

Progress in typhoid epidemiology

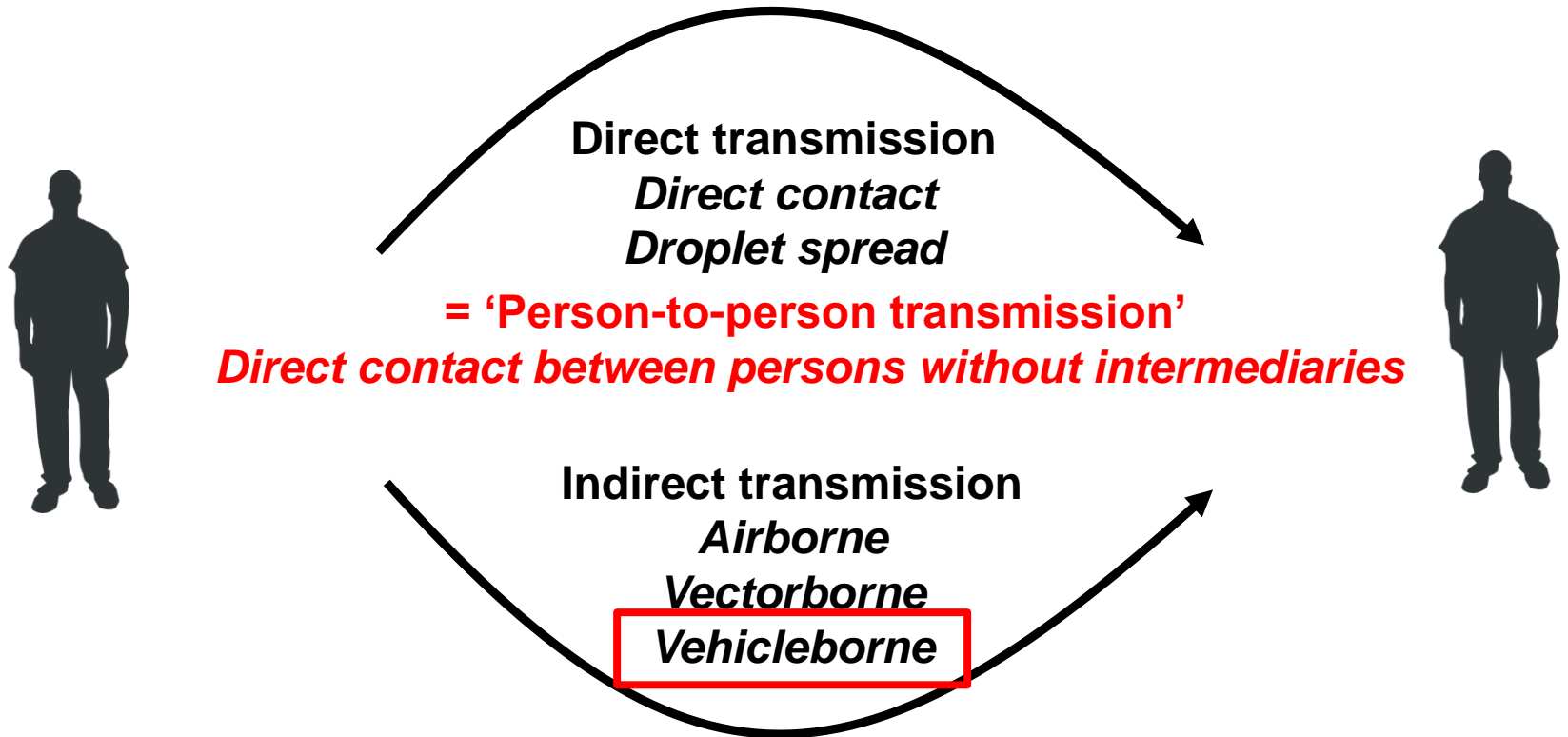
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**10th International Conference on Typhoid
and Other Invasive Salmonellosis
4 April 2017**

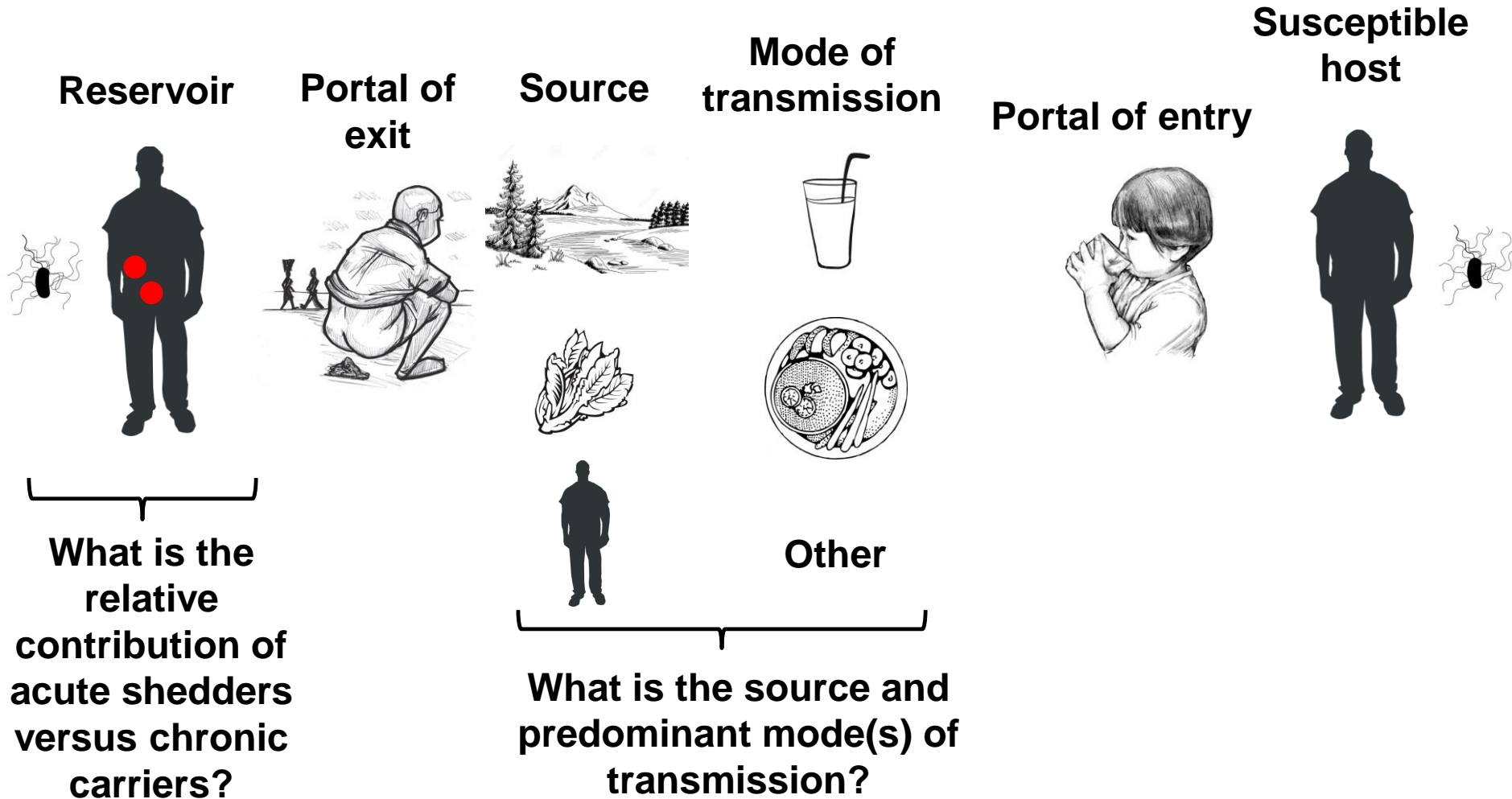
Overview

- **Mode of transmission and sources**
 - **Evidence and importance**
- **Burden of disease**
 - **Current estimates and trends**
 - **Extrapolation, uncertainty, and data gaps**
 - **Severe disease and death**
 - **Occurrence by age**

Modes of transmission



Chain of infection



Mode of transmission in aggregate

- **Mogasale systematic review and meta-analysis association between unimproved water and typhoid fever**
 - **Persons with unimproved water have 2.4 times odds of typhoid fever compared with those with improved water**
 - **Aggregating empiric studies is informative**
- **WHO Foodborne Diseases Epidemiology Reference Group Source Attribution Task Force, structured expert elicitation using Cooke's Classical Method**
 - **Water: 0.33-0.57**
 - **Food: 0.08-0.49**
 - **Other: 0.11-0.47**

Mode of transmission locally

- **Foodborne**
 - **Restaurant-associated outbreaks linked to chronic carriage in food handler in countries where typhoid is rare e.g., Colorado, United States**
- **Waterborne**
 - **Municipal water supplies e.g., Kathmandu, Nepal**
- **Waterborne and foodborne**
 - **Consuming surface water and produce grown in pit latrine seepage e.g., Central Division, Fiji**

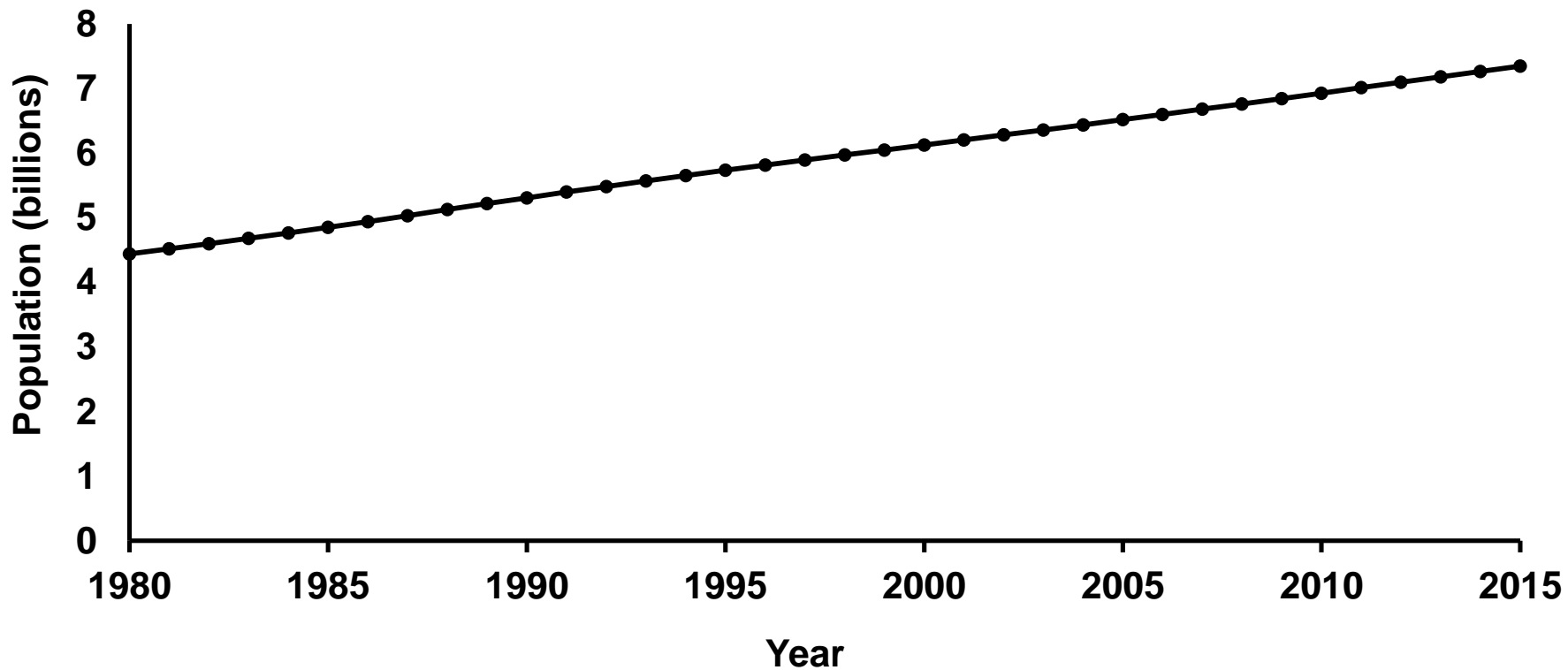
Role of infection class on transmission

- **Fecal shedding classes following onset of acute illness**
 - **Acute shedding: <3 months**
 - **Convalescent carriers: ≥3-12 months**
 - **Chronic carriers: >12 months**
- **Things that we ‘know’**
 - **At low force of infection a larger proportion of acute typhoid is in age groups more susceptible to becoming chronic carriers**
 - **As acute typhoid infections approach zero the role of chronic carriers as the reservoir approaches 100%**
 - **Much to learn**

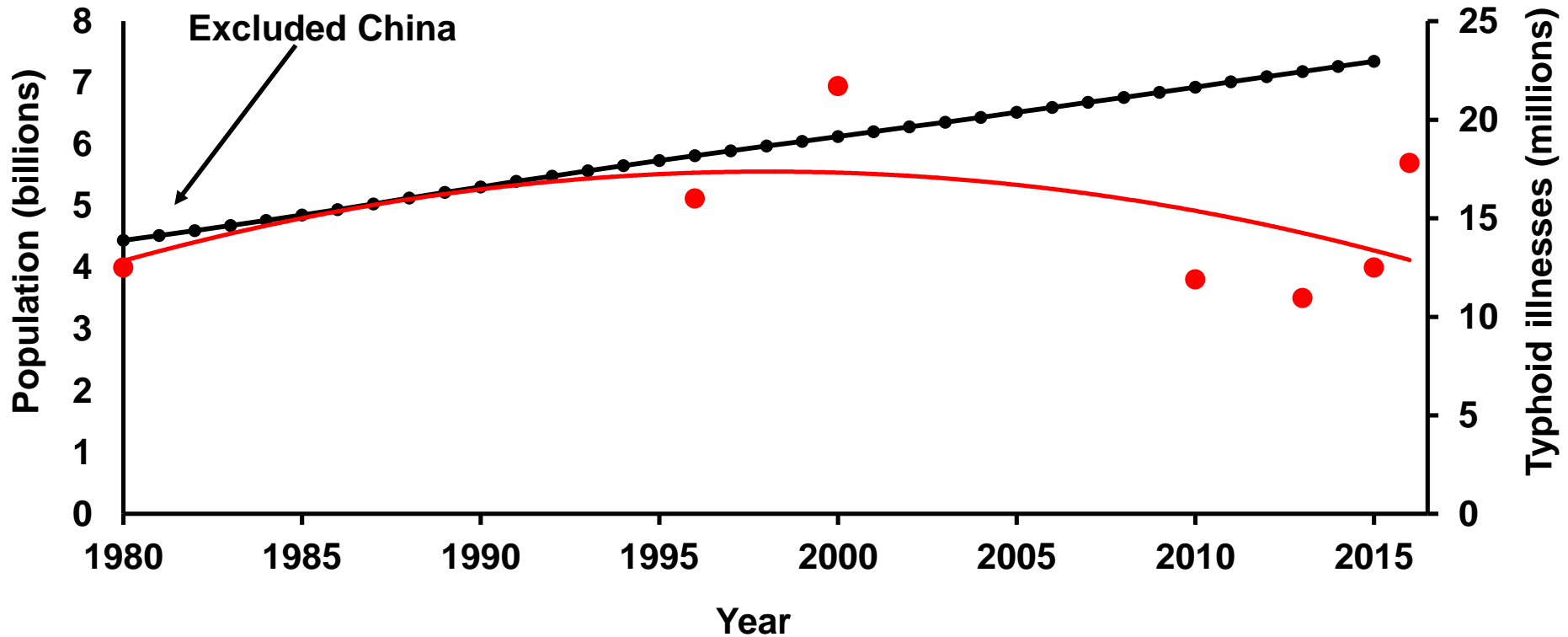
History of published estimates of typhoid burden

Metrics	Year									
	1980	1996	2000	2010	2010	2010	2010	2013	2015	2015
Origin	WHO	WHO	US CDC	IVI	JHU	WHO	IHME	IHME	IHME	Yale
Coverage	Global, except China	Global	Global	LMIC, unadjusted	Global	Global	Global, including paratyphoid	Global	Global	LMIC
Illnesses (millions)	12.5	16.0	21.7	20.6	26.9	20.1	-	11.0	12.5	17.8
DALYs (thousands)	-	-	-	-	-	10,292	12,239	11,128	10,576	-
Deaths	-	600,000	216,510	223,000	-	144,890	190,200	160,700	148,800	-

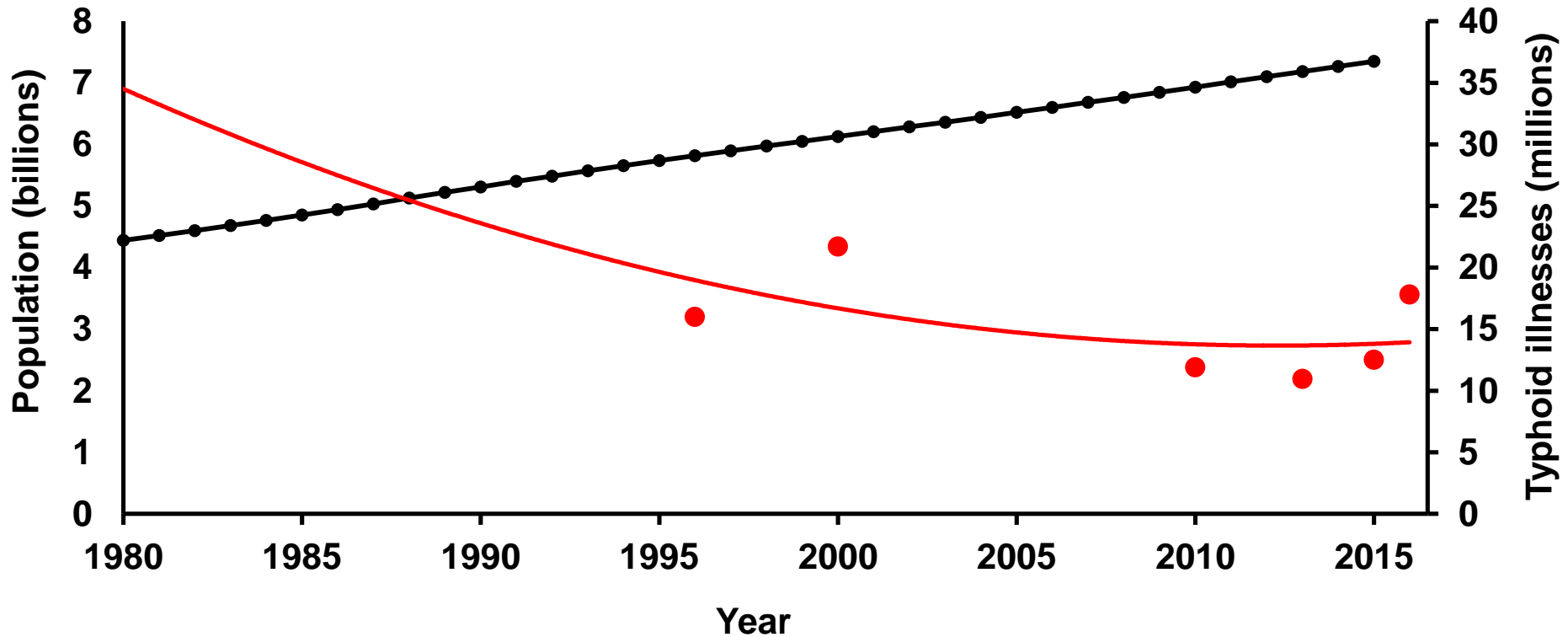
Global population, 1980-2015



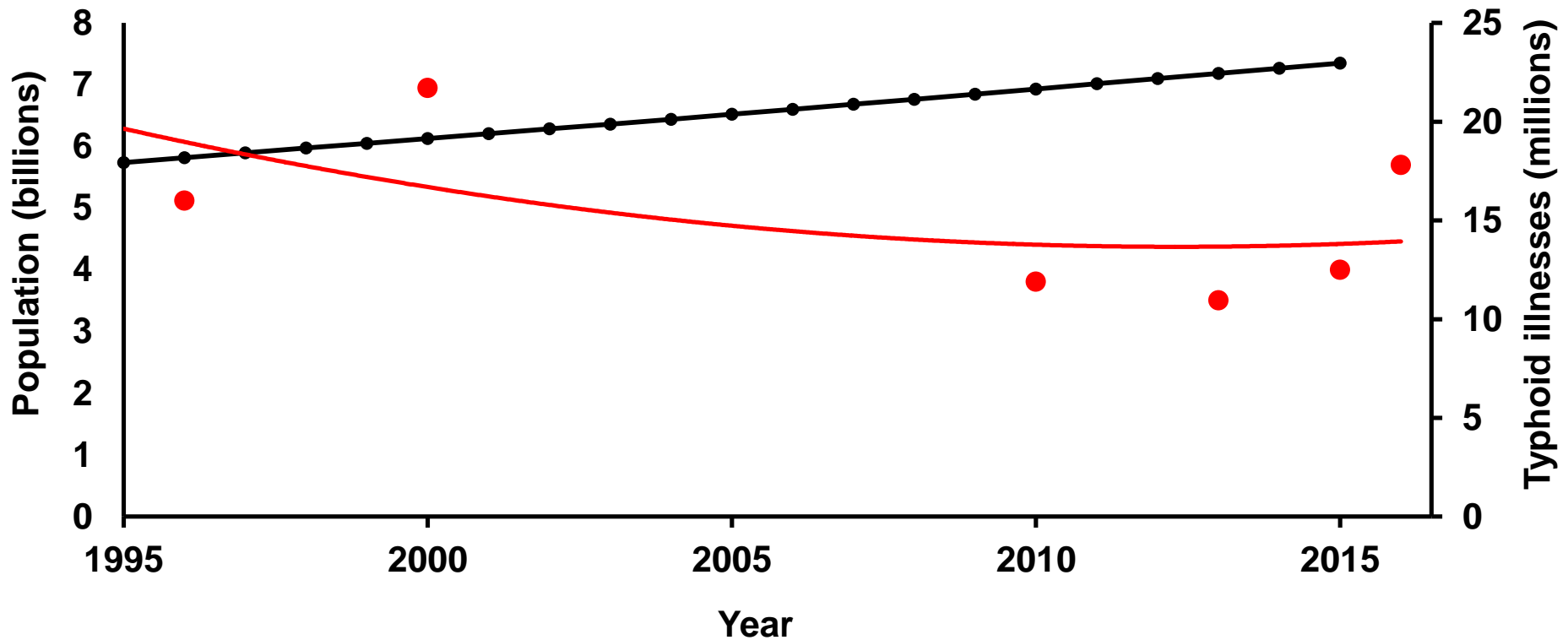
Global population and typhoid illness estimates 1980-2015



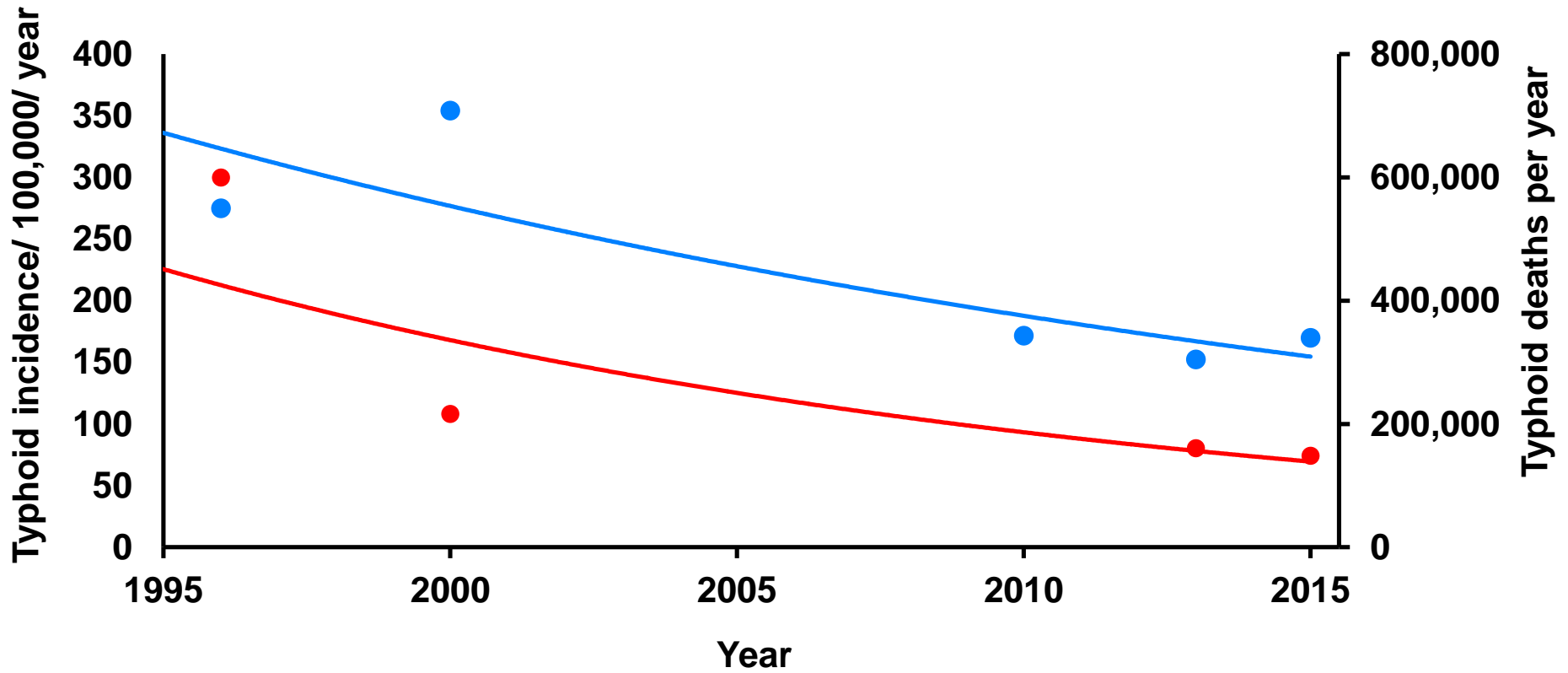
Global population and typhoid illness estimates 1980-2015



Global population and typhoid illness estimates 1995-2015



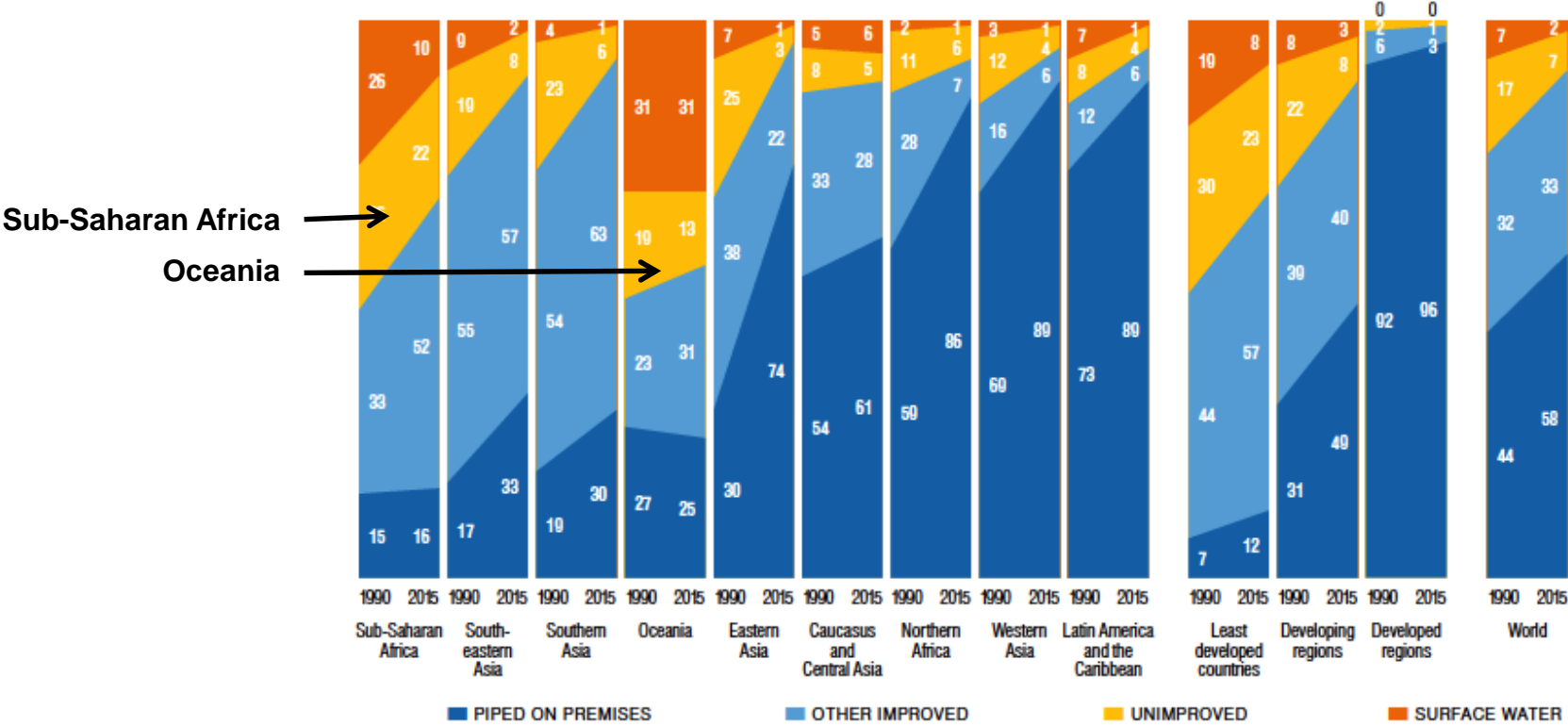
Typhoid incidence and deaths 1995-2015



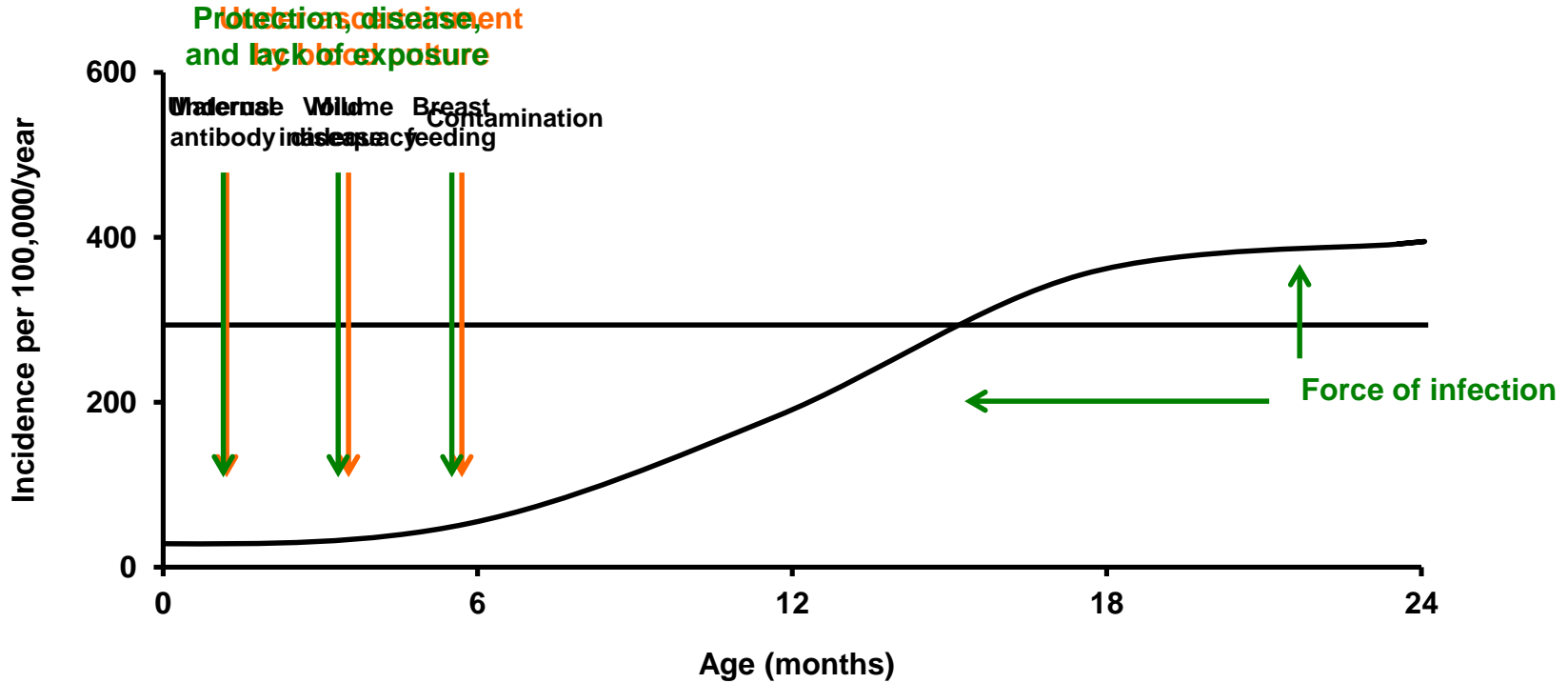
Extrapolation, uncertainty, and data gaps

- **Improvements in methods for extrapolation**
- **Estimating uncertainty**
- **Data gaps**
 - **Areas and age groups needing incidence data**
 - **More and better data on disability and death**
 - **The ‘hidden’ problem in Oceania**

Change in improved drinking water coverage by region, 1990 to 2015



Typhoid fever in infants and young children aged <2 years



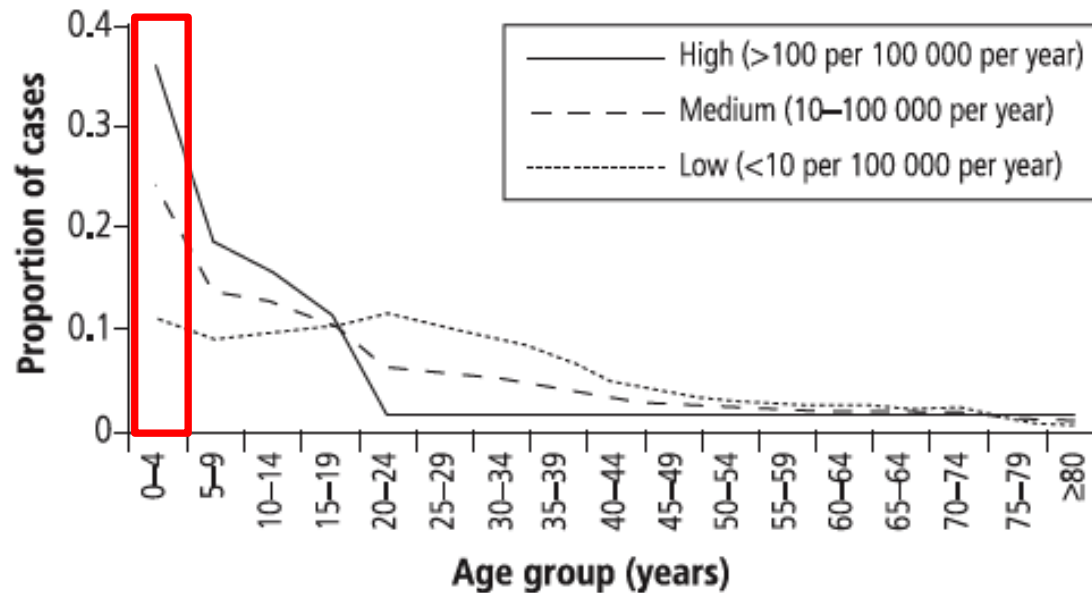


William Budd, b. 14 Sep 1811, d. 9 Jan 1880

Role of infection class in transmission

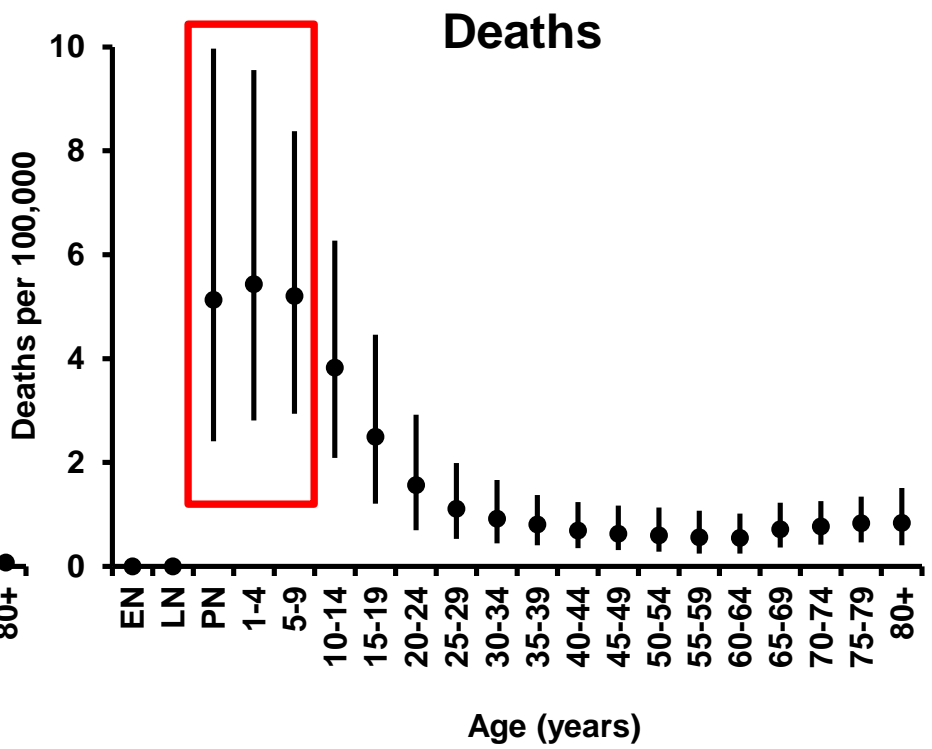
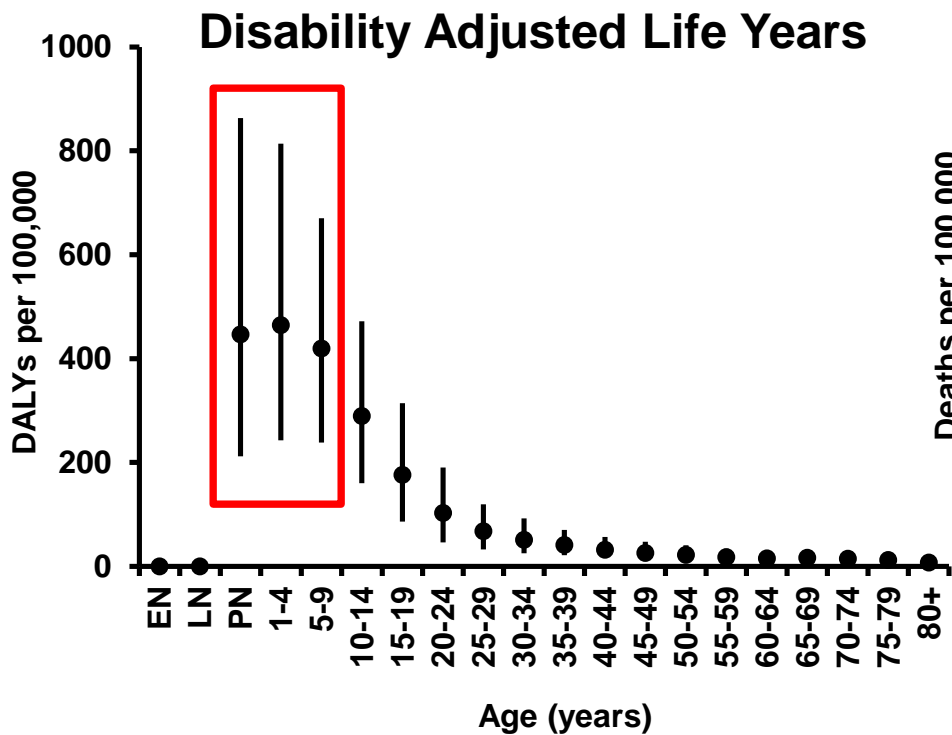
- **Things that we would like to know more about**
 - **Proportion stool cultures positive in acute disease vs. chronic carriage**
 - **Concentration of *Salmonella* Typhi in feces in acute disease vs. chronic carriage**

Distribution of typhoid fever by age group at various incidence levels, 2000



Typhoid fever DALYs and deaths by age

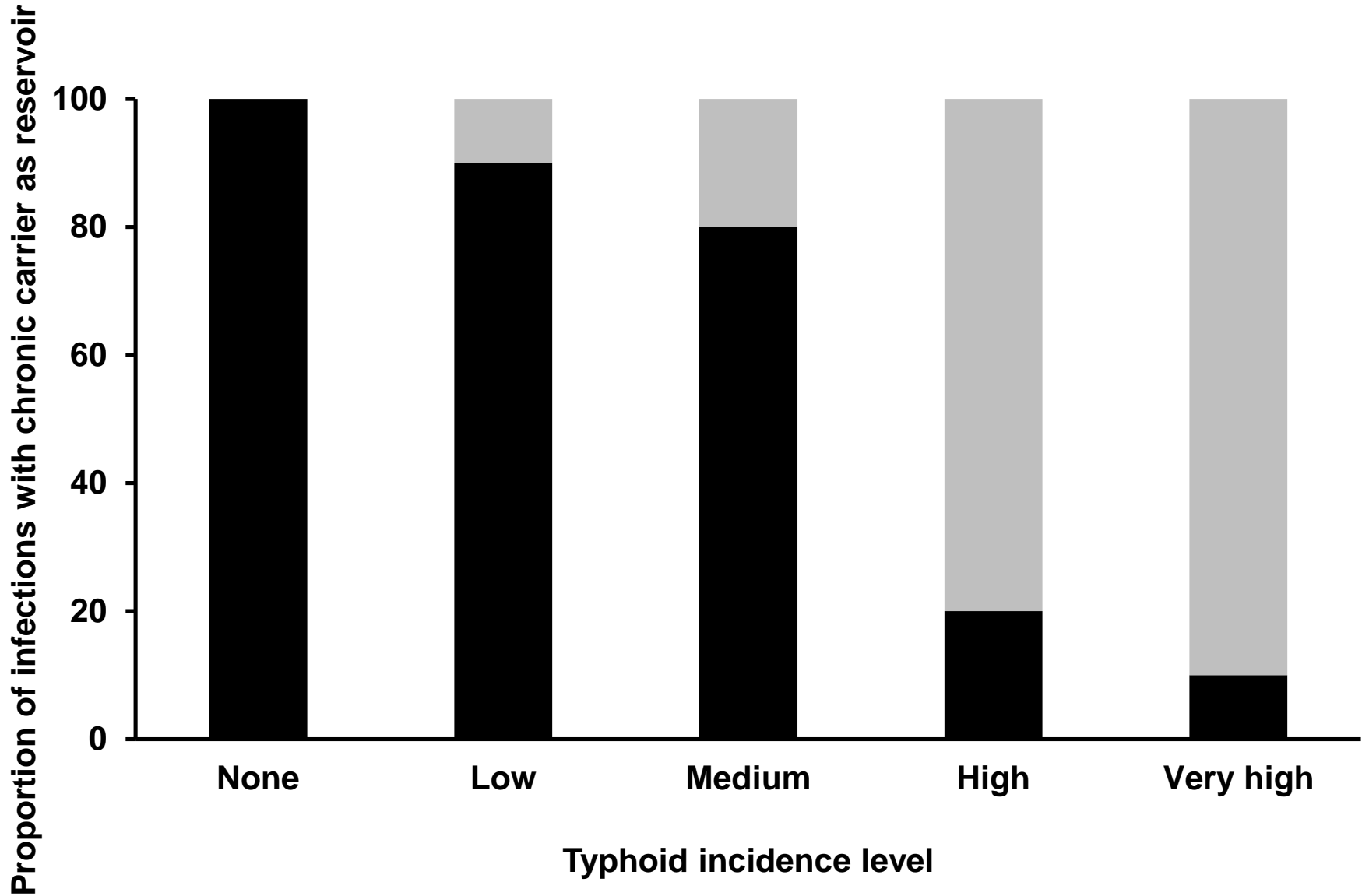
Global Burden of Disease 2015



Social inequity

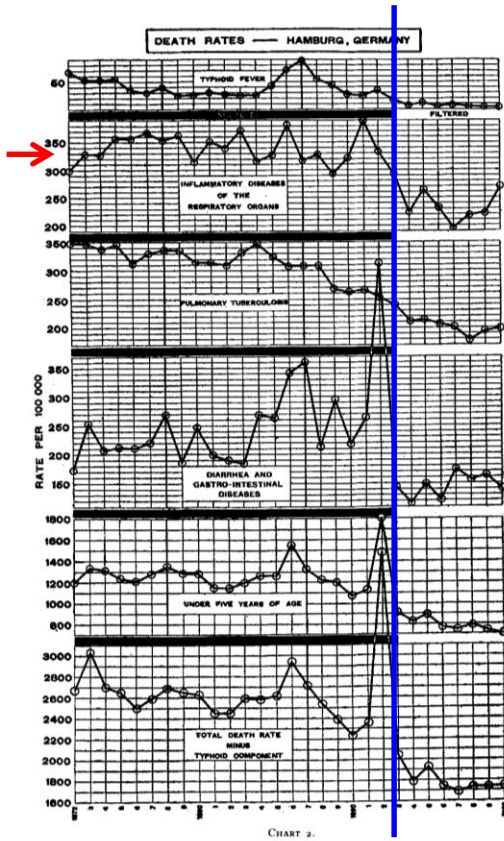
- **High-income countries**
 - Declined following increased access to safe water and food in urban areas
 - Disease of travelers, beneficiaries of typhoid vaccines
- **Low- and middle-income countries**
 - Poor sanitation, unsafe water and food
 - Crowding
 - Limited access to vaccines

Acute disease and chronic carriage as reservoir



Deaths by cause and age, Hamburg, Germany, 1872-1900

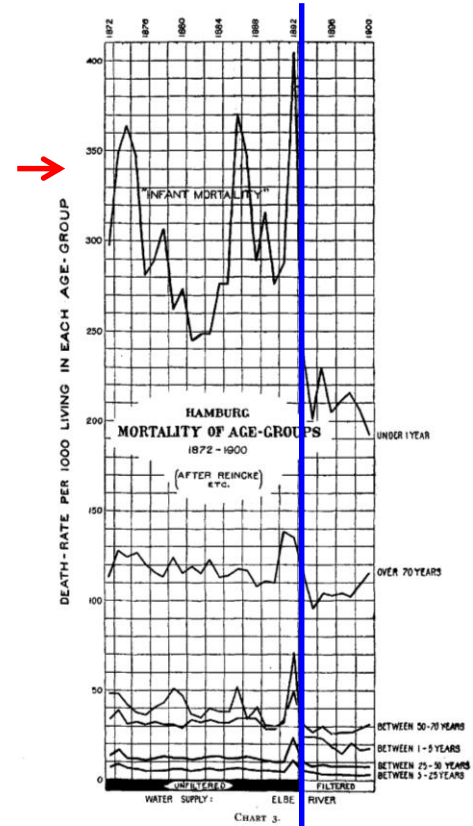
Typhoid fever deaths



1872

1900

Infant deaths

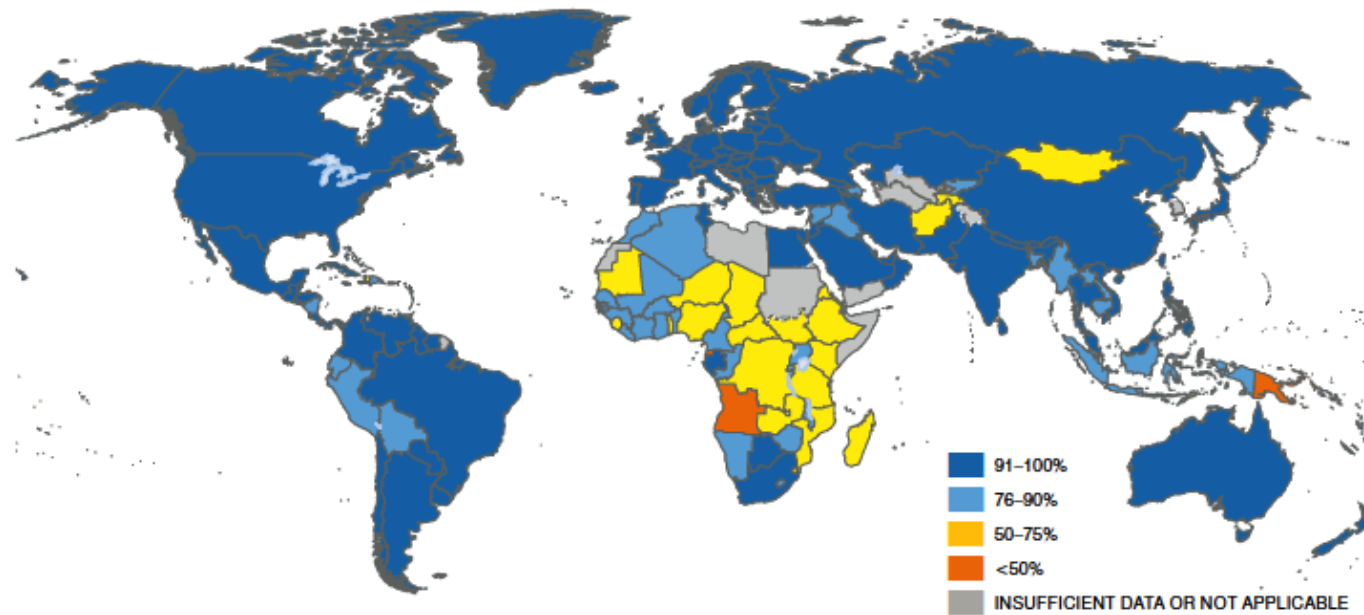


1872

1900

Elbe River water filtered

Improved drinking water coverage, global, 2015



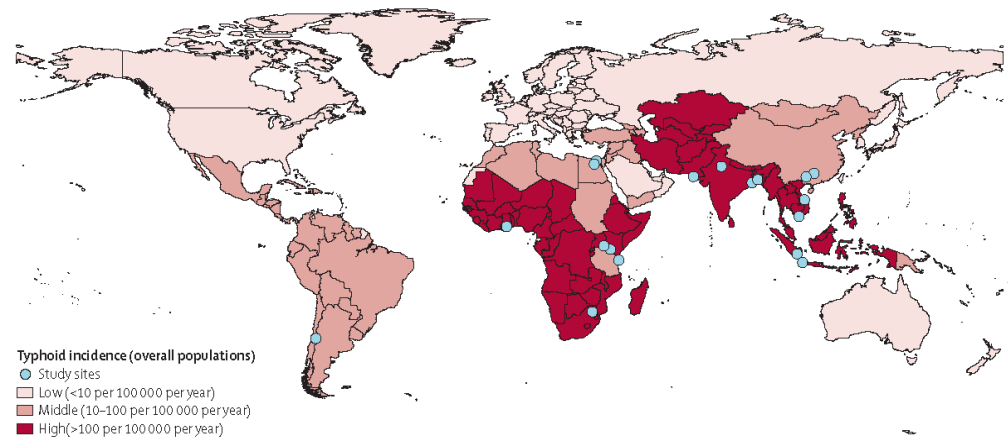
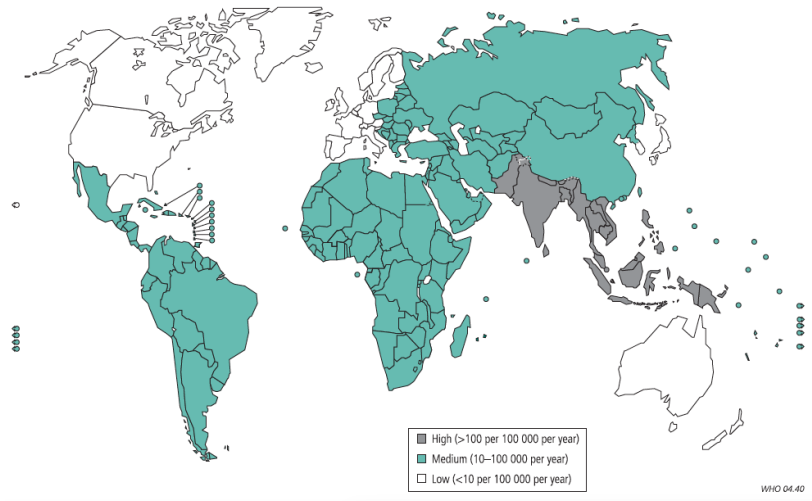
Data inequity

- **High-income countries**
 - **Laboratory confirmation**
 - **Notifiable disease with high reporting**
 - **Robust data**
- **Low- and middle-income countries**
 - **Dependence on clinical diagnosis**
 - **Weak surveillance with low reporting**
 - **Poor quality routine data**
 - **Special studies**

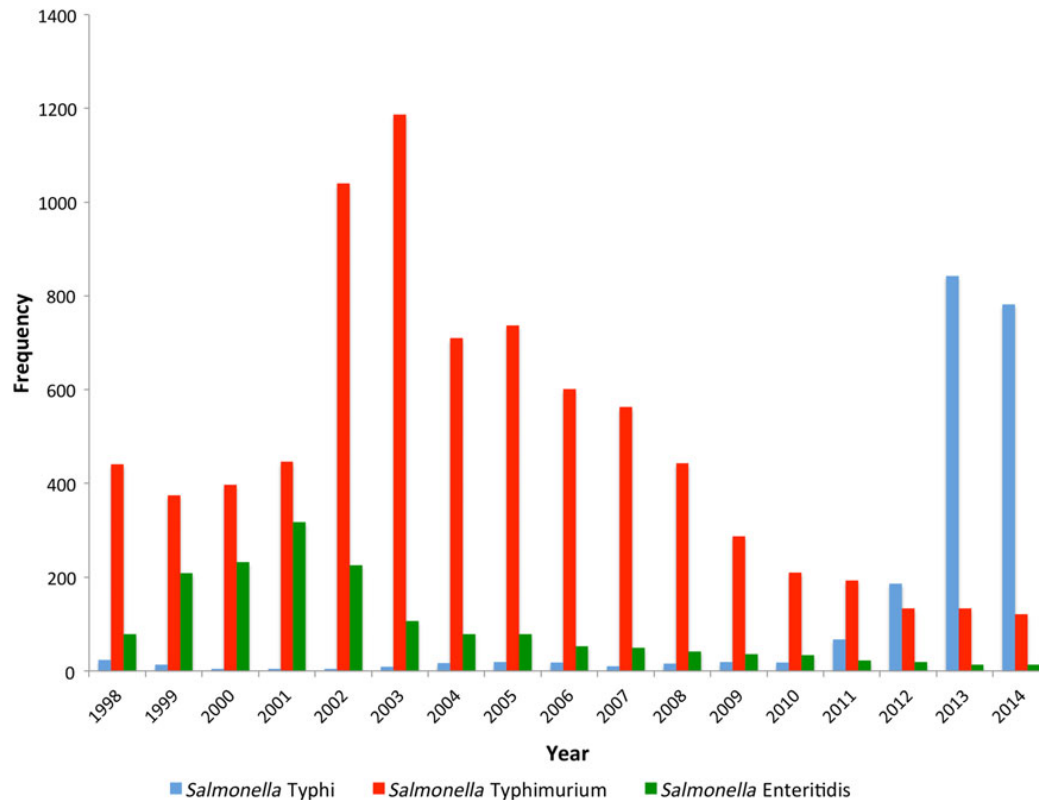
Moving targets for vaccine

- **Person, place, and time**
 - Vaccination of ‘high risk groups and populations’ based on ‘local epidemiologic situation’
 - Who should be vaccinated and where?
- **Age**
 - ‘Immunization of school-age and/or preschool-age children’
 - Typhoid conjugate vaccines can protect below 2 years of age
 - At what age should we vaccinate to prevent the most disease?

Global distribution of typhoid fever, 2000 vs. 2010



Salmonella enterica bloodstream infections, Queen Elizabeth Central Hospital, Blantyre, Malawi, 1998-2014



Conclusions

- **Current typhoid fever estimates are remarkably consistent, improving with**
 - **New data**
 - **Better extrapolation and modeling**
- **Data are weakest in areas with most disease**
 - **Complications and death**
- **Typhoid fever incidence varies in person, place, and time**
 - **Targeting vaccine is challenging**
 - **Need to understand more about disease in infants and young children**

Role of infection class in transmission

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Role of infection class in transmission

- Things that we would like to know more about
 - Proportion stool cultures positive higher in acute disease vs. chronic carriage?
 - Concentration of *Salmonella* Typhi in feces higher in acute disease vs. chronic carriage?
 - Chronic carriers (when positive): 10^6 - 10^{10} CFU/g (Merselis)
 - $<10^2$ - 10^7 (Thomson)