

Epidemiology and global burden of disease of typhoid fever

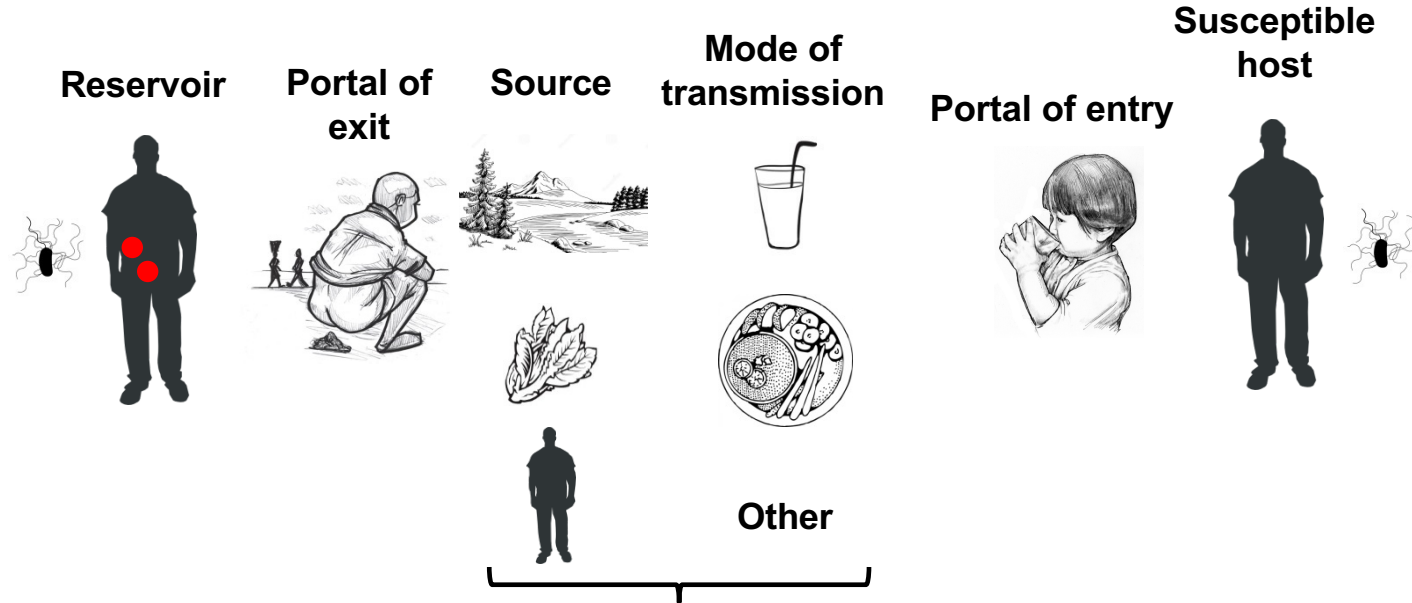
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**WHO SAGE: typhoid vaccines session
17 October 2017**

Outline

- **Epidemiology**
 - Chain of infection
 - Sources and modes of transmission
- **Global burden estimates**
 - Endemic disease
 - Occurrence by age
 - Geographic and temporal variation
 - Outbreaks

Chain of infection



What is the source and predominant mode(s) of transmission?

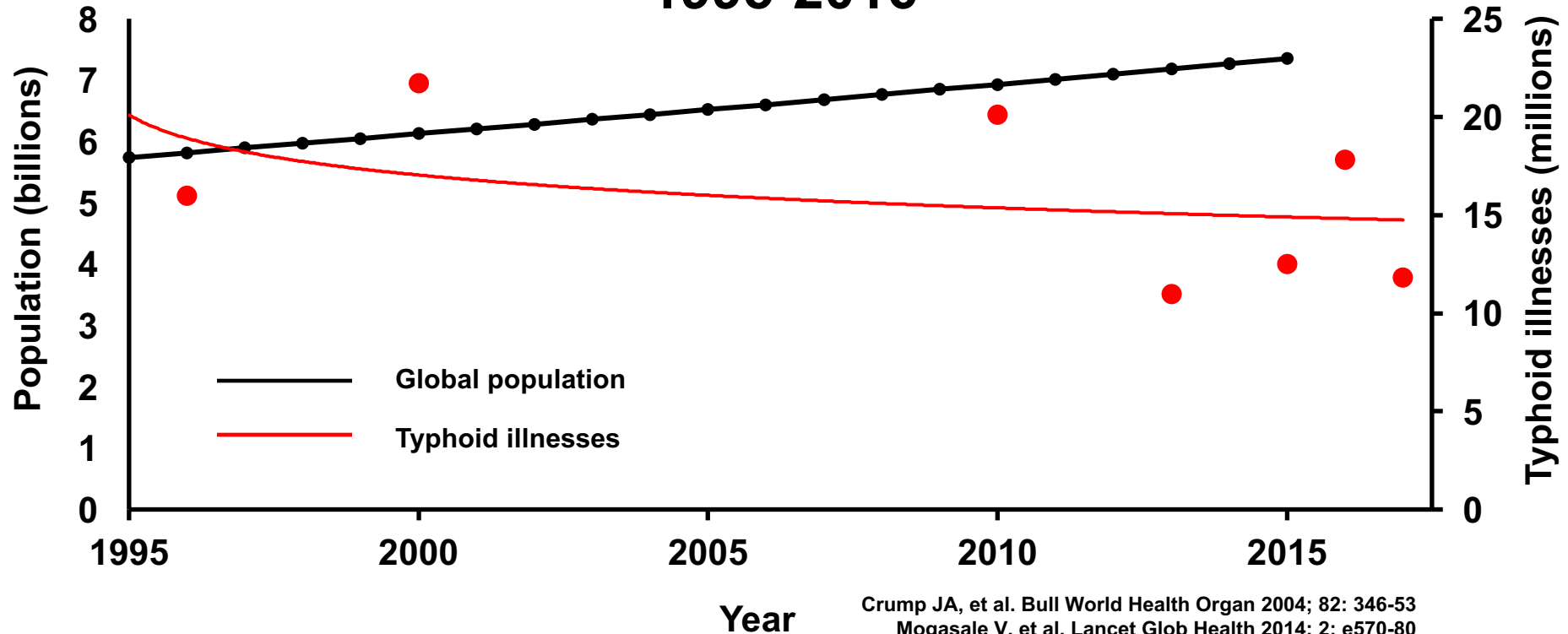
Mode of transmission locally

- **Waterborne**
 - **Municipal water supplies e.g., Kathmandu, Nepal**
- **Foodborne**
 - **Restaurant-associated outbreaks linked to chronic carriage in food handler in countries where typhoid is rare e.g., Colorado, United States**

Published estimates of typhoid burden, 1995-2016

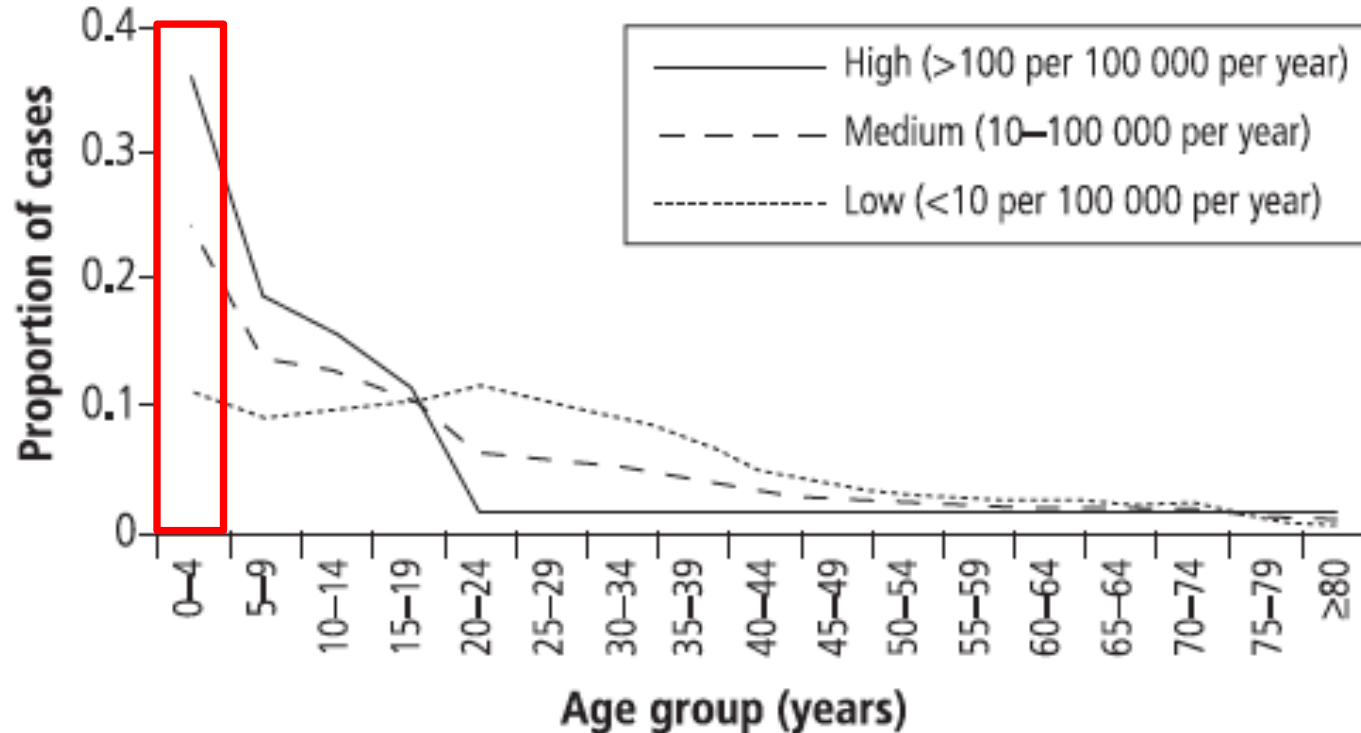
Metrics	Year									
	1996	2000	2010	2010	2010	2010	2013	2015	2015	2016
Origin	WHO	US CDC	IVI	JHU	WHO	IHME	IHME	IHME	Yale	IHME
Coverage	Global	Global	LMIC, unadjusted	Global	Global	Global, including paratyphoid	Global	Global	LMIC	Global
Illnesses, millions (95% CI)	16.0	21.7	20.6 (17.5-24.2)	26.9 (18.3-35.7)	20.1 (7.8-44.9)	-	11.0 (9.6-14.4)	12.5 (10.9-14.3)	17.8 (6.9-48.4)	11.8 (10.2-13.6)
DALYs, thousands (95% CI)	-	-	-	-	10,292 (3,805-22,028)	12,239 (1,702-23,043)	11,128 (6,014-18,315)	10,576 (5,896-17,598)	-	8,843 (4,902-14,436)
Deaths (95% CI)	600,000	216,510	223,000 (131,000- 344,000)	-	144,890 (53,519- 309,903)	190,200 (23,800- 359,100)	160,700 (85,900- 268,000)	148,800 (81,900- 249,700))	-	128,200 (70,100- 210,200)

Global population and typhoid illness estimates 1995-2016



Crump JA, et al. Bull World Health Organ 2004; 82: 346-53
Mogasale V, et al. Lancet Glob Health 2014; 2: e570-80
Buckle GC, et al. J Glob Health 2012; 2: 10401
Kirk MD, et al. PLoS Med 2015; 12: e1001921
IHME. GBD 2010, 2013, 2015, 2016. Lancet
Antillón M, et al. PLoS Neglect Trop Dis 2017; 11: e0005376

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



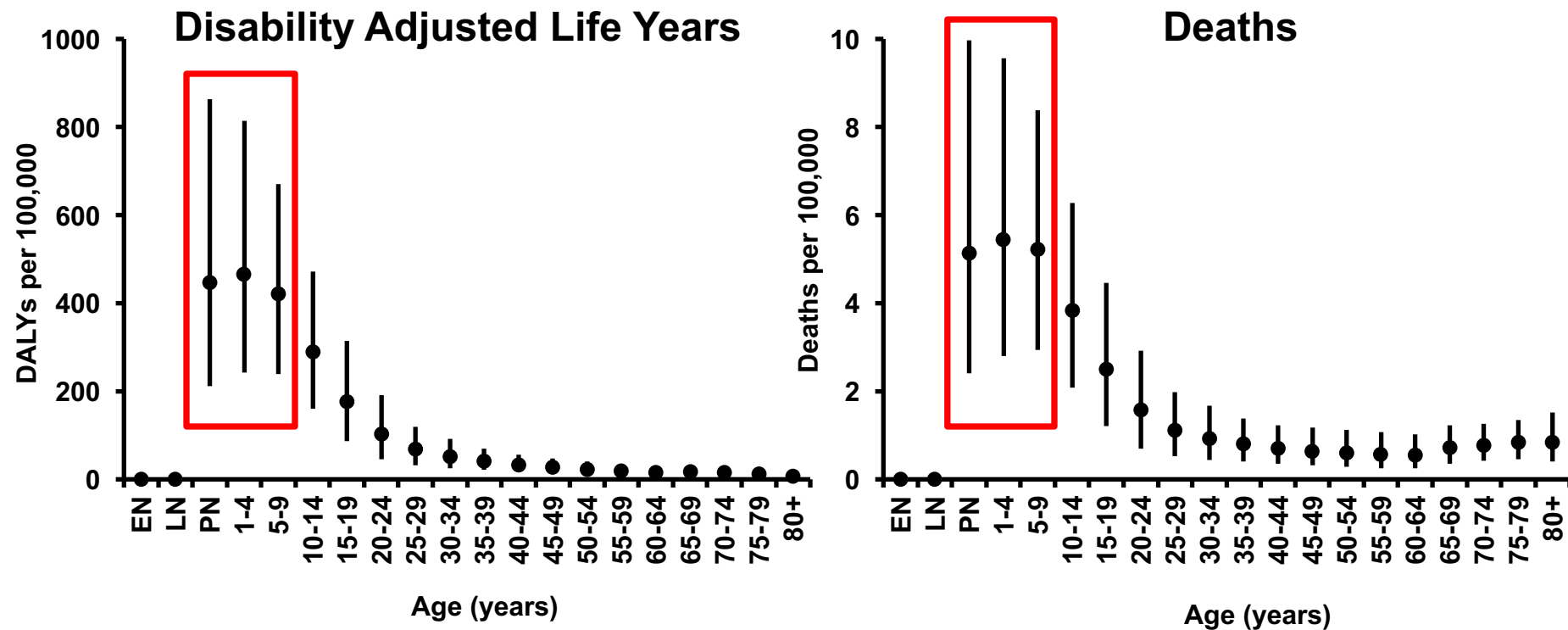
Crump JA, et al. Bull World Health Organ 2004; 82: 346-53

Azmatullah A, et al. J Glob Health 2015; 5: 020407

Britto C, et al. Clin Infect Dis 2017; 64: 1604-11

Typhoid fever DALYs and deaths by age

Global Burden of Disease 2015



EN: early neonatal, LN: late neonatal, PN: post-natal

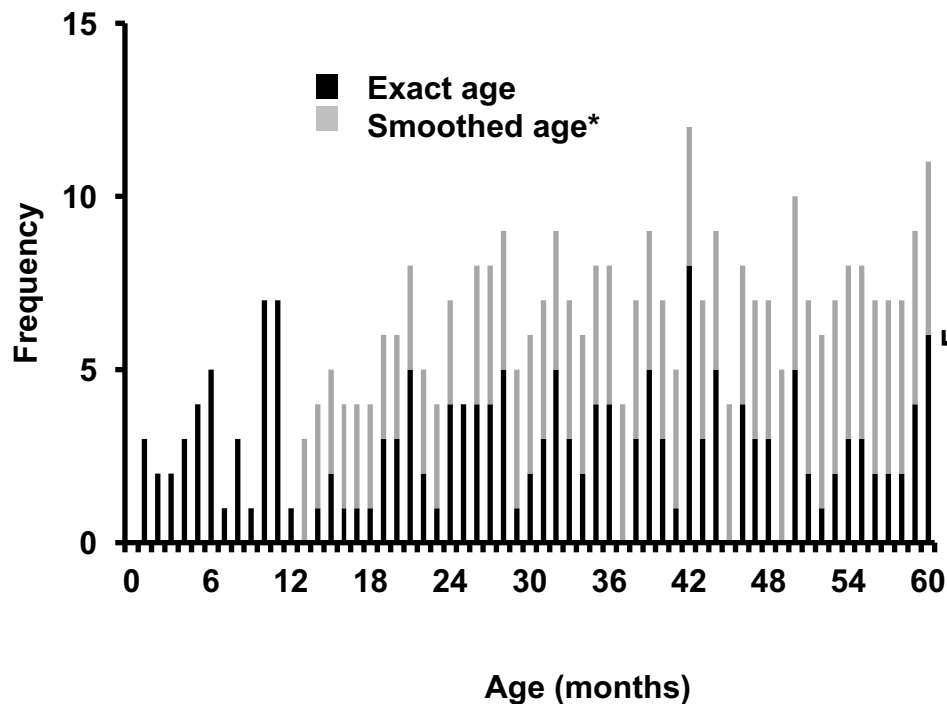
<http://vizhub.healthdata.org/gbd-compare/>

Typhoid in infants and young children

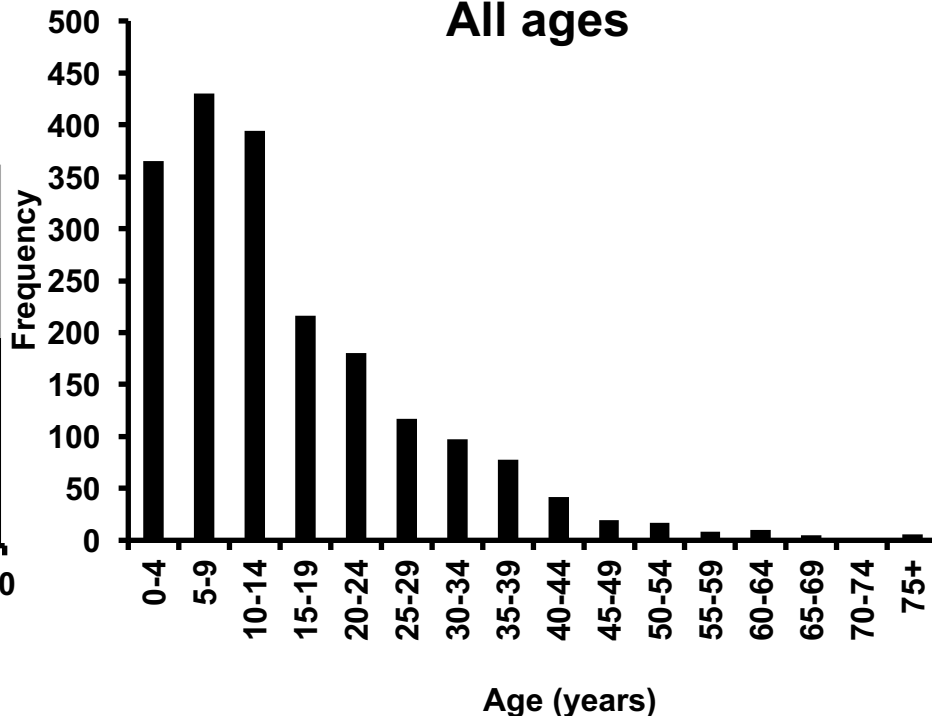
- **Typhoid <5 years of age**
 - Detailed understanding by month of age
 - Especially <2 years of age
 - Severity
- **WHO SAGE working group on typhoid vaccines undertook detailed review of unpublished data**

Typhoid fever by age <5 years and all ages inpatients Queen Elizabeth Hospital, Blantyre, Malawi, 1998-2014

Age <5 years by month



All ages



*Age known to year rather than month; age smoothed across all months of year

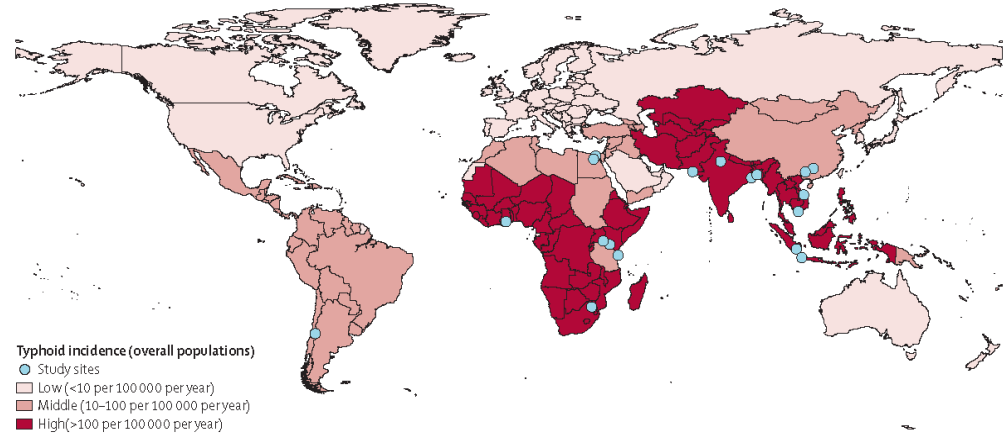
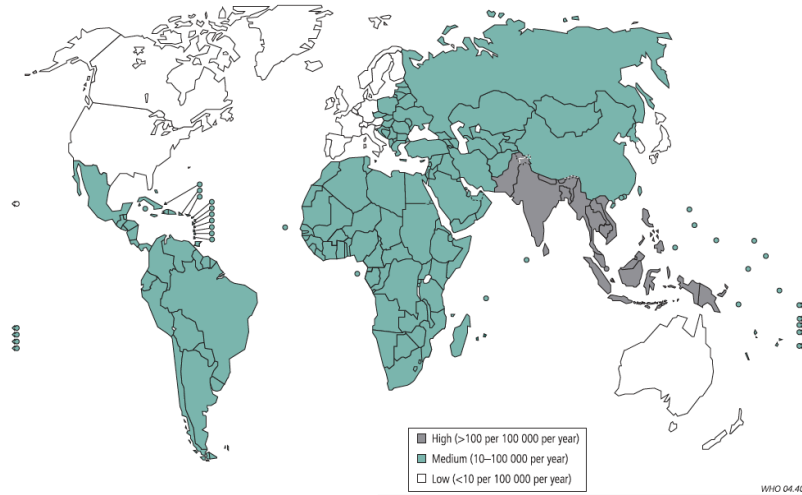
Summary of results

- **Data were received from 15 sources from Africa, Asia, and the Americas**
- **Available data were of inpatients, outpatients, or both, collected between 1998 and 2017 representing >10 000 blood culture confirmed episodes of typhoid fever**
- **Among studies of all age groups**
 - **27% of typhoid fever occurred in the age group 0-4 years**
- **In the age group 0-4 years, giving equal weighting to data in these studies**
 - **29.7% of typhoid fever episodes occurred at age ≤ 2 years**
 - **9.9% at age ≤ 1 year**
 - **2.9% at age ≤ 6 months**

Summary of typhoid occurrence <5 years of age

- Typhoid fever is uncommon but not absent ≤ 6 months of age
 - Neonatal disease is rare but documented
- Typhoid occurrence increases steeply between 6 and 12 months of age
- Typhoid fever is as common among 1-2 year olds as 2-5 year olds
- Typhoid fever is sufficiently severe among under 5 year olds to require outpatient and inpatient care

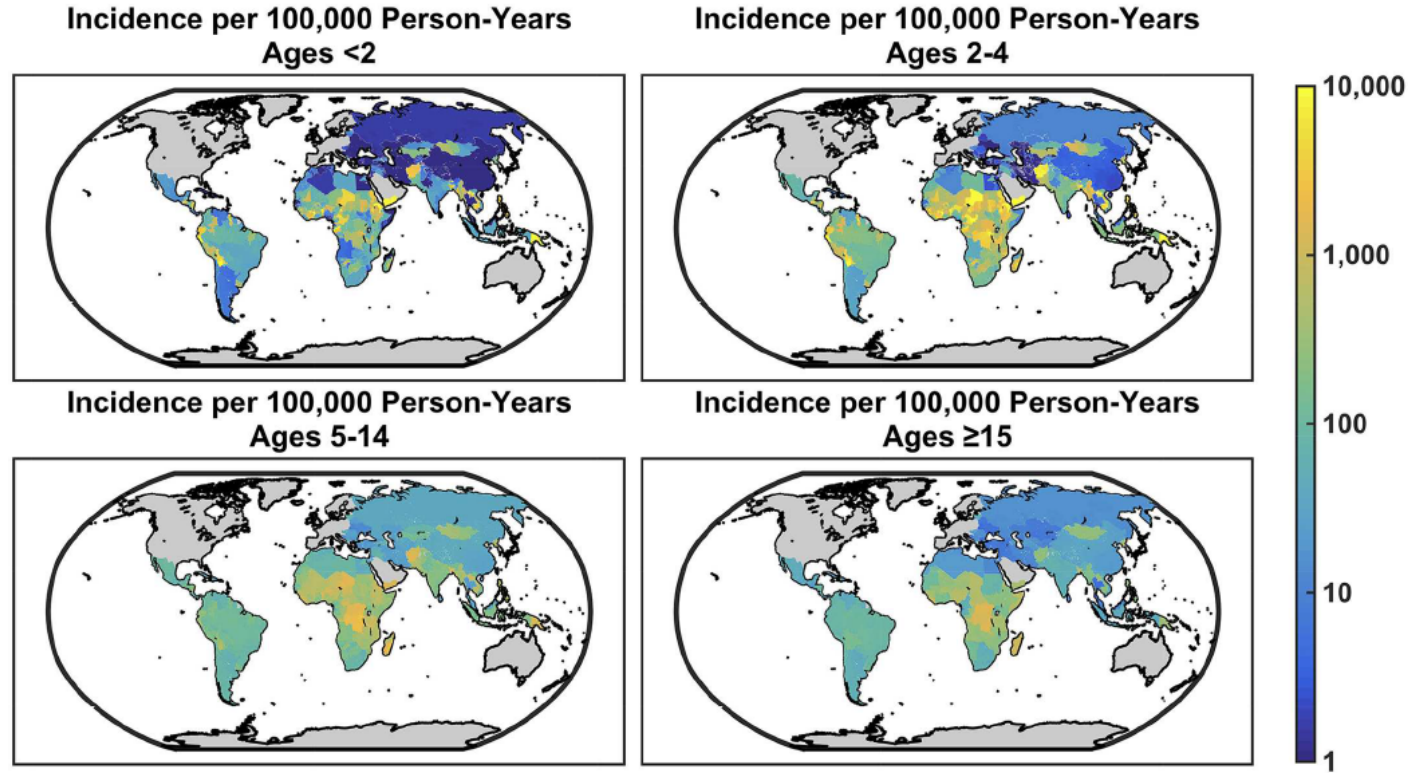
Global distribution of typhoid fever, 2000 vs. 2010



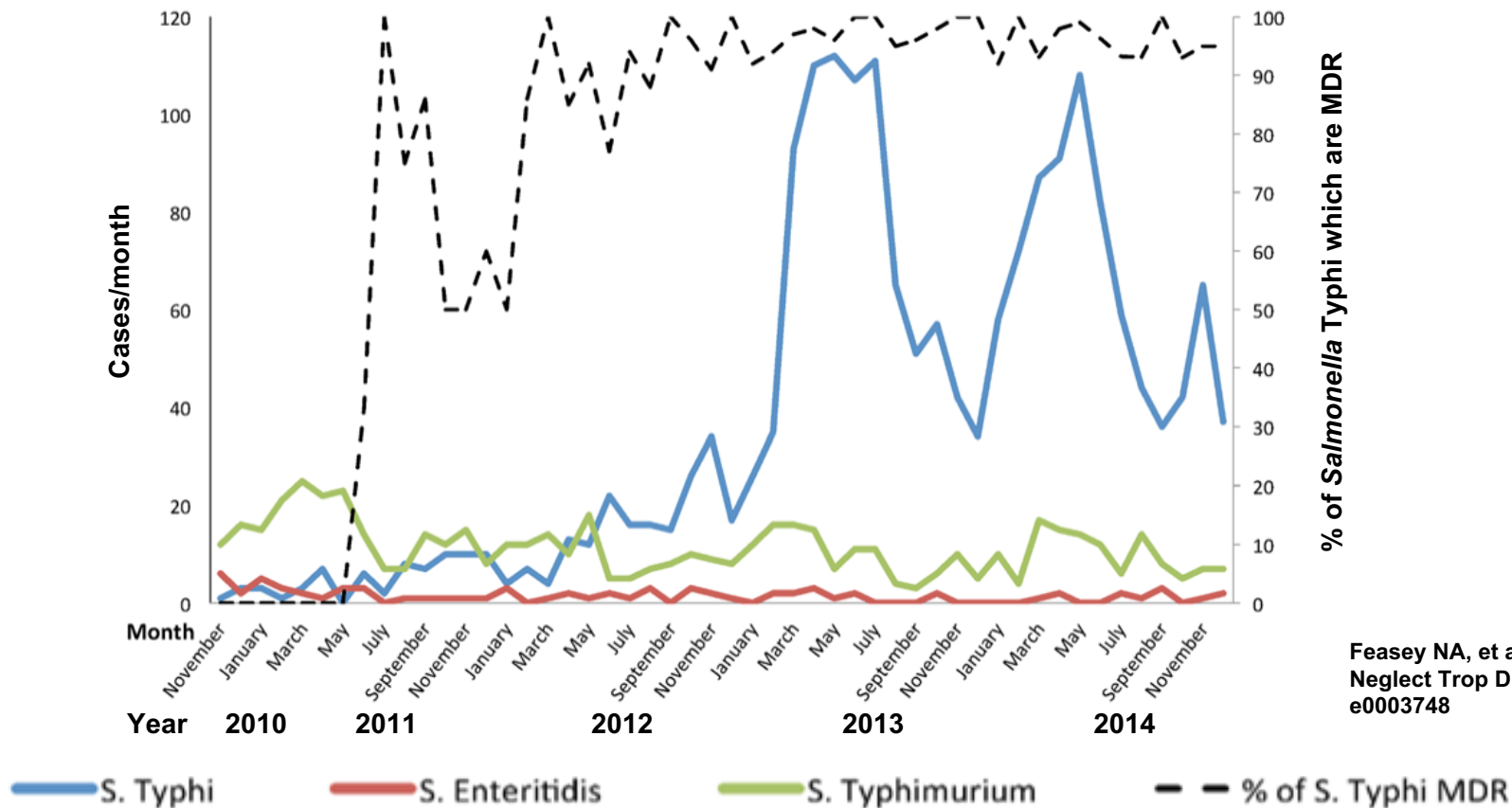
Typhoid Surveillance in Africa Programme (TSAP)
Marks F, et al. Lancet Global Health 2017; 5: e310-23

Model-predicted age-specific incidence per 100,000 person-years, 2015

The median posterior predicted incidence per 100,000 person-years in each of the age groups (<2 yrs, 2-4 yrs, 5-14 yrs, and ≥15 yrs) is mapped for all low- and middle-income countries (LMICs) with a resolution of 0.1 degrees



Monthly trends in bloodstream invasive *Salmonella* diagnosed at Queen Elizabeth Hospital, Blantyre, Malawi, November 2010-October 2014.



Feasey NA, et al. PLoS Neglect Trop Dis 2015; 9: e0003748

Typhoid outbreaks

- **Incidence during outbreaks excluded from most estimates of disease burden**
 - **Typhoid fever is epidemic prone**
- **The SAGE Working Group reviewed the available data on outbreaks**
 - **41 published reports 1990-2017**
 - **Mean 1,097 cases per outbreak**
 - **10 (28.6%) and 8 (22.9%) among 35 distinct outbreaks occurred in the WHO South-East Asia Region and African Region and respectively**
 - **14 (40.0%) of 35 outbreaks exceeded 100 days duration**
 - **Vaccine rarely deployed**

Conclusions

- **Typhoid epidemiology**
 - **Human reservoir, portal of exit stool**
 - **Transmission from fecally contaminated water and food**
- **Global typhoid cases have plateaued with 11-18 million illnesses and 128,000-190,200 deaths per year**
- **Severe typhoid is common below 2 years of age**
- **Typhoid incidence varies in place and time between and within countries**
 - **Heterogeneity is a critical consideration for vaccination strategy**
- **Typhoid outbreaks may be large and prolonged**
 - **Reactive vaccination seldom timely**

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