

# Cholera

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# History

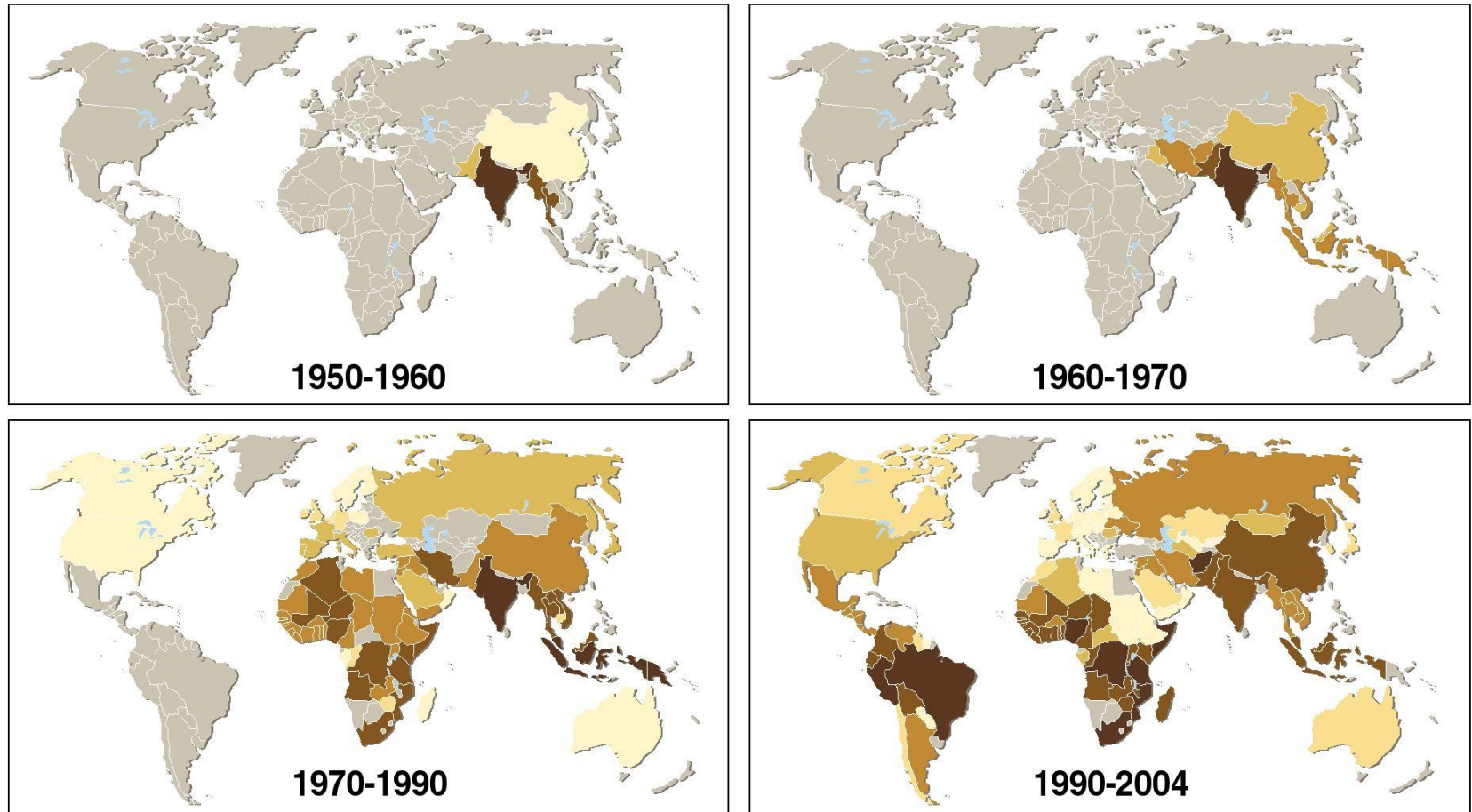
- Originated in Ganges River
- 19<sup>th</sup> century—six subsequent pandemics
  - Spread to all continents
  - Probably killed President James Polk in 1849 shortly after he left office



# Epidemiology

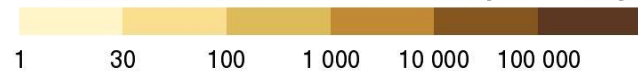
- 3-5 million cases per year, 100-120,000 deaths
- Endemic in resource poor areas of Asia and Africa
  - Worst cases in young children and elderly
- Epidemics have occurred in Asia, Middle East, South and Central America
  - 1991 Peru
- Mostly imported to US
  - 9% acquired via consumption of contaminated Gulf Coast seafood

# The spread of cholera 1950-2004

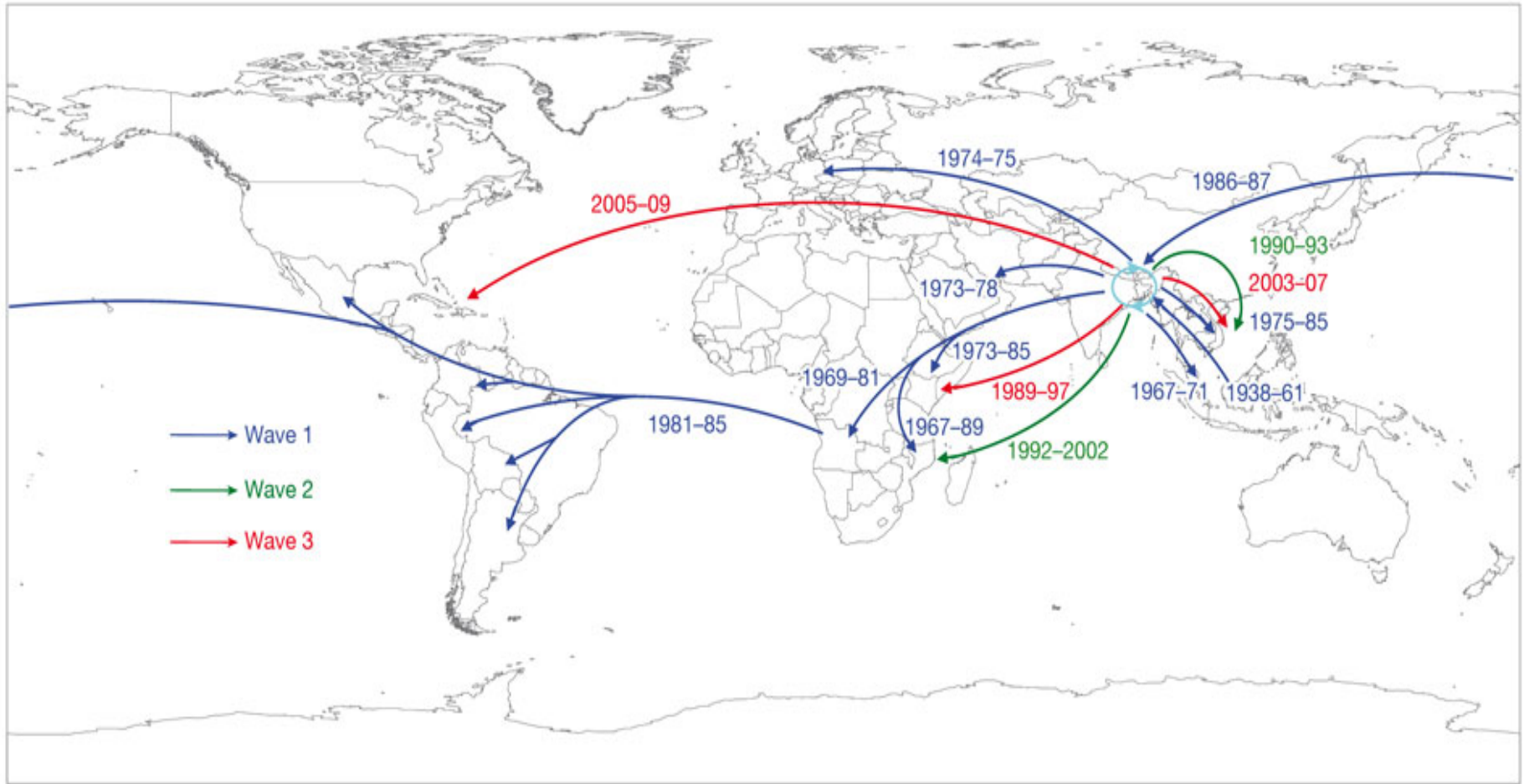


Source : Working group II and III, Synthesis report, IPCC, 2007.

Number of cholera cases declared per country



# Transmission events inferred for the seventh-pandemic of cholera phylogenetic tree



# Global map of countries reporting cholera in 2010



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Les appellations employées dans la présente publication et la présentation des données qui y figurent n'impliquent de la part de l'Organisation mondiale de la Santé aucune prise de position quant au statut juridique des pays, territoires, villes ou zones, ou de leurs autorités, ni quant au tracé de leurs frontières ou limites. Les lignes en pointillés sur les cartes représentent des frontières approximatives dont le tracé peut ne pas avoir fait l'objet d'un accord définitif.

Data Source: The Global Task Force on Cholera Control/WHO  
Map Production: Public Health Information and Geographic Information Systems (GIS)  
World Health Organization



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# Post-earthquake cholera epidemic in Haiti 2010

## AFFECTED AREAS

- Most affected
- Affected
- Possibly affected

Oct. 27



Oct. 28



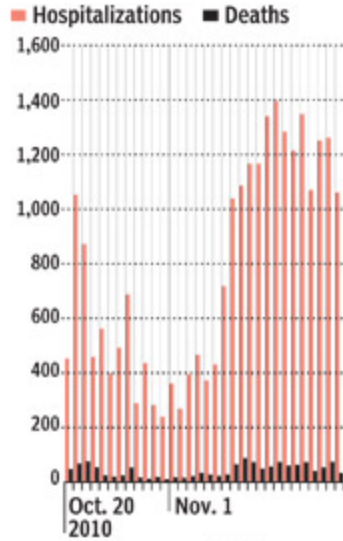
Oct. 29



Nov. 2

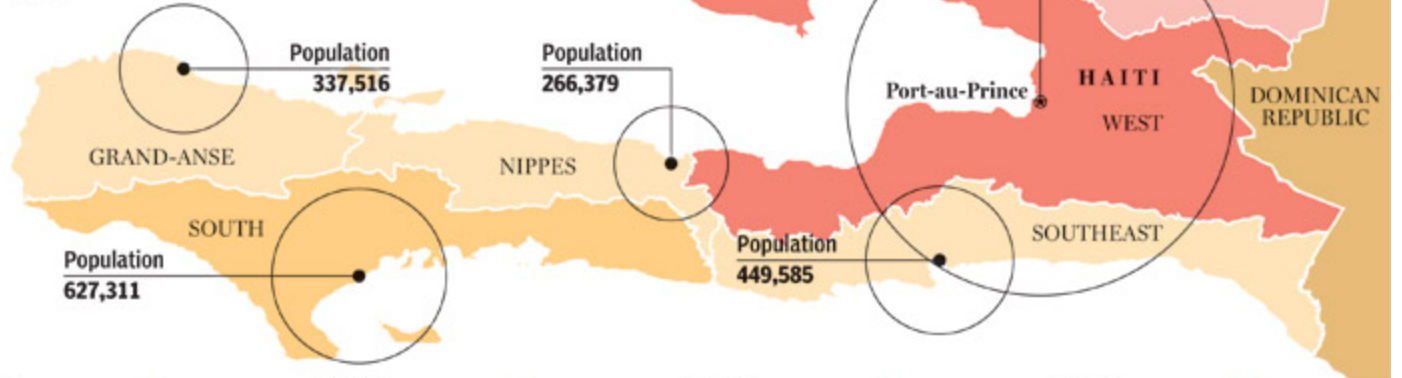


## TOTAL NUMBER OF DEATHS AND HOSPITALIZATIONS FROM OCT. 20 TO NOV. 20



## CURRENT CASE COUNT AS OF NOV. 20, 2010

- 4,068-13,162
- 1,649-4,067
- 92-1,648
- 10-91
- Less than 10



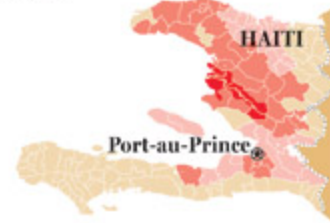
Nov. 3



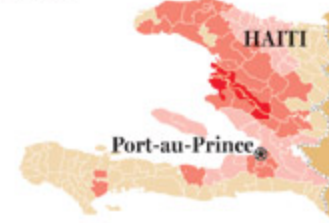
Nov. 8



Nov. 10



Nov. 16



# Cholera outbreak in Haiti

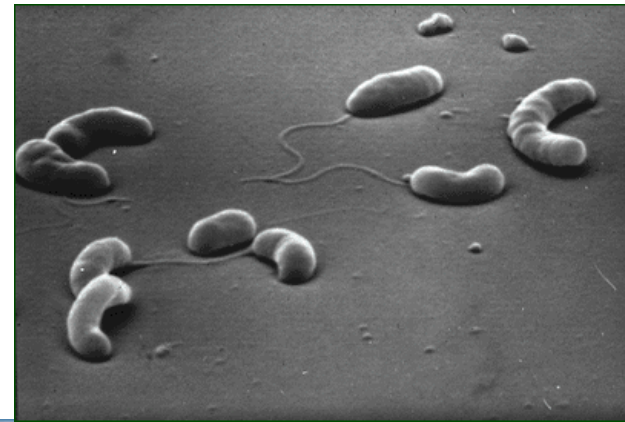
- Importation by Nepalese battalion (asymptomatic vs. symptomatic carriage)
- Spread through Artibonite river
- 5 clusters:  
~440,000 cases by Oct 2011
- Hyper virulent strains



Piarroux R, et al. Understanding the cholera epidemic, Haiti. *Emerg Infect Dis* 2011

# Microbiology

- Gram negative, curved, motile bacillus
- More than 190 serotypes
  - Only O1 and O139 responsible for epidemic cholera
- Cholera toxin—multimeric protein
  - Binds to enterocytes, increases cyclic AMP
  - Increased chloride secretion
  - Reduced sodium absorption
  - Massive loss of fluid and electrolytes



# Mode of Infection

- Humans only known natural host
  - Fecal-oral transmission
- Free-living ***V cholerae*** in aquatic environments
- Infections generally caused by ingestion
  - Water (infectious dose =  $10^9$ )
  - Food (infectious dose =  $10^3$ )
  - Person-to-person

# Clinical Manifestations

- Most *V. Cholera* infections are asymptomatic (75%)
  - *1 case per 30 to 100 infections in the E1 biotype*
  - *1 case per 2 to 4 infections with the classical biotype*
  - *shedding bacteria in feces for 7-14 days*
- **Mild disease** cannot be distinguished from typical gastroenteritis
  - Few episodes of watery diarrhea
  - +/- Nausea and diarrhea
  - Do not become clinically dehydrated
- **Incubation—few hours to 5 days**
  - Most present between 1-3 days
  - Incubation shortest with higher number of ingested organisms

# Characteristic Diarrhea

- Onset sudden or gradual
- “Rice Water”—watery with flecks of mucus
  - Mild “fishy” odor
  - High concentration of Na, K, Cl, bicarbonate
- Abdominal cramping but not severe
- Fever infrequently (non-invasive disease)

# Severe Cholera (“Gravis”)

- Massive volume loss—500-1000ml/hour
  - Can develop over a few hours
    - *Hypovolemic shock within 4-12 hours*
  - Most severe over first two days, then gradually improves over 4-6 days
  - Volume loss may be 100% of body weight
- Complications
  - Renal failure due to dehydration
  - Severe hypokalemia
    - *Arrhythmias, ileus, and leg cramps*
  - Metabolic acidosis
  - Hypoglycemia, seizures



Figure 2: A child, lying on a cholera cot, showing typical signs of severe dehydration from cholera

The patient has sunken eyes, lethargic appearance, and poor skin turgor, but within 2 h was sitting up, alert, and eating normally.

# Mortality

- Most infections none or mild symptoms
  - <5% with severe disease
- Untreated patients—50-70% mortality
  - Increased risk in children—10-fold increased
  - Increased risk in pregnant women
    - *50% fetal loss in 3<sup>rd</sup> trimester*
  - Death can occur within 2-3 hours of onset of symptoms
    - *Usually after 18 hours to a few days*



# Microbiological & Molecular Methods of Detection

- Microbiological culture-based methods using fecal or water samples
- Rapid Tests
  - Dark-field microscopy
  - Rapid immunoassays
  - Molecular methods - PCR & DNA probes



# Treatment

- ORAL REHYDRATION
  - Reduces mortality to less than 1%
  - Na and water absorption is facilitated by glucose even in the presence of cholera toxin
  - Oral rehydration solution from WHO
    - *Make your own: 1 liter water, 1 tsp salt, 8 tsp sugar*
    - *Don't use apple juice, chicken broth, tea, ginger ale*
    - *Approx 10ml/kg for each stool*
    - *Rice-based ORS may be more effective*
  - Use NGT if necessary

# IV rehydration

- Ringer's lactate if available
  - 20ml/kg bolus
- Watch for hypokalemia
  - Use potassium bicarb to correct metabolic acidosis if possible rather than only sodium bicarb (K driven into cells)
- Start oral rehydration as soon as patients able to drink

# Preventing Cholera: Vaccines

- Orochol
  - Contains  $2 \times 10^8$  viable cells of attenuated strain CVD 103-HgR in a lyophilized form
  - Oral immunization of children older than 2
  - Subunit A of the cholera toxin (CT) has been removed
- Dukoral
  - Protects against O1 Inaba and Ogawa, Classical & El Tor strains
  - Contains  $1 \times 10^{10}$  heat/formalin killed cells of strain WC/rBS



# Epidemic Control Measures

- Hygienic disposal of human waste
- Adequate supply of water
- Good food hygiene
  - Thoroughly cooking food
  - Eating food while it's hot
  - Preventing cooked foods from contacting raw foods (including water or ice)
  - Avoiding raw fruits or vegetables
  - Washing hands after defecation & before cooking

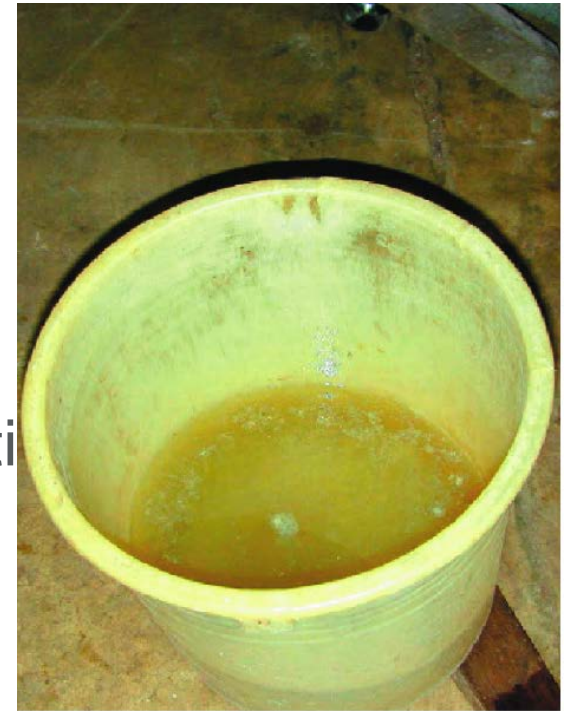


Figure 1: Bucket with typical rice-water stool from a patient with cholera

# Antimicrobials

- Adjunct to appropriate rehydration
- Use in severe cases
- Reduce volume by about half
- Decrease *Vibrio* excretion by one day
- Oral not IV/IM
- Consider local resistance patterns
  - Tetracycline 500mg Q6h x 3 days
  - Doxycycline 300mg x 1 dose
  - Ciprofloxacin 1gm x 1 dose
  - Children <8yrs: Erythromycin 10mg/kg TID x 3 days
    - *Azithromycin 20mg/kg x 1 dose*

# Zinc supplementation

- Reduces stool output and duration in children
- 179 Bangladeshi children with cholera
  - Erythromycin + zinc 30mg or placebo
  - 12% shorter duration of diarrhea
  - 11% less stool output

# Antibiotic Prophylaxis

- Appropriate for household contacts
  - Not recommended for mass community

# Vaccine

- Oral—not available in US
  - Short-term protection (2 years)
  - Active against 85–90% *V. cholerae* O1 among all age groups
  - Requires two doses 7 days-6 weeks apart
  - Protection 4-6 months after immunization

# Anatomy of an Outbreak--Haiti

- Haiti without *Vibrio cholerae* outbreak for decades
- Catastrophic earthquake in January 2010
  - Displacement of population
  - Disruption of already heavily fractured infrastructure
  - Massive tent communities with poor sanitation
- Outbreak of cholera in October 2010
  - South Asian strain
  - 440 deaths, approx 7,000 cases
- Impact of Tropical Storm Tomas

# Requirements for an Outbreak

- Significant breaches in the water, sanitation, and hygiene infrastructure permitting large-scale exposure to food or water contaminated with *Vibrio cholerae*
- Cholera must be present in the population

# Prevention

- Clean water
  - Boil water for at least one minute
  - Chlorine tablets commercially available
  - Bleach--8 drops of bleach for 1 gallon
    - *2 drops of bleach for every 1 liter of water*
    - *Wait 30 minutes before drinking*
- Wash hands, use latrines, cook food

# Technology in an epidemic

- Free texts in Creole
  - 80% have access to cellular phone
  - Information on symptoms
  - Information on prevention and clean water sources



# References

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[http://www.who.int/topics/cholera/publications/en/first\\_steps.pdf](http://www.who.int/topics/cholera/publications/en/first_steps.pdf)

# Slide title

- Bullet 1
- Bullet 2