appears approximately linear for positive ONI values, so a linear model was fit for ONI values > 0 and used to predict how cholera incidence in East Africa might respond to the strength of an El Niño event. There was a strong positive relationship between positive ONI values and cholera in East Africa from 1992-2014, with an increase of 29,226 cases (95 %CI: 9,403-49,049) for the seven countries in East Africa with increased rainfall in El Niño years (r^2 =0.48; Fig. S45A). The association between ENSO strength and cholera for countries with positive rainfall was weaker over the entire time period from 1970-2014 $(r^2=0.09;$ Fig. S44B), as was the association between ENSO strength and cholera in East Africa (r^2 =0.10; Fig. S45B). The $7th$ modern cholera pandemic only reached sub-Saharan Africa in 1970. As a result, during the first couple of decades following its reintroduction, cholera incidence in Africa was largely driven by the pattern of geographical spread and the occurrence of large epidemics in completely naïve populations, likely obscuring any climate influence on cholera epidemiology in the region. In addition, surveillance and reporting of cholera at the national level was inadequate in many African countries during this time period. Therefore, it is not surprising that we see stronger associations between ENSO and cholera from 1992- 2014 than we do for the entire time period.

Fig. S44. Association between ENSO strength (mean of three highest absolute ONI values) and detrended annual cholera cases for **(A)** 1992-2014 and **(B)** 1970-2014**.** Red circles are annual totals from countries with positive rainfall anomalies during El Niño years and blue circles are annual totals from countries with negative rainfall anomalies during El Niño years. Lines represent linear regression using a natural cubic spline with three degrees of freedom plus a 95% confidence interval.

Fig. S45. Association between ENSO strength (mean of three highest absolute ONI values) and detrended annual cholera cases in East Africa for **(A)** 1992-2014 and **(B)** 1970-2014**.** Red circles are annual totals from East African countries with positive rainfall anomalies during El Niño years and blue circles are annual totals from East African countries with negative rainfall anomalies during El Niño years. Red and blue

lines represent linear regression using a natural cubic spline with three degrees of freedom plus a 95% confidence interval. Green line in (A) is simple linear regression fit and 95% confidence interval for ONI values > 0.

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